EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMA's Regulatory Science Strategy to 2025

Mid-point achievements to end 2022

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Foreword by Emer Cooke, EMA Executive Director

Over the past two years, EMA has prioritised work to respond to the ongoing COVID-19 pandemic, which has had an unprecedented impact on many EMA activities. Recognition of the importance of this work in the response to this crisis has come in the form of an extension to EMA's legal mandate, including the work of Emergency Task Force, and the engagement with national competent authorities and stakeholders in tackling medicines shortages, as well as new tasks in the field of medical devices.

In parallel with this vital work the Agency, together with its Network partners, has being progressing implementation of its Regulatory Science Strategy to 2025 originally envisaged to enable regulators to be ready to support the development of increasingly complex medicines that more and more deliver healthcare solutions by converging different technologies to promote and protect human and animal health. Nothing has demonstrated the need to address dramatic acceleration in innovation than the COVID-19 pandemic with the interplay of vaccines, therapeutics, diagnostics and MedTech developments enabled by rapid open science exchange, dynamic regulatory reviews and unprecedented public information campaigns to build trust and confidence in these developments.

As such I am very pleased to present a mid-point achievements report that seeks to identify headline deliveries right across strategic goal areas advancing Regulatory Science in both the Human and Veterinary areas. The EMA plans to gradually lift its business continuity status through 2023 and will seek opportunities to focus more on delivering not just the RSS to 2025 but also the wider EMRN Network Strategy to 2025. I believe that by doing so we can evolve the Network capability to engage with and enable innovative science and technology within the current pharmaceutical framework and build towards the future framework beyond 2025.

Introduction

The motivation behind the Regulatory Science Strategy to 2025 was the recognition that the pace of innovation had accelerated dramatically in recent years and regulators needed to be ready to support the development of increasingly complex medicines that more and more deliver healthcare solutions by converging different technologies to promote and protect human and animal health. Furthermore with the advent of Big Data it was recognised that "Real World Evidence" would open up new sources of information on the use of medicines in healthcare settings and regulators would need to take action to address the challenges arising from collecting and processing these data from patients. Therefore the Agency undertook an extensive period of outreach, analysis and consultation with its scientific committees, stakeholders and EU regulatory partners via a public consultation and dedicated workshops[1] and published EMA's Regulatory Science to 2025 in March 2020[2].

The broad ambition expressed in this strategy was to advance EMA's engagement with regulatory science over the next five years, covering both human and veterinary medicines and to build a more adaptive regulatory system that will encourage innovation in human and veterinary medicine.

Implementation was organised via three streams. The first stream fed into the European Medicines Regulatory Network Strategy to 2025. This overarching network comprises 30 European Economic Area regulatory authorities, the European Commission and the EMA. The second, closely interconnected, stream was to embed the RSS deliverables in the (multi)annual work programmes/implementation plans of the EMA's scientific committees, working parties and other groups involved in the evaluation of medicines. The final stream was via the EMA's proposed mechanism to stimulate regulatory science research[3].

Implementation planning was undertaken to feed each core recommendation into these streams, and the EMA has enjoyed continued cooperation with stakeholders and EU regulatory partners in delivering this strategy.

This report provides an overview of main achievements, from March 2020 to December 2022 in a succinct form with links to more detailed information where available. It is structured along the strategic goals presented in the original strategy as they apply to both human and veterinary areas respectively. It starts by highlighting achievements for the top five human and top three veterinary recommendations thought to deliver the most significant change over the five-year course of the strategy as judged by the stakeholders consultation process. It should be noted that this report does not attempt to be exhaustive as to the achievements to December 2020 but rather to provide a point in time reference summary which will be further complemented in substance and delivery through the work to be undertaken in 2023-2025.

[1] https://www.ema.europa.eu/en/documents/leaflet/development-regulatory-science-strategy-2025_en.pdf
[2] EMA Regulatory Science to 2025 (europa.eu)
[3] Regulatory Science and Innovation Programme for Europe (ReScIPE): A proposed model (wiley.com)

1. Highlight on achievements for the top 5 (human) recommendations thought to deliver the most significant change over the course of the five-year strategy

Harald Enzmann
Chair of CHMP

"The unprecedented pace of innovation in the development of medicines during the COVID pandemic has set an example of what is possible – even in the current regulatory framework. Building on that positive experience, we will further advance regulatory science and its contribution to the development of innovative medicines and to patients' access in evolving healthcare systems."

1.1.1. Foster innovation in clinical trials

Driving collaborative evidence generation – improving the scientific quality of evaluations	
Core recommendations	**Underlying actions**
Foster innovation in clinical trials	• Establish a multi-stakeholder, neutral, platform, to enable new approaches to clinical studies and to position the EU as a preferred location for innovative clinical research;
	• Drive development and adoption of novel practices that facilitate clinical trial authorisation, GCP and HTA acceptance at EU and international level;
	• Work with stakeholders, the EU Medicines Regulatory Network and the European Commission to promote and facilitate the conduct of complex clinical trials and other innovative clinical trial designs;
	• Promote increased information sharing on clinical trial design, conduct, results and best practices. Build on this information and the multi-stakeholder platforms to enable further education, training and sharing of best practice in order to accelerate innovative change;
	• Critically assess the clinical value of new and emerging endpoints and their role in facilitating patients' access to new medicines;
	• Promote the inclusion of neglected populations such as pregnant women, the elderly and those of diverse ethnicity in clinical trials.

Achievements

- Launch of the Clinical Trial Information System (CTIS) enabling the applicability of the Clinical Trial Regulation (CTR):
  - Online training programme dedicated to sponsors and member states user to support user journey and activity in CTIS;

- Onboarding of the user community on the use of CTIS: enhance quality of CTA submission;
- Reorganised Clinical Trials Coordination Group (CTCG) and integration with SAWP, EU-IN, etc.;
- Publication of monthly Key performance indicators (KPIs) to monitor the European clinical trials environment.

- The establishment of Accelerating Clinical Trials in the EU (ACT EU) and associated work plan to 2026:
  - Establishment of the ACT EU Steering Group, with adoption of its mandate and membership;
  - Facilitate assessors community collaboration (assessors round table);
  - Publication of Q&A on Complex Clinical Trials;
  - Multistakeholder workshop on decentralised clinical trials held with publication of recommendation paper on decentralised clinical trials.
- 2022 HMA EU-IN workplan to improve and re-launch Simultaneous National Scientific Advice (SNSA) now under ACT-EU and clear focus on CTA:
  - SNSA first pilot with focus in CTA / pre-CTA advice;
  - Multiple stakeholder interactions on decentralised clinical trials during the pandemic.

1.1.2. Promote use of high-quality real-world data (RWD) in decision- making

Advancing patient-centred access to medicines in partnership with healthcare systems	
Core recommendations	**Underlying actions**
Promote use of high-quality real-world data (RWD) in decision-making	• The actions in this Regulatory Science Strategy relating to RWD are included within the 10 actions listed under Big Data. In addition, specific pilots of RWD analytics will be conducted and work on pharmacovigilance methods will continue: – Conduct a pilot of using rapid analytics of real-world data (including electronic health records) to support decision-making at the PRAC and CHMP; – Review of the utility of using electronic health records for detecting drug safety issues (including drug interactions);
	• Mapping of good examples of use of RWD in different phases of drug development to develop guidance on such use.

Achievements

- Establishment of DARWIN EU®

  The DARWIN EU® contract was awarded on 8 Feb 2022 to Erasmus University Medical Centre Rotterdam with a number of subcontractors, marking the start of the establishment of DARWIN EU®:

  - The Advisory board for DARWIN EU® has been in place since June 2021 and includes multi-stakeholder representation to advise on its implementation, linkages with other initiatives and communications with stakeholders;

  - Good progress in the delivery of the contract has been achieved –timelines for all deliverables and service levels have been achieved leading to the activation of Phase II on 10 Aug 2022;
  - Data partners have been shortlisted and onboarding of first 10 data partners is in progress (Sep 2022);
  - The first pilot studies have been initiated (4 planned in Phase I).
- Establishing and expanding a catalogue of observational data sources for use in medicines regulation:
  - The updated meta data list – which defines the structure of the catalogue – has been adopted and published; the data storage solution as the data repository in which the data underpinning the catalogues will be stored, has been developed and integrated into EMA architecture;
  - Work is ongoing with contractors on the enhancement of the data source catalogue and its integration into the EMA website with estimated delivery by DIGIT in Q4 2023;
  - Work is ongoing separately on the collection of detailed metadata about selected sources which will be included in the new catalogue:

    to provide a source of high-quality, validated real world data on the use, safety and efficacy of medicines;

    to address specific questions by carrying out high-quality, non-interventional studies, including developing scientific protocols, interrogating relevant data sources and interpreting and reporting study results.
- Progress on RWE International Collaboration Roadmap:
  - The June 2022 ICMRA workshop on RWE identified areas of opportunities for regulatory collaboration which could help address common challenges and further enable the integration of RWE into regulatory decision-making: Harmonisation of RWD and RWE terminologies, Convergence on RWD and RWE guidance and best practice, including readiness and transparency.
- Explore how DARWIN can capture and analyse Patient Experience Data such as PROs:
  - Learning initiatives workshop held. Objectives of the meeting were to:

    Learn from current experience of using real-world data for regulatory purpose;

    Discuss important challenges related to optimal use of real-world data, including data relevance, submission processes and training needs;

    Discuss means to support effective consultation with stakeholders, including industry, the regulatory network, academia, healthcare professionals and patients.

1.1.3. Reinforce patient relevance in evidence generation

Advancing patient-centred access to medicines in partnership with healthcare systems	
Core recommendations	**Underlying actions**
	• Revise the existing patient engagement methodology and review and update EMA's existing 'Framework for interaction with patients and patient organisations' to reflect EMA's evolving approach to

Advancing patient-centred access to medicines in partnership with healthcare systems	
Reinforce patient relevance in evidence generation	patient data and enhanced patient involvement in EMA scientific committees;
	• Explore and deploy additional methodologies to collect and use patient data for benefit-risk assessment;
	• Update existing, and develop new EMA guidelines on patient data collection;
	• Coordinate the approach to patient reported outcomes (PROs);
	• Promote use of core health-related quality-of-life PROs.

Achievements

- Framework for interaction with patients and their organisations has been updated to the current Engagement Framework Engagement framework: European Medicines Agency and patients, consumers and their organisations (europa.eu). The new engagement framework also refers to patient experience data and how it should be further incorporated during drug development and regulatory assessment.
- Multi-stakeholder workshop on Patient Experience Data (PED) held at EMA on 21 September 2022:
  - Executive summary published describing the key outputs of the workshop, which includes agreeing of a common understanding of what constitutes PED in the EU and EMA's agreement to prepare a reflection paper to provide advice on the best EU approach to generate and collect PED. This will help provide clarity on the process and support mechanisms at EMA, while further work on PED guidance at global (ICH) level continues.
  - Video recordings and presentations published.
- Mapping and analysis of existing methodologies for the collection and use of patient experience data through engagement of an academic collaborating expert: A group report (*An Overview of Patient Experience Data for Medicines Assessment*) from the faculty of pharmacy of the university of Lisbon has been prepared together with EMA. It has been used to plan related work, including the multi-stakeholder workshop mentioned above.
- Contribution to ongoing ICH discussion on guidelines for PED in medicines regulation[4]:

  The ICH Reflection Paper on Patient-Focused Drug Development (PFDD) has been prepared and published. It identifies key areas where incorporation of the patient's perspective could improve the quality, relevance, safety and efficiency of drug development and inform regulatory decision making. It also presents opportunities for development of new ICH guidelines to provide a globally harmonized approach to inclusion of the patient's perspective in a way that is methodologically sound and sustainable for both regulated industry and regulatory authorities.

[4] ICH_ReflectionPaper_PFDD_FinalRevisedPostConsultation_2021_0602.pdf

1.1.4. Contribute to HTA's preparedness and downstream decision making for innovative medicines

Advancing patient-centred access to medicines in partnership with healthcare systems	
Core recommendations	**Underlying actions**
Contribute to HTA's preparedness and downstream decision making for innovative medicines	• Ensure the evidence needed by HTAs and payers is incorporated early in drug development plans, including requirements for post-licensing evidence generation;
	• Enable information exchange with HTAs to support bridging from benefit-risk to relative effectiveness assessment;
	• Discuss with HTAs guidance and methodologies for evidence generation and review;
	• Collaborate with HTAs on the identification of priority products and technologies;
	• Monitor the impact of decision-maker engagement through reviews of product-specific experience;
	• Further develop the structured interaction between EMA and HTA bodies, respecting the respective remits.

Achievements

- Delivery, together with EUnetHTA, on agreed priorities under the joint work plan to 2021:
  - provided more than 60 parallel consultations to medicine developers to allow them to obtain feedback from regulators and HTA bodies on their evidence-generation plans to support decision-making on marketing authorisation and reimbursement of new medicines at the same time; (EUnetHTA Joint Action 3 (2016-2021));
  - exchanged information on the outcome of the regulatory assessment at the time of marketing authorisation as part of EUnetHTA's framework for production of relative effectiveness assessments;
  - worked on optimising post-authorisation data generation tools, such as patient registries, to serve data needs for various decision-makers;
  - provided joint guidance on "Regulatory and health technology assessment advice on PLEG" (Regulatory and health technology assessment advice on post-licensing and postlaunch evidence generation is a foundation for lifecycle data collection for medicines - Moseley - 2020 - British Journal of Clinical Pharmacology - Wiley Online Library);
  - explored how HTA bodies and regulators apply the concepts of unmet medical need and therapeutic innovation in view of possible synergies;
  - explored the conceptual similarities and differences between the significant benefit of orphan medicines versus their added therapeutic value (Assessment of significant benefit for orphan medicinal products by European regulators may support subsequent relative effectiveness assessments by health technology assessment organizations - ScienceDirect).

- Initiated preparation, from a methodological and operational perspective, for the coming into application of the Regulation on Health Technology Assessment (EU) 2021/228 through established a joint EMA / EUnetHTA 21 work plan until 2023.
- Completed joint research work on regulatory/HTA collaboration, comprised of desk review, analysis of product assessments as well as interviews, leading to an article on " Strengthening the Interface of Evidence-Based Decision Making Across European Regulators and Health Technology Assessment Bodies " (Strengthening the Interface of Evidence-Based Decision Making Across European Regulators and Health Technology Assessment Bodies (valueinhealthjournal.com)).

1.1.5. Support developments in precision medicine, biomarkers and 'omics

Catalysing the integration of science and technology in medicines development	
Core recommendations	**Underlying actions**
Support developments in precision medicine, biomarkers and 'omics	• Enhance early engagement with novel biomarker developers to facilitate regulatory qualification: – Critically review the EMA's biomarker validation process, including duration and opportunities to discuss validation strategies in advance, in order to encourage greater uptake and use;
	• Address the impact of emerging 'omics' methods and their application across the development life cycle;
	• Evaluate, in collaboration with HTAs, payers and patients, the impact of treatment on clinical outcomes measured by biomarkers;
	• Optimise the European research infrastructure for developing personalised medicine.

Achievements

- Process improvement platform for qualification of opinions – an R&D platform industry stakeholders focus group has been established and a workshop is in preparation for 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 be reported at the December 5th, 2023 R&D industry platform meeting.
- Support to developers via Innovation Task Force (ITF) and Business Pipeline Meetings (BPM), expanding early points of contacts to technologies and methods related to drug development (increase of number of support meetings and proportion on technologies).
- 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 now has a member in the Science and Innovation Panel (SIP) of the Innovative Health Initiative (IHI) who coordinates the EMA input to strategic research and innovation agendas and the drafting of funding proposals of IHI and other European Partnerships.
- 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".

2. Highlight on achievements for the top three veterinarian recommendations thought to deliver the most significant change over the course of the five-year strategy

Gerrit Johan Schefferlie
Chair of CVMP

"Veterinary medicines are benefiting from new technologies resulting in innovative medicines for animals and public health.

A constant challenge for regulators is to ensure that the knowledge in the network allows for the adequate scientific assessment of those innovative medicines without stopping progress. The publication of scientific guidelines is of key importance to overcome those challenges."

2.1.1. Transform the regulatory framework for innovative veterinary medicines

Catalysing the integration of science and technology in medicines development	
Core recommendations	**Underlying actions**
Transform the regulatory framework for innovative veterinary medicines	• Produce further guidance to implement the annex to the new veterinary legislation (Regulation (EU) 2019/6) that defines proportionate and future-proofed technical standards for novel veterinary therapies, particularly biologicals;
	• Ensure that the new regulatory environment is applied in a timely manner, in line with research for innovative products at national and European level provided through specific programs;
	• Develop standards for novel therapies and the promotion of new endpoints for the evaluation of efficacy;
	• Consider improving regulatory requirements for post-authorisation evidence generation for novel therapies;
	• Strengthen support to developers throughout the development lifecycle of novel therapies;
	• Contribute to, and share resources with, the human domain in the area of novel therapies, such as the approach to assessment of cell therapies, monoclonal antibodies, etc.;
	• Increase EU network capacity and capability in novel therapies drawing on knowledge and training from human experience.

Achievements

- More than 50 documents with guidance for the implementation of the Regulation (EU) 2019/6 have been produced before the implementation date of the Regulation, many of the documents refer to biologicals/immunologicals.

- The EMA/CVMP has worked with EFSA on risk assessment with a view to aligning methodology for estimating consumer exposure to residues, including dual-use substances. A draft guideline with the name "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 and gone through a consultation period, the document is currently under revision to consider the comments received and once finalised will be forwarded to the EC. Draft report
- The Novel Therapies & Technologies Working Party 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), bacteriophages (Draft Guideline on quality, safety and efficacy of bacteriophages as veterinary medicines), as well as working on nanomaterials. Most of the draft guidance is to be published for consultation before the end of 2022 or during the beginning of 2023.
- Quality Innovation Group established which will also address requests coming from veterinary companies.
- Assessment of the efficacy of the EMA policy on Minor Uses 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. A paper is to be published in the short term.

2.1.2. Develop new approaches to improve the benefit-risk assessment of veterinary medicinal products

Driving collaborative evidence generation - improving the scientific quality of evaluations	
Core recommendations	**Underlying actions**
Develop new approaches to improve the benefit-risk assessment of veterinary medicinal products	• Develop regulatory approaches to accommodate advances in technology such as whole genome sequencing and analytical methodology to access ever-lower limits of detection;
	• Develop methodology for the benefit-risk evaluation of novel medicines intended to promote, or manage, the health of herds, besides the health of the individual animal;
	• Promote systematic application of structured benefit-risk methodology and quality assurance systems in the approach to assessment and consistency of decision-making;
	• Develop criteria to accept non-conventional sources of data (e.g. real-world evidence);
	• Consider the regulatory framework and methodology to evaluate the efficacy of a veterinary medicine which is used to produce an improvement in human health, where benefit to the animal might be secondary;

	• Optimise quality and consistency of outputs from EMA and maximise their dissemination to relevant stakeholders, especially for novel technologies.

Achievements

- Launch of the European Veterinary Big Data Strategy 2022-2027.
- Ongoing work towards publication of the revised guideline on the evaluation of the benefit-risk balance of veterinary medicinal products – public consultation expected for 1st quarter 2023.

2.1.3. Collaborate with stakeholders to modernise veterinary pharmacoepidemiology and pharmacovigilance

Driving collaborative evidence generation - improving the scientific quality of evaluations	
Core recommendations	**Underlying actions**
Collaborate with stakeholders to modernise veterinary pharmacoepidemiology and pharmacovigilance	• Encourage increased stakeholder involvement in modernising veterinary pharmacovigilance and enhance international coordination;
	• Using data on the sales of veterinary products, develop methodology to collate, analyse and communicate information about the incidence of adverse reactions related to medicines' use;
	• Together with stakeholders, develop new and improved continuous surveillance and signal detection methodology using the network's pharmacovigilance database;
	• Establish stakeholder expert groups for different food-producing species to access actual-use data of products in the field, both off and on label;
	• Facilitate development of methodology using new technology, such as veterinary practice management systems and mobile phone apps, to increase reporting rates of adverse events.
	• Improve communication of veterinary pharmacovigilance to the general public.

Achievements

- The Union pharmacovigilance database system has been developed to support the requirements of Regulation (EU) 2019/6. It consists of an enhanced database for recording suspected adverse event reports (EVVet3), supplemented by an IRIS-based module for the submission of identified signals and of annual statements of signal detection having been carried out:
  - Training workshops on the pharmacovigilance system have been carried out and remain available on the EMA website;
  - Improvements to the system will continue to be delivered, but Marketing Authorisations Holders can notify the outcome of their signal detection activities.

- Scientific advice was developed by the Agency in support of the relevant implementing regulation on Good veterinary pharmacovigilance practice (Commission Implementing Regulation (EU) 2021/1281 of 2 August 2021 laying down rules for the application of Regulation (EU) 2019/6 of the European Parliament and of the Council as regards good pharmacovigilance practice and on the format, content and summary of the pharmacovigilance system master file for veterinary medicinal products).
- The new Pharmacovigilance IT system (EVVet3) - based on signal detection – has been implemented, a new methodology for veterinary pharmacovigilance:
  - Further procedures and opportunities for collaboration between Member States are being developed.
- Stakeholder groups as mandated by Regulation (EU) 2019/6 to improve pharmacovigilance for specific animal species are being established.
- Publication of guidelines:
  - Guideline on veterinary good pharmacovigilance practices (VGVP) Collection and recording of suspected adverse events for veterinary medicinal products;
  - Guideline on veterinary good pharmacovigilance practices (VGVP) Controls and pharmacovigilance inspections;
  - Guideline on veterinary good pharmacovigilance practices (VGVP) Pharmacovigilance systems, their quality management systems and pharmacovigilance system master files;
  - Guideline on veterinary good pharmacovigilance practices (VGVP) Signal management;
  - Guideline on veterinary good pharmacovigilance practices (VGVP) Veterinary pharmacovigilance communication.
- Significant efforts have been made to relate suspected adverse event reports for same or similar products in a smart way to enable meaningful analysis of veterinary pharmacovigilance reports (so-called 'recoding' of products).

3. Achievements for Human Strategy

3.1. Goal 1: Catalysing the integration of science and technology in medicines development

3.1.1. Support translation of advanced therapy medicinal products (ATMPs) into patient treatments

Ilona G. Reischl
Chair of CAT

"Advanced Therapy Medicinal Products are innovative medicines which bring new hope for the treatment of diseases, with the promise that they not only manage the symptoms of severe, disabling or life-limiting conditions but may transform and save lives. By extending opportunities to provide assistance with planning, method development and clinical evaluation through early engagement with regulators we support streamlined development to facilitate efficacious transformative therapies reaching the patients faster and address their unmet medical needs."

Catalysing the integration of science and technology in medicines development	
Core recommendations	**Underlying actions**
Support translation of advanced therapy medicinal products (ATMPs) into patient treatments	• Identify therapies that address unmet medical need;
	• Provide assistance with early planning, method development and clinical evaluation;
	• Address the challenges of decentralised ATMP manufacturing and delivery locations;
	• Support evidence generation, pertinent to downstream decision-makers;
	• Evaluate and improve interactions with European institutions (research, financial and environmental);
	• Raise global awareness of ATMPs to maximise knowledge sharing, promote data collection;
	• Engage with other international regulatory agencies to foster global convergence of requirements for ATMPs.

Achievements

- Launch of pilot providing enhanced support to academic ATMP development in September 2022.
- ATMP cluster meetings held with FDA, PMDA and Health Canada.
- Fostering of novel manufacturing methods with the establishment of the Quality Innovation Group.
- QIG survey and ITF review summarising novel technologies.
- 23 ITF and Business Pipeline meetings were held for ATMPs from 2020 to 2022:
  - 10 BP: 5 in 2020, 3 in 2021 and 2 in 2022 and
  - 13 ITF meetings: 3 in 2020, 8 in 2021 and 2 in 2022.

- From 1 January 2020-30 Jun 2022, 44% of products which received PRIME eligibility were ATMPs (18 ATMPs /41 products).
- Guidance (checklists and flowcharts) on quality, non-clinical and clinical development for ATMPs published in November 2021.
- Dedicated training modules on navigating the regulatory requirements and Scientific Advice for ATMPs.
- Actionable objectives for the Cooperation between the European Medicines Agency (EMA) and the European Innovation Council (EIC) agreed in December 2022.

3.1.2. Promote and invest in the PRIME scheme

Paolo Foggi
Chair of SAWPh

"Results from the first five years of Europe's Priority Medicines Scheme have shown that PRIME has given patients earlier access to transformative treatments that can make a real difference to their health. We must further strengthen this initiative introducing a more adaptable process and leveraging the knowledge built during the development to enable better downstream decision making by regulators, HTAs and payors resulting in increased patient access to these treatments."

Catalysing the integration of science and technology in medicines development	
Core recommendations	**Underlying actions**
Promote and invest in the PRIME scheme	• Improve external communication to better explain and promote PRIME;
	• Review the scientific advice provided in PRIME with a view to allow more flexibility in the procedure and identify opportunities for more agile discussions;
	• Optimise the current regulatory system that supports PRIME in order to enable a shortened time frame for development and MA review while ensuring high quality evidence generation plans to improve access for patients;
	• Review the performance of the scheme after 5 years, to ensure that it delivers the expected impact on public health (i.e. faster access to patients of priority medicines), and adapt its scope and features, if applicable;
	• Explore opportunities for further engagement and collaboration with patients, healthcare professionals, academia and international partners;
	• Explore possible impact and benefits of expanding the earliest possible entry to the PRIME scheme to a wider range of applicants, including for new indications of existing products.

Achievements

- 5 years PRIME review and report with recommendations published in March 2022 (period covered by the analysis: Launch of PRIME in March 2016 until end June 2021).
- Recommendations for enhancement of PRIME scheme presented to PRIME oversight group and to SAWP/CHMP/CAT in July and September 2022.
- Detailed activities plan (2022-2025) adopted by SciCoBo in June 2022 covering planned and on-going activities to strengthen the PRIME scheme.
- Work on-going to update guidance, templates, processes and communication by Q4, 2022 for implementation of changes as of 2023 to strengthen support provided for PRIME products.
- A set of metrics and performance indicators has been developed to monitor the achievement of PRIME objectives and strategic goals.
- A risk analysis and action plan has been developed to ensure the RSS 2025 PRIME core recommendations and underlying actions are met.
- Publication in Therapeutic Innovation & Regulatory Science comparing PRIME and Breakthrough therapy designation applications 'Considering global development? Insights from applications for FDA Breakthrough Therapy and EMA PRIME designations'.
- Recommendations to pursue PRIME applications in the Regulatory Science and Innovation Task Force's (TRS) Early Point of Contact (EPOC) meetings including providing regulatory and scientific recommendation on best way to achieve a positive PRIME designation.

3.1.3. Facilitate the implementation of novel manufacturing technologies

Kora Doorduyn - van der Stoep
Chair of CMDh

"Pharma 4.0 is a vision to apply emerging technologies to e.g. digitalise pharmaceutical manufacturing leading 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. In this respect it is important to find the optimal balance between facilitating innovation by allowing greater flexibility while at the same time ensuring that appropriate controls remain in place to maintain adequate oversight of manufacturing activities."

Catalysing the integration of science and technology in medicines development	
Core recommendations	**Underlying actions**
Facilitate the implementation of novel manufacturing technologies	• Recruit and develop expertise, in novel manufacturing technologies and develop training and tools to enhance the assessment process;
	• Identify potential bottlenecks and strengthen early interaction, transparency and communication with stakeholders on regulatory requirements for novel manufacturing technologies;

Catalysing the integration of science and technology in medicines development	
	• Address regulatory challenges through modernisation of relevant regulations and guidelines to facilitate novel manufacturing technologies, including through international harmonisation activities;
	• Encourage the use of risk-based approaches to manufacturing processes and control strategies throughout the product lifecycle;
	• Facilitate a flexible and fit for purpose approach in application of Good Manufacturing Practice;
	• Support the development of greener manufacturing technologies in line with the EU's 'Strategic Approach to Pharmaceuticals in the Environment'.

Achievements

- Establishment of the Quality Innovation Group - see 3.1.1.

  QIG: Industry survey on expected key innovative manufacturing technologies finalised and reported. QIG mandate and selection membership criteria of QIG developed, Kick-off meeting organised in September 2022. Further stakeholder engagement (including listen and learn focus groups planned for early 2023.

- International activities relating to Pharmaceutical Quality Knowledge Management System (PQKMS):
  - PQKMS: The Pharmaceutical Quality Knowledge Management System (PQ KMS) Working Group established at ICMRA in June 2021 and a paper on Global Pharmaceutical Quality Knowledge Management: Enhancing Regulatory Reliance and Agility was published by ICMRA;
  - A reflection paper on the Regulatory Pharmaceutical Quality Knowledge Management System (PQ KMS) to Enhance the Availability of Quality Medicines has been published by ICMRA in July 2022;
  - Enable use of risk-based approaches to manufacturing and control strategies by implementing ICH Q12 (e.g. trainings on Pharmaceutical Quality System (PQS) effectiveness) and participation in the ICH Q9 revision [continues through 2023].

- GMP and manufacturing topics input at international level:
  - Publication of Annex 1 Manufacture of sterile medicinal products (harmonised with PIC/s, and WHO) in July 2022 clarifying how manufacturers can take advantage of new possibilities deriving from the application of an enhanced process understanding by using innovative tools as described in the ICH Q9 and Q10 guidelines and facilitating introduction of new and innovative manufacturing technologies;
  - Enhance submission, assessment, and post-approval change management (ICH M4Q R2 - structured data in module 3);
  - Agree globally harmonised principles for regulatory acceptance of Continuous Manufacturing technologies (ICH Q13);

- An ICMRA-Industry Virtual Workshop was held in July 2021 and a report on Enabling Manufacturing Capacity in the COVID-19 Pandemic was published by ICMRA;
- Pilot on collaborative hybrid inspections have been developed through ICMRA. Status: terms of reference for collaborative hybrid inspections developed, a call for applications launched and pilot inspections planned for the first half of 2023 with reporting on the outcome of the pilot at the end of 2023;
- A pilot on collaborative assessment has also been launched with applications received and planned to be assessed in latter half of 2022 with reporting on the outcome of the pilot at the end of 2023.

3.1.4. Create an integrated evaluation pathway for the assessment of medical devices, in vitro diagnostics and borderline products

Catalysing the integration of science and technology in medicines development	
Core recommendations	**Underlying actions**
Create an integrated evaluation pathway for the assessment of medical devices, in vitro diagnostics and borderline products	• Facilitate the regulatory pathway between notified bodies and medicines' regulators: – Establish a process for multi-stakeholder scientific advice to support development of medicine-device combinations, qualification methodologies and the use of companion diagnostics; – 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; – Adapt consultation processes to address emerging digital technologies and wearables;
	• Build a network of expertise to regulate and provide support throughout the product lifecycle;
	• Define how benefit-risk of borderline products is assessed and communicated;
	• Gain insight in innovation on drug-device combination products via horizon scanning.

Achievements

- Establish 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;
    EMA to review such analysis and hold a follow-up call with industry participants, with a view to shape a pilot for such advice;

EMA to 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 MDR/IVDR implementation, however the necessary collaborative interactions with EC MDCG and 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 and considered at present. Amendments to their scope/procedure/expertise are being discussed (e.g. Focus Group on QoNM as part of the R&D stakeholder platform and the upcoming EMA workshop on QoNM in March 2023) and will be implemented.

3.1.5. Develop understanding of, and regulatory response to, nanotechnology and new materials in pharmaceuticals

Catalysing the integration of science and technology in medicines development	
Core recommendations	**Underlying actions**
Develop understanding of, and regulatory response to, nanotechnology and new materials in pharmaceuticals	• Raise awareness of new nanomedicines and materials via the EU-Innovation Network, and foster collaboration with DG JRC and other international partners (e.g. IPRP), to share knowledge and harmonize regulatory practices: – Generate guidance addressing PK/PD (including modelling) requirements and long-term efficacy and safety; – Develop and standardise new testing methods related to the quality and safety assessment of nanomedicines; – Understand the critical quality attributes (CQA) of a given product and the relationship between those and the biological activity and in-vivo behaviour of the product;

Achievements

- Creation of the Quality Innovation Group - see 3.1.1.
- Ongoing horizon scanning deep dive report on nanotechnology as part of collaboration between EU-IN and EMA.

3.1.6. Diversify and integrate the provision of regulatory advice along the development continuum

Marianne Lunzer
Chair of CTCG

"31st January 2022 was a true milestone in the evolution of the EU regulatory system with the entry into force of the Clinical Trials Regulation, the establishment of the CTCG and the launch of the ACT EU programme all aimed to develop the European Union further as a competitive centre for innovative clinical research and enhancing evidence generation capabilities. A key priority action of this programme is to reinforce scientific advice coordination between clinical trial authorisation and clinical trial design. This is being effectively delivered by enhanced collaboration between the CTCG, the SAWP/ETF / EU-IN (SNSA via the national innovation offices) and enriched with the establishment of a multistakeholder platform."

Catalysing the integration of science and technology in medicines development	
Core recommendations	**Underlying actions**
Diversify and integrate the provision of regulatory advice along the development continuum	• Create complementary and flexible advice mechanisms to support innovative product development also expanding multi-stakeholder consultation platforms;
	• Facilitate a more iterative advice framework that better addresses the continuum of evidence generation. Make general advice on new technological trends publicly available;
	• Promote more integrated medicines development aligning scientific advice, clinical trials approval and Good Clinical Practice oversight;
	• Advance acceptance of digital endpoints through exploring a multistakeholder platform to generate feedback on their utility;
	• Facilitate translation of innovation via a re-engineered Innovation Task Force and synergy with an evolving EU-Innovation Network platform.

Achievements

- Establishment of ACT EU – work plan to 2026 – Priority Action 1: Mapping & Governance.
- Aligning scientific advice, clinical trials approval and Good Clinical Practice oversight.
- Focus Group with industry associations on practical application of integrated development support held in 2021 reaching a number of recommendations. See 3.1.4.
- Launch of parallel joint scientific consultations (JSCs) with HTA bodies/EUnetHTA 21 and publication of EMA and European HTA bodies joint work plan (2021-2023).
- Establishment of rapid scientific advice to support COVID-19 developments and of the ETF-led scientific advice foreseen in Regulation (EU) 2022/123 on a reinforced role for the European Medicines Agency in crisis preparedness and management for medicinal products and medical devices.

- Continuous improvement of the SAWP/PDCO interaction, clarifications of the scope of scientific advice in public guidance *and planned novel mode of SAWP involvement in PDCO procedures.*
- Acceptance of questions relating to medical devices in scientific advice requests and initiation of process development and medical device decision-maker engagement towards setting up scientific and regulatory advice on medical devices – see 3.1.4.
- Implementation of Notified Bodies on applicant side - first in ITF meetings and Scientific Advice.
- Patient experience data in EU medicines development and regulatory decision-making workshop held on 21/09/2022 – see achievements under "Further develop external engagement and communications to raise awareness of EMA's work and promote trust and confidence in the EU regulatory system".
- Re-engineered Innovation Task Force and synergy with an evolving EU-Innovation Network platform.
- Advance acceptance of digital endpoints - multistakeholder platform (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).
- Published recommendations to prepare for new technologies (Genome editing, Artificial Intelligence Horizon Scanning reports, https://doi.org/10.1038/d41573-022-00190-3).

3.2. Driving collaborative evidence generation – improving the scientific quality of evaluations

3.2.1. Leverage non-clinical models and 3Rs principles

Driving collaborative evidence generation – improving the scientific quality of evaluations	
Core recommendations	**Underlying actions**
Leverage non-clinical models and 3Rs principles	• Stimulate developers to use novel pre-clinical models, including those adhering to the 3Rs: – Cooperate with other EU agencies/bodies to fund research and (access to) standardised repositories for alternative methods and models; – Development of clear guidance to encourage and prioritise the use of New Approach Methodologies (NAMs) that can be used to fulfil testing requirements in lieu of traditional animal tests and that take the 3Rs into serious consideration;
	• Re-focus the role of the Joint 3Rs working group (J3R WG) to support qualification of new alternative 3R-compliant methods/models including in silico and novel in vitro assays;
	• Implement/develop IT tools to exploit the added value of SEND for the re-analyses of non-clinical studies to support clinical trials, marketing authorisation and improved evidence generation.

Achievements

- 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).
- Implement 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.

3.2.2. Develop the regulatory framework for emerging clinical data generation

Driving collaborative evidence generation – improving the scientific quality of evaluations	
Core recommendations	**Underlying actions**
Develop the regulatory framework for emerging clinical data generation	• Develop methodology to incorporate clinical care data sources in regulatory decision-making;
	• Clarify questions on data ownership and data security;
	• Modernise the GCP regulatory oversight to enable decentralised models of clinical trials coupled with direct digital data accrual;
	• Develop the capability to assess complex datasets captured by technology such as wearables;
	• Facilitate training and understanding of healthcare professionals and patients to access and participate effectively in such trials;
	• Support the development of robust digital endpoints through qualification, scientific advice, and the establishment of a multi-stakeholder platform to obtain feedback on their utilisation.

Achievements

- 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 clinical trial authorisation, GCP and HTA acceptance at EU and international level;

Comments from the Expert Working Group and selected stakeholders are being reviewed related to the principles and Annex 1 (traditional clinical trials). A new Regulatory Chair was appointed to the Expert Working Group (EWG) in September. Annex 2 (decentralised and novel type trials) will be developed, likely in the new year. The principles and Annex 1 guidance is targeted to be put to public consultation likely early 2023.

- 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 one month of public consultation expected in early 2023).
- EMA expert base expanded in the areas of digital, biomechanics and devices.

3.2.3. Expand benefit-risk assessment and communication

Driving collaborative evidence generation – improving the scientific quality of evaluations	
Core recommendations	**Underlying actions**
Expand benefit-risk assessment and communication	• Include patient preferences to inform the benefit-risk assessment: – Develop guidance building on recent developments (e.g., IMI PREFER) of appropriate methods for patient preference study design, conduct, analysis, and presentation for regulatory purposes, ensuring high quality methodology and independence; – Provide guidance on the roles of patient preferences in the different therapeutic contexts and regulatory decisions, i.e., how preferences can help regulators interpreting clinical trial outputs, how they can inform shared decision-making; how to handle heterogenous or conflicting preferences; how to communicate patient preferences in regulatory decisions;
	• Promote systematic application of structured benefit-risk methodology and quality assurance systems in the approach to assessment and consistency of decision-making;
	• Enhance structured assessment of benefits, harms, and uncertainties to improve communication to the public;
	• Develop the capability for analysing individual patient data to support decision-making;
	• Improve communication with HTAs and payers regarding therapeutic context, comparison vs. placebo/active-control, patient perspective.

Achievements

- EMA launched the Cancer Medicines Forum in March 2022 with academia to optimise cancer treatments in clinical practice:
  - EMA, in collaboration with the European Organisation for Research and Treatment of Cancer (EORTC), has launched the Cancer Medicines Forum (CMF). Bringing together representatives from academic organisations and the European medicines regulatory network, the forum aims at advancing research into optimising cancer treatments and will contribute to foster high standards in cancer care in the European Union (EU).
- Pilots conducted applying quantitative benefit-risk assessment for initial marketing authorisations and associated communication tools for quantitative benefit-risk assessment. Updated guidance for key regulatory outputs (assessment reports, labelling) to enhance usefulness for down-stream decision makers:
  - Mini project agreed with CAT and CHMP; pilot to complete in 2023.
- In-depth review of experience with product-specific discussion between regulators and HTAs at time of licensing to understand the impact and enable optimisation:
  - Discussions ongoing with HTA and payers.
- Process for enhanced interaction between EMA and payers to debrief on regulatory outcomes:
  - Process being established; aiming for a workshop on oncology single-arm trials and endpoints in 2023;
  - Network capability to analyse raw data – project ongoing:

    Pre-pilot on raw data analysis completed;

    Design initiated by CHMP pilot for clinical raw data analysis of MAAs;

    Advisory Group on Raw Data established;

    Scientific information dossier pilot on advanced analytics initiated;

    Discussion on Clusters of Excellence;

    AI Workshop held.
  - Application of multi-state models to estimate benefits and harms of cancer drugs in oncology trials (collaboration EMA-UMCG-HOVON), abstract accepted ASH and DIA EU;
  - Survey on trade-offs for PFS with doctors and regulators (EMA-EORTC-UMCG-HIOVON), presented at DIA 2022, manuscript being prepared;
  - Survey on cancer patient trade-offs - IQVIA tender (ongoing; survey launched);
  - Study on validating external controls for assessing benefits and harms in cancer trials using RCTs - IQVIA tender (ongoing; manuscript being written);
  - Setting up pilot webinar on conversations with cancer patients about benefits and harms of drugs (first webinar in multiple myeloma expected in 2023).

3.2.4. Invest in special populations initiatives

Violeta Stoyanova-Beninska
Chair of COMP

"We can be more confident that medicines are effective and safe for everyone if clinical research includes diverse patient population groups, as has been most recently demonstrated during the COVID-19 pandemic.

In addition, clinical trials are becoming more innovative with respect to their design allowing for more patient centred approaches to be applied and capturing diversity in treatment populations. This will increase clinical trial efficiency.

We are investing in a number of parallel initiatives to focus on special population needs seeking to address long term health inequalities and utilising new sources of evidence generation such as RWE from healthcare systems to complement clinical trials."

Driving collaborative evidence generation – improving the scientific quality of evaluations	
Core recommendations	**Underlying actions**
Invest in special populations initiatives	• Focus on accelerating access for patient (sub-)populations in urgent need whilst ensuring high quality data to evaluate efficacy and safety of medicines;
	• Identify areas of highest unmet needs where clinical care data can supplement clinical trial data;
	• Foster input of patients/patient representatives and carers in the regulatory process and enhance multi-stakeholder advice in collaboration with patients, HCPs, payers and HTAs;
	• Progress implementation of the geriatric medicines strategy;
	• Progress implementation of the joint EMA/EC paediatric medicines action plan: – Participate in multi-stakeholder initiatives on neonatal medicines to further the understanding of disease mechanisms and natural history and develop disease progression models to support innovative clinical trial design, biomarkers and endpoints that accurately capture treatment benefit;
	• Develop a strategic initiative in maternal-foetal health to better understand and communicate risks, benefits and uncertainties of medicines use in pregnancy and breastfeeding, in collaboration with other regulators and international stakeholders: – Such an initiative should include considerations regarding PK/PD modelling, epigenetics, reproductive toxicity studies, clinical trial design as well as post-authorisation follow-up methods;

Driving collaborative evidence generation – improving the scientific quality of evaluations	
	• Encourage research to improve the efficiency and effectiveness of detecting drug safety issues (signal detection) in pregnant women and the elderly.

Achievements

- 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.
- Finalisation of good pharmacovigilance practice (GVP) P. III on 'Product- or population-specific considerations: pregnancy and breastfeeding' following public consultation in 2020 as well as the Annex to GVP XVI on pregnancy prevention programs.
- Publication of Annex 2 to the Guide on Methodological Standards in Pharmacoepidemiology: Guidance on methods for the evaluation of medicines 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" and the related Concept Paper outline, with an informal WG to be established by the end of 2022. – Meeting minutes
- Development & 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 & 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 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.
- Symposium session 'Post-Authorization Regulatory Strategies to Evaluate Drug Safety in Pregnancy: How to Optimize the Design of Registries & Database Studies' at 2022 annual conference of the international society for pharmacoepidemiology (ISPE).
- EMA-FDA-MHRA regulatory cluster has been set up and is meeting monthly to collaborate on strategy development & 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 the CHMP pilot on RWE and the CHMP workplan makes reference to geriatric use cases. We will do a number of RWE studies relevant to geriatric use 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.

3.2.5. Optimise capabilities in modelling, simulation and extrapolation

Brian Aylward
Chair of PDCO

"Children are not small adults, but they are small people. As such, it is possible to use data from some people to assess and predict drug behaviour in others. Better modelling and extrapolation methods can facilitate the characterisation and authorisation of medicines in children, and such measures are in line with the spirit of the paediatric regulation."

Driving collaborative evidence generation – improving the scientific quality of evaluations	
Core recommendations	**Underlying actions**
Optimise capabilities in modelling, simulation and extrapolation	• Enhance modelling and simulation and extrapolation use across the product lifecycle and leverage the outcome of EU projects;
	• Develop guidance and standards on the use of AI in modelling and simulation for regulatory submissions;
	• Deploy advances in RWD, modelling, simulation and extrapolation to benefit special populations particularly neglected patient populations;
	• Promote development and international harmonisation of methods and standards via a multi-stakeholder platform;
	• Increase capability and redesign the operations of relevant working parties to ensure wider knowledge exchange: – Invest in Centres of Excellence in regulatory science at an EU level, to work with regulatory agencies to provide training and research on modelling & simulation tools; – Enhance collaboration with external partners/consortia with expertise in modelling and simulation, and EU funded or co-founded projects e.g. IMI, Horizon 2020;
	• Investigate possibilities for conducting modelling and simulation analyses to address key regulatory questions as part of product specific assessment or development of guidelines and policies;
	• Consider working with stakeholders to foster data sharing through developing data standards and platforms for data exchange.

Achievements

- 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 to be published Q1 2023;
- Technical advice to research funders on this topic area.

3.2.6. Exploit digital technology and artificial intelligence in decision making

Driving collaborative evidence generation – improving the scientific quality of evaluations	
Core recommendations	**Underlying actions**
Exploit digital technology and artificial intelligence in decision making	• Establish a digital innovation lab to explore, pilot and develop solutions and processes, across the drug regulation spectrum, that leverage novel digital technology and artificial intelligence to support increase in efficiency and regulatory decision-making;
	• Develop capacity and expertise across the regulatory network through curriculum development and knowledge-sharing initiatives on data science, digital technologies and artificial intelligence-related solutions, products and endpoints, and their applications in the regulatory system;
	• Create and maintain a Health Data Science and AI forum to engage with a diverse set of stakeholders in novel digital technologies and artificial intelligence. This will include the technical, ethical, legal, regulatory and scientific perspectives of the use of digital technologies, and AI-powered applications;
	• Establish a dedicated framework for the development of guidelines and recommendations. The framework should address which guidelines are a priority, how the guidelines should be developed and which areas might be impacted, as well as the acceptability metrics or success factors;
	• Engage in efforts (e.g. via standardisation activities) for achieving greater global alignment with other regulators (e.g. FDA) on these topics;
	• Implement the priority recommendations of the HMA-EMA joint Big Data Task Force in the area of analytics.

Achievements

Digitalisation: in a constant evolving environment, the Agency is embracing Digital Transformation to ensure a proper response. In 2020, in the context of the Future Proofing programme, a Digital Business Transformation task force was created with the mandate to develop and execute a digitalisation strategy for the Agency. In 2021 the Agency continued to develop digitalisation activities by:

- Accelerating the development of Digital and Analytics Solutions through the creation of the Analytics Centre of Excellence (ACE) and the Digital Innovation Lab (DigiLab):

- Analytics Centre of Excellence is a digital toolbox experimentation hub where the Agency tests and expands its capacity to experiment with new analytics technologies such as artificial intelligence (AI) and machine learning in relation to business-process design, automation, information, and knowledge management. Automated recognition of personal data in documents, reengineering the procurement process, and utilising AI to find anomalies between submission data in documents and databases are just a few examples of initiatives;

  Five pilot projects were implemented: QR code, Discoverer tool, two validation tools to compare documents and a tool to automate registration of applications submitted to EMA;

  Other initiatives have been developed in parallel: Speech to Text, the implementation of Chatbots at EMA deploying the first chatbot at EMA for Talent Acquisition, Improvements in the ASK-EMA automatic triage system, the implementation of a Product Name validation for the new vet regulation, PEDAR to identify personal data, etc.

- Digital Innovation Lab (DigiLab) is a framework designed to identify opportunity spaces for digital innovation across the Agency, and to bring people together to ideate, design and prototype potential digital innovation solutions. DigiLab projects aim to either improve, or radically change the way we work, the latter through the introduction of technologies new to the Agency;

  Over 50 ideas for digitalisation and automation have been collected across the Agency;

  Fourteen new projects received green light for kick-off and aim to realise efficiency gains through automations;

  Ongoing DigiLab projects include i) experimentation with virtual reality to deliver security training, ii) piloting generating and using QR codes, iii) using Microsoft power apps to develop a self-service process to subscribe for newsletters, iv) process redesign to replace excel based workflows, v) use of robotic process automation to automate email management in Outlook, vi) use of robotic process automation to build clinical breakpoint data tables *etc.*

- Digital transformation programme and oversight, digital change management and digital capability and capacity building:
  - The Digital Business Transformation Task Force drives complex digital change initiatives that impact on the strategy of EMA, its structure and operations in relation to the network, its partners and stakeholders. Its objective is to adapt EMA operations to fundamental changes brought by legislative initiatives, digital technologies and global trends, to meet stakeholders' needs and expectations.
  - Continuation of EMA core business process digitalisation via IRIS – a modern and secure online platform to handle knowledge and regulatory and scientific procedures. The platform integrates data and information from other EMA systems to provide an efficient and user-friendly portal for regulatory network users and applicants.
- Establishment of a digital academy to develop a digital skills framework for EMA and lead on digital capability building:
  - Increasing digital literacy and stimulating the development of digital skills in order to support digital capability and capacity building at EMA and in the network, by defining crucial digital skills;
  - Building awareness around these skills and their importance for EMA and the network;

- Creating, maintaining and growing collections of learning offers to further develop these skills and encouraging staff to explore skills of interest to them;
- Providing these collections to EMA and Network staff through a single platform which acts as entry point to the content.

- Establishment of the Coordination Group on Artificial Intelligence:
  - Joint HMA/EMA workshop on AI in Medicines regulation[5];
  - Support in the preparation of the ICMRA Horizon Scanning Assessment Report on AI;
  - Scientific, technical and regulatory experience and knowledge sharing;
  - Advice on training initiatives, e.g. toward development of a "Data Science curriculum";
  - Leveraging expertise toward development of AI guidance in the form of a reflection paper;
  - Support to interactions with stakeholders, including Interagency collaboration on AI (including consideration for organising data science challenge).

3.3. Advancing patient-centred access to medicines in partnership with healthcare systems

3.3.1. Bridge from evaluation to access through collaboration with payers

Advancing patient-centred access to medicines in partnership with healthcare systems	
Core recommendations	**Underlying actions**
Bridge from evaluation to access through collaboration with payers	• Enable involvement of payers' requirements in the prospective discussion of evidence generation plans, including post-licensing evidence generation;
	• Contribute to the preparedness of healthcare systems by creating opportunities for collaboration on horizon scanning;
	• Establish more structured interaction between EMA and payers to support information flow, whilst respecting remits;
	• Collaborate with stakeholders to monitor the performance (safety and effectiveness) of products newly launched on the market (learning healthcare system), and link to the planning of evidence through risk management plans (RMPs).

Achievements

- Establish cooperation priorities with healthcare payer organisations, covering exchange on medicines' approvals (including ATMP), post-licensing evidence planning and DARWIN.
- Engagement of EMA Horizon scanning 1) with the International Horizon Scanning Initiative (IHSI) on methodological aspects (signal detection and multi-disciplinary assessment of challenges), and 2) collaboration in the context of the EUnetHTA21 work programme.
- Regular contribution to meetings of MEDEV on CHMP outcomes.

[5] https://www.ema.europa.eu/en/documents/report/report-joint-hma/ema-workshop-artificial-intelligence-medicines-regulation_en.pdf

3.3.2. Develop network competence and specialist collaborations to engage with big data

Sabine Straus
Chair of PRAC

"The pace of change in pharmacovigilance is rapid and it is our hope that Big Data's contribution will lead to a strengthened regulatory system that can efficiently integrate data analysis into its assessment processes. Knowing when and how to have confidence in the evidence generated from Big Data will benefit public health and will enable faster access to life-saving treatments for patients and for these treatments to be used more effectively and safely."

Advancing patient-centred access to medicines in partnership with healthcare systems	
Core recommendations	**Underlying actions**
Develop network competence and specialist collaborations to engage with big data	• Deliver a sustainable platform to access and analyse healthcare data from across the EU (Data Analysis Real World Interrogation Network -DARWIN). Build the business case with stakeholders and secure funding to establish and maintain a secure EU data platform that supports better decision-making on medicines by informing those decisions with robust evidence from healthcare;
	• Establish an EU framework for data quality and representativeness. Develop guidelines, a strengthened process for data qualification through Scientific Advice, and promote across Member States the uptake of electronic health records, registries, genomics data, and secure data availability;
	• Enable data discoverability. Identify key meta-data for regulatory decision-making on the choice of data source, strengthen the current ENCePP resources database to signpost to the most appropriate data, and promote the use of the FAIR principles (Findable, Accessible, Interoperable and Reusable);
	• Develop EU Network skills in Big Data. Develop a Big Data training curriculum and strategy based on a skills analysis across the Network, collaborate with external experts including academia, and target recruitment of data scientists, omics specialists, biostatisticians, epidemiologists, and experts in advanced analytics and AI;
	• Strengthen EU Network processes for Big Data submissions. Launch a 'Big Data learnings initiative' where submissions that include Big Data are tracked and outcomes reviewed, with learnings fed into reflection papers and guidelines. Enhance the existing EU PAS register to increase transparency on study methods;
	• Build EU Network capability to analyse Big Data. Build computing capacity to receive, store, manage and analyse large data sets including patient level data (PLD), establish a network of analytics

Advancing patient-centred access to medicines in partnership with healthcare systems	
	centres linked to regulatory agencies, and strengthen the Network ability to validate AI algorithms;
	• Modernise the delivery of expert advice. Build on the existing working party structure to establish a Methodologies Working Party that encompasses biostatistics, modelling and simulation, extrapolation, pharmacokinetics, real world data, epidemiology and advanced analytics, and establish an Omics Working Party that builds on and reinforces the existing pharmacogenomics group;
	• Ensure data are managed and analysed within a secure and ethical governance framework. Engage with initiatives on the implementation of EU data protection regulations to deliver data protection by design, engage with patients and healthcare professionals on data governance, and establish an Ethics Advisory Committee;
	• Collaborate with international initiatives on Big Data. Support the development of guidelines at international multilateral fora, a data standardisation strategy delivered through standards bodies, and bilateral collaboration and sharing of best practice with international partners;
	• Create an EU Big Data 'stakeholder implementation forum'. Dialogue actively with key EU stakeholders, including patients, healthcare professionals, industry, HTA bodies, payers, device regulators and technology companies. Establish key communication points in each agency and build a resource of key messages and communication materials on regulation and Big Data.

Achievements

- Review and establishment of BDSG workplans (Workplan 2020, Workplan 2021-2023, Workplan 2022-2025).
- Publication of the Big Data Steering Group (BDSG) 2022 report (europa.eu)
- Data quality:
  - Multi-stakeholder workshop on Data quality framework for medicines regulation held on 7 April 2022;
  - Engage with European Commission via EHDS and its joint action TEHDAS;
  - Published EU Data quality framework v1.0 following public consultation;
- EU Network Skills:
  - Big data training signpost made available in EU-NTC;
  - Explore EU Network training needs via Survey of skills completed;

  - Biostatistics, Pharmacoepidemiology and Data science curriculum adopted;
  - Market research for training delivery outsourcing completed and roll-out of training delivery started.
- Network capability to analyse:
  - Establishment of the multi-disciplinary Advisory group on raw data with members from CHMP, EMA Working Parties, patients' representatives;
  - Proof-of-concept pilot completed and CHMP pilot on raw data launched to receive, store, manage and analyse raw data to ultimately support decision making;
  - Launch enhancement of safety data analysis to support decision making;
  - Cluster of excellence paper, exploring how data analysis at national level can be fostered including through mutual support and sharing of good practice, endorsed by HMA;
  - Proof-of-concept pilot completed on data driven interrogation of scientific information submitted as part of scientific advice requests and MAAs and collaboration initiated with ICH M11 on the development of a logical model for clinical study protocols;
  - Joint HMA/EMA workshop on artificial intelligence in medicines regulation held, see also 3.2.6. ;
  - Initiated & 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 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;
  - Selection of Danish Medicine Agency (DKMA) as the analytics service provider to support the clinical trials raw data pilot. DKMA will serve as EMA's contractor in conducting individual patient data analyses for three out of ten regulatory procedures included in the pilot. The other pilot procedures will be undertaken by either NCA assessment teams or EMA staff. This split in assessment models is a key feature of the pilot to enable conclusions to be reached on the optimal resourcing approach (or blend).
- EU Stakeholder implementation forum:
  - 2nd and 3rd Big Data multi-stakeholder forum held – report of the 3rd workshop expected 1st quarter 2023.
- Delivery of expert advice:
  - Establishment of Methodology Working Party (MWP) and appointment of its members. First virtual meetings held twice monthly since April 2022.
- Governance framework:
  - Establishment and review of the Big Data Steering Group (BDSG) mandate and membership;
  - Support European Commission via EHDS and its joint action TEHDAS, assess impact of EHDS;
  - Support European Commission on the revised Pharmaceutical Strategy;
  - Review options for to strengthen BDSG expertise on ethics.
- International initiatives:
  - European Medicines Regulatory Network Data Standardisation Strategy published;

- Finalisation of the " data standardisation roadmap implementation workplan" targeted for 1st quarter 2023;
- Continued International collaboration with regulators (FDA, Health Canada, PMDA) and other stakeholders' engagement;
- Global regulators call for international collaboration to integrate real-world evidence into regulatory decision-making, published by the International Coalition of Medicines Regulatory Authorities (ICMRA).

- Bi-annual Industry meeting held in 2022.

3.3.3. Deliver improved product information in electronic format (ePI)

Emiel Van Galen
Chair of HMPC

"Development of the ePI common standard within the EU creates the technical foundation for the dissemination of trustworthy, regulator-authorised product information in the growing digital world, which will provide patients / consumers and HCPs with an additional and personalised approach for information on medicines. It enables more efficient retrieval of information the user is looking for in searches and facilitating the use of their preferred e-platforms. It also offers the possibility to streamline, simplify and speed up the regulatory processes involved in the creation and updating (variation) of PI such that patients/consumers and HCPs can be provided with the most up to date information about the safe and effective use of their medicines."

Advancing patient-centred access to medicines in partnership with healthcare systems	
Core recommendations	**Underlying actions**
Deliver improved product information in electronic format (ePI)	• Enable real-time interactivity within the Summary of Product Characteristics and Patient Leaflet;
	• In conjunction with healthcare providers, patients and pharmaceutical industry representatives, develop a strategic plan to deliver a sustainable ePI system;
	• Enable the reuse of structured medicinal product information by third parties through development of trustworthy source(s) and a standardised interface for access;
	• Address the need for improvements in PI content, such as package leaflet layout and readability, and user testing, identified in the EC report;
	• Plan for interoperability and interactivity of ePI with other eHealth systems and telematics initiatives, ensuring data portability;
	• Explore how digitalisation of medicines information could be harnessed to address key EU Network priorities, such as initiatives to avoid and manage supply problems.

Achievements

- European medicines regulatory network adopts EU common standard for electronic product information:
  - The EU ePI Common Standard was developed in 2021. This technical standard, based on Fast Healthcare Interoperability Resources (FHIR), will enable harmonised ePI across the EU. A proof-of-concept exercise established that the EU ePI Common Standard can be used to create accessible, user-friendly, multilingual ePI;
  - Following a public consultation, the EU ePI Common Standard was adopted by the EU Network Data Board on behalf of the European Medicines Regulatory Network, in September 2021;
  - Development of a 'minimum viable product' that will be piloted for creation of ePI began in 2022 supported by the EU's funding programme EU4Health and involving project team members from EMA, and Spanish, Danish, Dutch, and Swedish National Competent Authorities, as well as the pharmaceutical industry.

3.3.4. Promote the availability and support uptake of biosimilars in healthcare systems

Advancing patient-centred access to medicines in partnership with healthcare systems	
Core recommendations	**Underlying actions**
Promote the availability and support uptake of biosimilars in healthcare systems	• Further develop strategic communication campaigns to healthcare providers and patient organisations to reinforce trust and confidence;
	• Enhance training of non-EU regulators in the evaluation of biosimilars with extension to all therapeutic areas;
	• Address regulatory challenges in manufacturing e.g., statistical assessment of CQAs in the comparability exercise and the evolution of multisource biologicals/biosimilars;
	• Further develop the biosimilar framework, adapting the clinical part of the development to the latest scientific knowledge concerning the comparability assessment.

Achievements

- EMA scientific position statement and press release on biosimilar interchangeability in the EU (19 September 2022).
- Ongoing discussions with all stakeholder groups to ensure adequate information on biosimilars is available in different EU languages to support trust and uptake in MSs.
- Establishment of the HMA group on biosimilar medicines to facilitate smooth uptake of biosimilars in the EU:
  - Position statement published: Statement on the scientific rationale supporting interchangeability of biosimilar medicines in the EU (europa.eu);
  - News item published and social media campaign launched;
  - EMA webpage on biosimilars updated;

- Dissemination campaign to stakeholders and partners coordinated via stakeholders' database and ENS;
- Further discussions planned within PCWP/HCPWP in 2022/23;
- Publication and presentation to BMWP, SAWP and CHMP of A Data Driven Approach to Support Tailored Clinical Programs for Biosimilar Monoclonal Antibodies - PubMed (nih.gov) – Report produced by a collaborating expert.

- Translation of the biosimilar video into Slovenian with external webpage updated. Ongoing translation of the video into Estonian and Czech.
- Biosimilars Working Party has been repositioned within the Quality Domain and will be reconstituted with a new work plan for 2023-2025.

3.3.5. Further develop external engagement and communications to promote trust and confidence in the EU regulatory system

Advancing patient-centred access to medicines in partnership with healthcare systems	
Core recommendations	**Underlying actions**
Further develop external engagement and communications to promote trust and confidence in the EU regulatory system	• Develop content strategy in key public health areas and hot topics in regulatory science: – Enhance professional outreach through scientific publications & conferences; – Design communication campaigns in collaboration with relevant stakeholders to proactively approach to key public-health areas (e.g. vaccines); – Improve communications for patients, healthcare professionals and other stakeholders including HTAs and payers;
	• Develop more targeted and evidence-based communication facilitated by updated web content and format;
	• Conduct research on optimising the impact of risk communication in changing the behaviour of patients and healthcare professionals, including as part of risk management and pharmacovigilance.

Achievements

- Develop content strategy in key public health areas and hot topics:
  - Design communication campaigns in collaboration with relevant stakeholders to proactively approach to key public-health areas (e.g. vaccines) Ongoing for COVID-19 and monkeypox;
  - Improve communications for patients, healthcare professionals and other stakeholders including HTAs and payers;
  - Enhance professional outreach through scientific publications & conferences Ongoing, list of priorities for Scientific publication Strategy presented to Strategic Communication Review Group (SCORE);

- Contribute and support initiatives on the Agency's plans and strategies, both internally and with external stakeholders:
  - Support drafting of strategy documents (Strategic plan for stakeholder engagement drafted and endorsed by Scientific Coordination Group (SCG) and SCORE).
- Further develop external engagement and communications to raise awareness of EMA's work and promote trust and confidence in the EU regulatory system:
  - Multi-stakeholder workshop on Patient Experience Data organised and workshop communication materials and recording published: EMA workshop on patient experience data in medicines development and regulatory decision-making - YouTube (for more information see achievements under the recommendation "Diversify and integrate the provision of regulatory advice along the development continuum");
  - Implement a consolidated approach to scientific publications at EMA, including improving oversight of the key priorities for scientific publication, enhancing support for Open Access and increasing external visibility of EMA's key scientific articles;
  - Multi-stakeholder workshop on EMA's Extended Mandate.

3.4. Addressing emerging health threats and availability/therapeutic challenges

3.4.1. Implement EMA's health threats plan, ring-fence resources and refine preparedness approaches

Marco Cavaleri
Co-Chair of ETF

"The COVID-19 pandemic has provided a significant boost to research that has significantly advanced our regulatory science agenda in the area of vaccines, anti-infectives, clinical trials and use of real-world evidence."

Addressing emerging health threats and availability/therapeutic challenges	
Core recommendations	**Underlying actions**
Implement EMA's health threats plan, ring-fence resources and refine preparedness approaches	• Enhance coordination of scientific and regulatory activities within the EU network;
	• Evaluate preparedness for emerging pathogens and 'disease X';
	• Advance understanding of the role of novel technology in responding to emerging health threats, to ensure appropriate regulatory support and oversight;
	• Work with EU regulatory partners to harmonise the regulatory framework for vaccine clinical trials, including during emergencies: – Strengthen collaboration with international partners and stakeholders on the identification, development, authorisation

Addressing emerging health threats and availability/therapeutic challenges	
	and post-authorisation follow-up of relevant medicinal products; – Effective and timely communication to regulatory partners, healthcare professionals and the public;
	• Develop methodology for the surveillance and detection of abuse of medicines including of opiates (pharmacovigilance).

Achievements

- Creation of Health Threats and Vaccines Strategy Advisory Function.
- Formalisation of the EMA Pandemic Task Force (ETF) and EMA's role in managing it in the new Regulation (EU) 2022/123:
  - Enhanced coordination of scientific and regulatory activities within the EU network;
  - Involvement of civil society representatives in the ETF;
  - Evaluated preparedness for emerging pathogens and 'disease X';
  - Advanced understanding of the role of novel technology in responding to emerging health threats, to ensure appropriate regulatory support and oversight;
  - Worked with EU regulatory partners to harmonise the regulatory framework for vaccine clinical trials, including during emergencies*;*
  - Strengthened cooperation with the EC and ECDC that has bene put in place in the context of COVID-19.

3.4.2. Continue to support development of new antibacterial agents and their alternatives

Addressing emerging health threats and availability/therapeutic challenges	
Core recommendations	**Underlying actions**
Continue to support development of new antibacterial agents and their alternatives	– Encourage new business models that provide "pull" incentives or different approaches beyond the current "funding research" strategy in the EU, including financial schemes to sustain availability of new and old antibiotics;
	• In collaboration with HTAs and payers, define the evidence requirements for new antibacterial medicines;
	• Evolve regulatory guidance and support alternative approaches to new antibacterial drug development as well as innovative approaches for prevention and treatment of infections;
	• Support the development and application of rapid diagnostic tools;
	• Support initiatives, such as the clinical trials network, to facilitate and accelerate clinical development.

Achievements

- Provision of ITF AMR platform to support development of novel antibacterial agents.
- Collaboration with ICMRA for the production of an Antimicrobial Resistance Best Practices Working Group report and case studies in November 2022.
- Generated an EMA Horizon scanning deep dive report on AMR for the information of the EMRN and of the EMA AMR strategy under development by the Health Threats and Vaccines Strategy Advisory Function in collaboration with the Veterinary division, applying a One Health approach.

3.4.3. Promote global cooperation to anticipate and address supply problems

Addressing emerging health threats and availability/therapeutic challenges	
Core recommendations	**Underlying actions**
Promote global cooperation to anticipate and address supply problems	• Build on deliverables from the work plan of the HMA/EMA Task Force on availability of authorised medicines;
	• Explore mechanisms to increase manufacturing capacity in Europe and internationally, in particular for essential medicines;
	• Enhance collaboration with international regulators in the area of supply disruptions due to manufacturing quality issues;
	• Promote greater knowledge exchange with international stakeholders on shortages due to quality/manufacturing issues;
	• Continue to engage with all stakeholders to address the causes and consequences of lack of medicines' availability;
	• Support international harmonisation of regulatory science standards for complex generic medicines addressing bioequivalence, waivers and modelling;
	• Improve monitoring of shortages and enhance communication of supply problems to EU citizens, their representatives and HCPs.

Achievements

- Set up of the Supply and Availability Work Stream under the TRS Task Force.
- Set-up of the various governance structures (MSSG, SPOC WP, iSPOC etc.) under the EMA extended mandate.
- Investment in the development of the European Shortage Monitoring Platform (ESMP).
- Monitoring of events and shortages that my lead to Major events. Monitoring of supply and demand for medicines in the critical list for COVID-19 and MPOX.
- Management of critical shortages in the EU/EEA by putting in place EU coordinated actions to mitigate these shortages, such as engaging with MAHs to increase production capacity in cases of unexpected increase in demand.
- Communication on supply disruptions to patients and HCPs.
- Relaunch of the Joint EMA/HMA Task Force on the availability of medicines:

- Adoption and publication of the updated mandate, transforming the TFAAM to function as a supply and availability hub, tracking progress on the medicine availability and shortage-related activities at EU/EEA level;
- The work programme of the TFAAM to 2025;
- Good Practice Guidance for patient and healthcare professional organisations on the prevention of shortages (published in July 2022);
- Meeting of the TFAAM with Industry Associations on 12 September 2022;
- Meeting of the TFAAM with Patients/Consumers Working Party and Healthcare Professionals Working Party on 15 November 2022.
- International communication clusters – Global Regulatory Working Group on shortages, FDA, Health Canada and ICMRA.

3.4.4. Support innovative approaches to the development, approval and post-authorisation monitoring of vaccines

Addressing emerging health threats and availability/therapeutic challenges	
Core recommendations	**Underlying actions**
Support innovative approaches to the development, approval and post-authorisation monitoring of vaccines	• Establish a platform for EU benefit-risk monitoring of vaccines post-approval;
	• Communicate proactively with key stakeholders on benefit-risk using evidence-based tools to tackle vaccine hesitancy;
	• Examine innovative clinical trial approaches to expedite vaccine development;
	• Advance methods/tools to characterise immune response and support definition of vaccine quality attributes;
	• Foster the development of improved delivery systems based on novel technologies;
	• Engage with public health authorities and NITAGs to better inform vaccine decisions;
	• Advance understanding of the role of novel technology (such as platform technologies) in responding to emerging health threats, in order to ensure appropriate regulatory support and oversight;
	• Harmonise the regulatory framework for vaccine clinical trials, including during emergencies.

Achievements

Background:

- Post-authorisation vaccine monitoring studies are a fundamental source of information to support public health and regulatory decisions with regard to the vaccine use in real-life settings. Approaches for post-authorisation monitoring and assessment of the impact of vaccines and their use in immunisation programmes in the EU has been fragmented in time, efforts, stakeholder

involvement and financing. Need for a sustainable framework at EU-level to quickly initiate observational studies to support decision making by public health and regulatory authorities.

Milestones:

- 2019-2020 - EMA and ECDC request resources for vaccine monitoring platform to SANTE.
- 2020 - EMA and ECDC discuss further funding for COVID-19 vaccine studies with SANTE.
- Nov. 2020 - EC adopts 'Health Union Proposal'- including a mandate for vaccine monitoring platform.
- 26 April 2021 - Kick off meeting which led to a joint declaration of joining forces to enhance post-marketing monitoring od COVID-19 vaccines in Europe (comms item on agencies' websites).
- January 2022: first case study of the VMP: Comparative effectiveness of heterologous and homologous primary- and booster SARS-CoV-2 vaccination schedules in the Nordic countries.
- Following the European Commission initiative on a new health security framework in the form of a European Health Union, based on the experience of dealing with COVID-19, the new extended mandates of the EMA and the ECDC were endorsed in March 2022 and October 2022, respectively.
- "EMA shall coordinate independent monitoring studies on the use, effectiveness and safety of medicinal products intended to treat, prevent or diagnose diseases related to the public health emergency, using relevant data, including, where relevant, data held by public authorities. …coordination as regards vaccines shall be conducted in conjunction with the ECDC, in particular, through a new vaccine monitoring IT platform".
- "The [ECDC] Centre shall coordinate independent post-marketing effectiveness and safety monitoring studies collecting new information and/or using the relevant data collected by competent bodies. That work shall be conducted jointly with the European Medicines Agency and notably through a new vaccine monitoring platform".
- The VMP Steering Group is established during the Kick-off face-to face meeting between the two agencies, which took place in Amsterdam on 16th May 2022.
- October 2022: second case study of the VMP: Effectiveness and safety of monkeypox Vaccination (SEMVAc study).
- October 2022: the Immunisation and Vaccine Monitoring Advisory Board, the VMP advisory board, is established. First meeting will take place in December 2022.
- 2023 and beyond:
  - Studies – number to reflect needs and resources;
  - More IVMAB meetings (tentative date for 2023);
  - Communications items: landing page on both Agencies' websites, press releases to reflect VMP activities, transparency (SG minutes publicly available).

3.4.5. Support the development and implementation of a repurposing framework

Addressing emerging health threats and availability/therapeutic challenges	
Core recommendations	**Underlying actions**
Support the development and implementation of a repurposing framework	• Enhance scientific and regulatory advice on evidence generation and MAA submission;
	• Develop methodological principles for third-party data-pooling, relevant RWD and historical non-clinical datasets;
	• Translate experience with EMA's registry pilot to guide RWD collection;
	• Explore utility of low-intervention clinical trials for evidence generation.

Achievements

- EMA and the Heads of Medicines Agencies (HMA) launched a pilot project to support the repurposing of medicines as a follow-up to the European Commission's Expert Group on Safe and Timely Access to Medicines for Patients (STAMP) discussions.

3.5. Enabling and leveraging research and innovation in regulatory science

3.5.1. Develop network-led partnerships with academic/research centres to undertake research in strategic areas of regulatory science

Enabling and leveraging research and innovation in regulatory science	
Core recommendations	**Underlying actions**
Develop network-led partnerships with academic/research centres to undertake research in strategic areas of regulatory science	• Develop and implement a roadmap that clarifies, where and how partnerships with academia can best contribute to the human and veterinary RSS. This should build on existing networks and consider how best to support academics developing medicines while identifying practical actions that facilitate interaction at strategic, tactical and operational level;
	• Identify, in consultation with research institutions, academia and other relevant stakeholders, fundamental research and associated training/education topics in strategic areas of regulatory science relevant to patients (such as PROs, omics-based diagnostics, epigenetics, drug-device combinations, modelling and simulation, Big Data, and artificial intelligence);
	• Proactively engage with DG Research & Innovation, DG-SANTE, DG CONNECT, the Innovative Health Initiative, the ENVI Agencies and Member State funding agencies to propose and issue calls to establish research collaborations;
	• Further develop research and evaluation of the impact of pharmacovigilance and risk management planning including:

Enabling and leveraging research and innovation in regulatory science	
	– Conduct, results and impact of post authorisation safety studies; – Impact on labelling changes and utility for significant product issues evaluation of periodic safety update reports; – Impact of different types of reports of suspected adverse drug reactions including spontaneously reported non-serious and patient reports in order to optimise detection of new safety issues; – Impact research following major regulatory action where additional risk minimisation measures are introduced. Such research should include both quantitative and qualitative approaches.

Achievements

- Published EMA's Regulatory science research needs in December 2021:
  - Engaged with academia, EFPIA as industry association, national and international funding organisations as well as other external parties (e.g., solution providers) on their potential contribution to delivering on the regulatory science research needs.
- Engaged with DG Research & Innovation, DG-SANTE, DG CONNECT, the Innovative Health Initiative, the 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, including: HORIZON-HLTH-2022-TOOL-11-02 (RWD for regulatory decision-making), HORIZON-HLTH-2022-STAYHLTH-01-04-two-stage (AI, obesity, mental health), HORIZON-HLTH-2022-DISEASE-06-03-two-stage (next generation vaccines), HORIZON-HLTH-2022-TOOL-11-01 (biomarkers for non-cancer authorised medicines), HORIZON-MISS-2022-CANCER-01-03 (pragmatic cancer trials), EU4H-2021-PJ-06 (EHDS2 Pilot use cases), HORIZON-HLTH-2021-DISEASE-04, HORIZON-HLTH-2021-IND-07 (competitive health industry);
  - Published research and evaluation of the impact of pharmacovigilance and risk management planning;
  - Completed study of the experience of the European Medicines Agency from involvement in multi-stakeholder regulatory science research projects based on semi-structured interviews with staff members and project coordinators, submitted for publication.

3.5.2. Leverage collaborations between academia and network scientists to address rapidly emerging regulatory science research questions

Enabling and leveraging research and innovation in regulatory science	
Core recommendations	**Underlying actions**
Leverage collaborations between academia and	• Ring-fence EMA funding to address rapidly emerging regulatory science research questions;

Enabling and leveraging research and innovation in regulatory science	
network scientists to address rapidly emerging regulatory science research questions	• Ensure close interaction between network scientists, academia and learned societies to deliver tangible impact through translation of this applied research into new drug products and regulatory tools;
	• Actively engage, through these applied projects, in training early-career researchers in regulatory science (e.g., via placements within the network);
	• Create a bridging action plan to feed iterative and interactive engagements between these stakeholders as a core strategy of the EMA, National (HMA and EU-IN) and global (ICMRA) regulatory authorities.

Achievements

- Ring-fenced EMA funding to address rapidly emerging regulatory science research questions:
  - Budget of 33 million together with the research tender to identify providers in quality, non-clinical, methodology, clinical and pharmacovigilance;
  - Research providers identified for 5 out of 6 of these areas;
  - 16 studies initiated on this contract basis.
- Published EMA's Regulatory science research needs see 3.5.1.

3.5.3. Identify and enable access to the best expertise across Europe and internationally

Enabling and leveraging research and innovation in regulatory science	
Core recommendations	**Underlying actions**
Identify and enable access to the best expertise across Europe and internationally	• Explore the creation of a 'shared environment' in which novel insights and experiences are shared among all stakeholders, including innovator and generic (complex) drug manufacturers, regulatory bodies and academia;
	• For rare diseases, foster collaboration with European Reference Networks and propose a collaboration plan that includes definition of necessary resourcing and objectives;
	• Propose a framework that allows for adequate identification and involvement of independent experts and ensures a rigorous conflicts of interest policy;
	• Develop a knowledge management system to track innovation, share information, enable linkages and create new insights across the product lifecycle.

Achievements

- Developing Topic Relationships Identification Proposition (TRIP) as a knowledge management system to track innovation, share information, enable linkages and create new insights across the product lifecycle:
  - This product is currently prioritised for delivery in 2023 under the new agile methodology. Epic hypothesis was presented and signed off at Portfolio Board in 4th quarter 2022.
- Launch and operation of the Collaborating Expert programme:
  - Actively engage, through these applied projects, in training early-career researchers in regulatory science;
  - So far 29 collaborating experts have contributed to regulatory science projects across the Agency (21 in 2021, 8 so far in 2022).
- Mapping NCA expertise (qualitative and quantitative) using the EMA expert database and developing a heat map:
  - Remodelled working parties and European Special Expert Communities (ESECs) through 2021 and 2022;
  - Mapping EU Reg Network expertise within the Innovation Offices.

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

Enabling and leveraging research and innovation in regulatory science	
Core recommendations	**Underlying actions**
Disseminate and exchange knowledge, expertise and innovation across the network and to its stakeholders	• Engage with academia to develop regulatory training modules, including describing innovation of new medicines and their progression from laboratory to patient;
	• Collaborate with the EMRN to: – Identify gaps in training and learning objectives; – Work with academic institutions to build and provide regulatory training modules or courses;
	• Conduct horizon scanning in key areas of innovation via collaborations with academia, the EU-Innovation Network and ICMRA;
	• Drive a data-sharing culture to foster open science which is mutually beneficial for all stakeholders.

Achievements

- EU NTC Learning Ecosystem roadmap and approach for an updated service model and related technology ecosystem adopted by EXB in July 2021.
- EU NTC Strategy 2022-2025 endorsed by HMA in November 2021.
- Surveys to 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 provided 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 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 EATRIS;
  - EMA/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.
- Established EMA horizon scanning as a systematic activity and delivered several published or internal reports on topics of high regulatory interest via engagement with external horizon scanning initiatives (ICMRA, EU-IN, IHSI, WHO, JRC):
  - Horizon Scanning published reports on Artificial Intelligence and on Genome Editing, as Rapporteur and in collaboration with ICMRA and EU-IN, respectively (journal publications: https://doi.org/ 10.1038/d41573-021-00130-7 and https://doi.org/10.1038/d41573-022-00190-3), and supports implementing the recommendations in policy and practice;
  - A report assessing international horizon scanning signals from JRC and WHO, published under https://doi.org/10.3389/fmed.2022.1064003;
  - Identification of new technologies via HS, ITF and scientific advice activities.

4. Achievements for Veterinary Strategy

4.1. Catalysing the integration of science and technology in medicines development

4.1.1. Reinforce and further embed application of the 3Rs principles

Catalysing the integration of science and technology in medicines development	
Core recommendations	**Underlying actions**
Reinforce and further embed application of the 3Rs principles	• Apply the highest possible 3Rs standards when implementing the new veterinary regulation as well as other legislative documents/guidelines to stimulate developers to use novel approaches adhering to 3Rs standards;
	• Strengthen cooperation between all stakeholders and international partners: – Cooperate with other EU agencies/bodies to fund research and (access to) standardised repositories for alternative methods and models;
	• Promote in silico methodology (e.g. modelling), novel in vitro assays and systematic reviews to reduce animal use, particularly in toxicology/epidemiology and batch control: – Re-focus the role of the Joint 3Rs working group (J3R WG) to support qualification of new alternative 3R-compliant method/models including in silico and novel in vitro assays; – Development of clear guidance to encourage and prioritise the use of NAMs that can be used to fulfil testing requirements in lieu of traditional animal tests and that take the 3Rs into serious consideration;
	• Promote regulatory acceptance and training.

Achievements

- Innovation Task Force support for 3R methodologies:
  - In September 2021, EMA opened up its Innovation Task Force (ITF) to the discussion of methodologies that minimise animal testing during medicines development.
- The joint human and vet 3RsWP has now been set and restarted.

4.1.2. Facilitate implementation of novel manufacturing models

Frida Hasslung Wikström
Chair of SAWPv

"Veterinary medicines are leading development in areas of public and animal health, such as the reduction of antimicrobial use.

The generation of guidance for novel manufacturing methods like the multi-strain dossiers for inactivated veterinary vaccines or bacteriophages should further enhance such leadership."

Catalysing the integration of science and technology in medicines development	
Core recommendations	**Underlying actions**
Facilitate implementation of novel manufacturing models	• Recruit and develop expertise, in novel manufacturing technologies and develop training and tools to enhance the assessment process;
	• Identify bottlenecks and propose modernisation of relevant regulations and guidance to facilitate novel manufacturing models, and novel approaches to traditional manufacturing. This should include guidance on strengthened early interaction, transparency and communication with stakeholders on regulatory requirements for novel manufacturing technologies;
	• Address regulatory challenges in point-of-care manufacturing such as responsibility for the manufacturing process, the concept of batch control, and the role of the Qualified Person;
	• Encourage the use of risk-based approaches to manufacturing processes and control strategies throughout the product lifecycle;
	• Facilitate a flexible and fit for purpose approach in application of Good Manufacturing Practice with respect to novel therapies;
	• Support the development of greener manufacturing technologies in line with the EU's 'Strategic Approach to Pharmaceuticals in the Environment'.

Achievements

- A comprehensive review of Annex 4 of the GMP Guide manufacture of veterinary medicinal products other than immunologicals has started and a concept paper was published for stakeholder consultation in October 2021.
- Similarly, a comprehensive review of Annex 5 of the GMP Guide manufacture of veterinary immunological medicinal products has started and a concept paper was published for stakeholder consultation in October 2021. Both updates include extending the underlying GMP concepts to include new areas of technology (e.g. novel therapy products), new processing methods, new products not previously covered.

- 2 GMP guidelines have been published by the European Commission during 2022:
  - Annex 1 – Manufacture of Sterile products;
  - Annex 21 – Importation of Medicinal products.
- Q&A's on GMP for Veterinary medicines were published by EMA during 2022.
- GMDP IWG regularly participating in ITF meetings on manufacturing related topics.

4.2. Driving collaborative evidence generation - improving the scientific quality of evaluations

4.2.1. Update Environmental Risk Assessments in line with the latest scientific knowledge

Driving collaborative evidence generation - improving the scientific quality of evaluations	
Core recommendations	**Underlying actions**
Update Environmental Risk Assessments in line with the latest scientific knowledge	• Contribute to the evaluation of novel approaches to ERA, and the EC considerations on the feasibility of establishing active substance monographs for all substances, including legacy active substances of which there is limited environmental information, providing input as required;
	• Develop further guidance on when the use of persistent, bioaccumulative and toxic substances in animals can be justified;
	• Develop additional guidance on the ERA of active substances used in aquaculture, including use of antimicrobials under the 'prescribing cascade';
	• Cooperate with DG RTD to fund ERA-related research relevant to veterinary medicines, such as antimicrobial and antiparasitics resistance in the environment, and environmental effects of endocrine disruptors and contaminants (e.g. metals that co-select for antimicrobial resistance);
	• Provide scientific support to the European Commission and the EU network to ensure that a "One Health" approach is applied to ERA;
	• Increase cooperation in the field of ERA with European agencies, particularly ECHA, EFSA and with EEA, and establish cooperation with international institutions, academic organisations and relevant initiatives;
	• Strengthen capacity and capability to evaluate the environmental fate and effects of novel veterinary therapies, and to apply ERA to combinations of substances.

Achievements

- A number of guidelines has been produced during the last months:
  - Publication of Reflection paper on antimicrobial resistance in the environment: considerations for current and future risk assessment of veterinary medicinal products;

- Publication of criteria for determining that an active substance is essential when considered in the context of Article 37(2)(j) of Regulation 2019/6;
- Publication of interpretation of Article 72 of Regulation (EU) 2019/6;
- Publication of higher tier testing to investigate the effects of parasiticidal veterinary medicinal products on dung fauna;
- Publication of interpretation of Article 18(7) of Regulation (EU) 2019/6.

4.2.2. Apply the latest scientific principles to the assessment of the safety of residues of veterinary medicines

Driving collaborative evidence generation - improving the scientific quality of evaluations	
Core recommendations	**Underlying actions**
Apply the latest scientific principles to the assessment of the safety of residues of veterinary medicines	• Develop methodology to evaluate the consumer safety of biologically active substances for use in veterinary medicines for food producing animals;
	• Engage with EU and international risk assessment bodies with a view to aligning methodology for estimating consumer exposure to residues, including dual-use substances;
	• Engage with the EC's Directorate General Research and Innovation (DG RTD), other bodies and EU agencies to fund research relating to safety of residues;
	• Work to increase capability in modelling, simulation and extrapolation (with applications in toxicological assessment, dose optimisation, environmental fate and residue depletion), for example, by seeking out and developing relevant training materials;
	• Maintain awareness of developments in scientific thinking on cumulative or combined exposure to chemicals and reflect on relevance for the evaluation of safety of residues.

Achievements

- Publications:
  - Guideline on safety and residue data requirements for applications for non-immunological veterinary medicinal products intended for limited markets submitted under Article 23 of the Regulation (EU) 2019/6;
  - Concept paper for the revision of residues guidelines to align with the definitions for withdrawal periods provided in Regulation (EU) 2019/6;
  - Concept paper on the development of a guideline on determination of the need for an MRL evaluation for biological substances.

- Protecting consumers:

  In 2021, positive opinions were adopted recommending the establishment of MRLs for the following active substances:

  - Bambermycin in poultry tissues;
  - Toltrazuril in poultry eggs.

4.2.3. Develop new and improved communication and engagement channels and methods to reach out to stakeholders

Laetitia Le Letty
Chair of CMDv

"The recent implementation of the Veterinary Regulation 2019/6 required enhanced communication with stakeholders to discuss and explain its impact in many aspects of the authorisation of veterinary medicinal products.

New online technologies have greatly contributed to ensuring frequent meetings of the regulatory network with stakeholders during recent exceptional times and will be used in the future."

Driving collaborative evidence generation - improving the scientific quality of evaluations	
Core recommendations	**Underlying actions**
Develop new and improved communication and engagement channels and methods to reach out to stakeholders	• Address the need for improvement in product information content, including package leaflet layout and readability;
	• Promote electronic formats of veterinary medicinal product information (veterinary ePI) that is readily and easily accessible and can be updated rapidly, making best use of new and digital technologies;
	• Address the matter of under-reporting in veterinary pharmacovigilance using new communication tools and channels;
	• Clearly inform the public of the scientific underpinning of new veterinary medicines and technologies, such as biological products including DNA vaccines or gene therapy;
	• Ensure authoritative communication on key issues, particularly on issues where stakeholder concerns could be helped by better information;
	• Promote better engagement with all stakeholders, especially those impacted by the CVMP opinions, i.e. animal owners.

Achievements

- Development and implementation of new communication tools, such as "CVMP highlights", specific veterinary infographics, social media activities to promote initiatives and events, especially on LinkedIn, as well as other website updates to streamline information related to veterinary medicines.
- Development of a dedicated veterinary stakeholder newsletter with more than 500 contacts, focusing on the implementation of the new legislation.

- More systematic involvement of veterinary stakeholders in multi-stakeholder engagement activities on the Agency's key priorities such as shortages, antimicrobial resistance, 3Rs, etc.
- Development and implementation of a strategic plan for veterinary stakeholder engagement. Consequently, more activities (trainings, webinars and meetings) are ongoing, such as the Big Data Veterinary Stakeholder Forum, which aims to raise awareness on the use of innovative digital technologies in the veterinary regulatory environment.

4.3. Addressing emerging health threats and availability/therapeutic challenges

4.3.1. Continue to promote the responsible use of antimicrobials and their alternatives

Addressing emerging health threats and availability/therapeutic challenges	
Core recommendations	**Underlying actions**
Continue to promote the responsible use of antimicrobials and their alternatives	• Work in partnership with EC, other EU Agencies and regulators and international bodies to promote the responsible use of antimicrobials and their alternatives;
	• Enhance the promotion of the responsible use of antimicrobials via updated and/or new regulatory guidance and scientific opinion;
	• Develop a regulatory approach/framework to promote alternatives to conventional antimicrobials and novel paradigms;
	• Explore the possibility of new funding models to generate data to support existing authorised products and to incentivise new product development;
	• Provide scientific and regulatory support to encourage development of veterinary antimicrobials and alternatives, to fill therapeutic gaps, without adversely impacting public health;
	• Foster development of rapid pen-side diagnostics to support responsible use.

Achievements

- EMA’s committee for veterinary medicines (CVMP) adopted a strategy on antimicrobials for 2021-2025;
- Published guidelines:
  - Guideline on the summary of product characteristics (SPC) for veterinary medicinal products containing antimicrobial substances;
  - Reflection paper on promoting the authorisation of alternatives to antimicrobial veterinary medicinal products in the EU;
  - Reflection paper on the use of aminopenicillins and their beta-lactamase inhibitor combinations in animals in the European Union: development of resistance and impact on human and animal health;

  - Concept paper for the development of a guideline on quality, safety and efficacy of veterinary medicinal products specifically designed for phage therapy published for public consultation; the guideline is expected in 2023.

- Advice to the Commission delivered on:
  - Criteria to designate antimicrobials as reserved for treatment of certain conditions in human;
  - A list of antimicrobials to be reserved for treatment of certain conditions in humans.
- Advice to the Commission under development by end 2022:
  - A list of antimicrobials which shall not be used under Articles 112-114 or which may be used under these Articles subject to certain conditions.
- Information sheet on the AMEG categorisation of antimicrobials in support of responsible use in veterinary medicine has been published in 23 official languages of the EU.
- EMA/FVE webinar on the AMEG categorisation delivered and available on YouTube.
- A draft reflection paper on the prophylactic use of antimicrobials in animals was published for public consultation.

4.3.2. Coordinate network activities to improve data collection on antimicrobial use in animals

Addressing emerging health threats and availability/therapeutic challenges	
Core recommendations	**Underlying actions**
Coordinate network activities to improve data collection on antimicrobial use in animals	• Define requirements for harmonised sales and use data collection for antimicrobial medicinal products used in animals;
	• Adjust the methodology for analysis of antimicrobial data, by considering approaches developed internationally;
	• Develop methodology to collate, analyse and communicate data on antimicrobial use per species;
	• Inform policy decisions via enhanced cooperation with European institutions (EFSA, ECDC) to collate data on antimicrobial use with information on AMR in animals, humans and food;
	• Participate in international initiatives to reduce the risk of AMR.

Achievements

- Annual reports on sales of veterinary antimicrobials continue to be published, with the report in 2021 covering 2 years (2019 and 2020) in preparation of meeting the requirements of Regulation (EU) 2019/6.
- Joint inter-agency antimicrobial consumption and resistance analysis (JIACRA) report:
  - 3rd report published in June 2021;
  - 4th report under preparation; expected by end 2023.
- Advices to the Commission published on:

- Requirements for the collection of data on antimicrobials used in animals in preparation of Commission Delegated Regulation (EU) 2021/578 of 29 January 2021 supplementing Regulation (EU) 2019/6 of the European Parliament and of the Council with regard to requirements for the collection of data on the volume of sales and on the use of antimicrobial medicinal products in animals;
- Format for the collection of data on antimicrobials used in animals in preparation of Commission Implementing Regulation (EU) 2022/209 of 16 February 2022 establishing the format of the data to be collected and reported in order to determine the volume of sales and the use of antimicrobial medicinal products in animals in accordance with Regulation (EU) 2019/6 of the European Parliament and of the Council Antimicrobial use data reporting per animal categories (numerator);
- Manual for reporting the data to the Agency Antimicrobial Sales and Use data base and data collection system under development.

- Establishment of technical estimates in preparation of the JIACRA III report Relevant collaborating experts projects completed.
- Contribution to TATFAR 2016-2020 progress report.
- Contribution to development of TATFAR work plan 2021-2026, lead of action number 1.1 1. Contributions to the TATFAR campaign during World Antimicrobial Awareness Week in November, and other global initiatives to combat antibiotic resistance, such as the Transatlantic Taskforce on Antimicrobial Resistance (TATFAR).
- To mark European Antibiotic Awareness Day in 2021, EMA launched a social media campaign to highlight the importance of using antibiotics prudently and participated in events organised by ECDC Keynote presentation on Responsible use of antibiotics in the context of European policy at the 5th international conference on Responsible Use of Antibiotics in Animals - 7-9 June 2021.

4.3.3. Engage with stakeholders to minimise the risks of antiparasitic resistance

Addressing emerging health threats and availability/therapeutic challenges	
Core recommendations	**Underlying actions**
Engage with stakeholders to minimise the risks of antiparasitic resistance	• Cooperate with other EU agencies / bodies on initiatives concerning antiparasitic resistance, e.g. the EC's Directorate General – Research and Innovation (DG RTD) on research into reliable tests to detect or measure resistance, or monitoring of antiparasitic use or resistance in food-producing species and non-food producing animals;
	• Participate actively in international initiatives that aim to develop strategies to combat antiparasitic resistance and to establish best practices on the use of veterinary antiparasitic medicines;
	• Promote responsible use of antiparasitics in the EU.

Achievements

- Publications by EWP-V:

- Revised guideline on the summary of product characteristics for antiparasitic veterinary medicinal products published in December 2021;
- Guideline on data requirements for veterinary medicinal products intended to reduce the risk of transmission of vector-borne pathogens in dogs and cats;
- Contributions to the revision of 9 VICH guidelines on efficacy of anthelmintics.

- Webinars conducted by EWP-V:
  - Training on the 'Guideline on the summary of product characteristics for antiparasitic veterinary medicinal products' (prudent use warnings).
- New EMA project started regarding the screening for future antiparasitic veterinary medicines to identify gaps in regard to medicines availability and guidance for future dossier (collaborating expert project initiated).
- Contribution to OIE / WOAH activities relating to guidance regarding prudent use of antiparasitic veterinary medicines: Responsible and prudent use of anthelmintic chemicals to help control anthelmintic resistance in grazing livestock species.

4.3.4. Promote and support development of veterinary vaccines

Addressing emerging health threats and availability/therapeutic challenges	
Core recommendations	**Underlying actions**
Promote and support development of veterinary vaccines	• Interact collaboratively with industry and other stakeholders to focus development on areas where vaccines are most needed;
	• Acknowledge that different benefit-risk approaches are required for assessment of specific vaccine types (e.g. vaccines for zoonotic diseases, limited markets, exceptional circumstances);
	• Develop a regulatory framework for authorisation, under exceptional circumstances, of vaccines for emerging health threats and benefit-risk monitoring post-approval;
	• Clarify when field efficacy trials to support marketing authorisation applications for new vaccines could be omitted;
	• Explore feasibility of establishing a framework for using epidemiological modelling data to support the demonstration of vaccine efficacy;
	• Develop appropriate and proportionate guidance to maximise opportunities offered by Regulation (EU) 2019/6 for promoting availability of vaccines (vaccine antigen master files, vaccine platform technology master files and multi-strain dossiers);
	• Advance understanding of the science behind novel technologies to ensure appropriate regulatory oversight and foster ability to exploit added value of new technologies.

Achievements

- Publications:

- Guideline on efficacy and target animal safety data requirements for applications for non-immunological veterinary medicinal products intended for limited markets submitted under Article 23 of the Regulation (EU) 2019/6;
- Guideline on clinical trials with immunological veterinary medicinal products;
- Guideline on data requirements for authorisation of immunological veterinary medicinal products under exceptional circumstances;
- Guideline on data requirements for applications for immunological veterinary medicinal products intended for limited markets submitted under Article 23 of the Regulation (EU) 2019/6.

4.4. Enabling and leveraging research and innovation in regulatory science

4.4.1. Develop network-led partnerships with academic/research centres to undertake research in strategic areas of regulatory science

Enabling and leveraging research and innovation in regulatory science	
Core recommendations	**Underlying actions**
Develop network-led partnerships with academic/research centres to undertake research in strategic areas of regulatory science	• Develop and implement a roadmap that clarifies where and how partnerships with academia can best contribute to the human and veterinary RSS. This should build on existing networks and consider how best to support academics developing medicines while identifying practical actions that facilitate interaction at strategic, tactical and operational level;
	• Identify, in consultation with research institutions, academia and other relevant stakeholders, fundamental research and associated training/education topics in strategic areas of regulatory science;
	• Proactively engage with DG Research & Innovation, DG-SANTE, the Innovative Health Initiative, the ENVI Agencies and Member State funding agencies to propose and issue calls to establish research collaborations;
	• Evaluate the conduct, results and impact of imposed and voluntary post authorisation safety studies;
	• Systematically conduct impact research following major regulatory action where additional risk minimisation measures are introduced. Such research should include both quantitative and qualitative approaches.

Achievements

- Publication of EMA's Regulatory Science Research Needs (RSRN).
- Systematic engagement with research funders across Europe and including DG RTD and IHI.
- Completion of a study of the experience of the European Medicines Agency 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.

4.4.2. Leverage collaborations between academia and network scientists to address rapidly emerging regulatory science research questions

Enabling and leveraging research and innovation in regulatory science	
Core recommendations	**Underlying actions**
Leverage collaborations between academia and network scientists to address rapidly emerging regulatory science research questions	• Ring-fence EMA funding to address rapidly emerging regulatory science research questions;
	• Ensure close interaction between network scientists, academia and learned societies to deliver tangible impact through translation of this applied research into new drug products and regulatory tools;
	• Actively engage, through these applied projects, in training early-career researchers in regulatory science (e.g., via placements within the network);
	• Create a bridging action plan to feed iterative and interactive engagements between these stakeholders as a core strategy of the EMA, National (HMA and EU-IN) and global (ICMRA) regulatory authorities.

Achievements

- Publication of EMA's Regulatory Science Research Needs (RSRN) to ensure interaction between network scientists, academia and learned societies.

4.4.3. Identify and enable access to the best expertise across Europe and internationally

Enabling and leveraging research and innovation in regulatory science	
Core recommendations	**Underlying actions**
Identify and enable access to the best expertise across Europe and internationally	• Explore the creation of a 'shared environment' in which novel insights and experiences are shared among all stakeholders, including innovator and generic (complex) drug manufacturers, regulatory bodies and academia;
	• Propose a framework that allows for adequate identification and involvement of independent experts and ensures a rigorous conflicts of interest policy;
	• Develop a knowledge management system to track innovation, share information, enable linkages and create new insights across the product lifecycle.

Achievements

- Launched the Collaborating Expert Scheme to facilitate involvement of independent experts.

- Developing an early innovation knowledge management system: TRIP.

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

Enabling and leveraging research and innovation in regulatory science	
Core recommendations	**Underlying actions**
Disseminate and exchange knowledge, expertise and innovation across the network and to its stakeholders	• Engage with academia to develop regulatory training modules, including describing innovation of new medicines and their progression from laboratory to patient;
	• Collaborate with the EMRN to: – Identify gaps in training and learning objectives; – Work with academic institutions to build and provide regulatory training modules or courses;
	• Conduct horizon scanning in key areas of innovation via collaborations with academia, the EU-Innovation Network and ICMRA;
	• Drive a data-sharing culture to foster open science which is mutually beneficial for all stakeholders.

Achievements

- Horizon scanning reports in areas related to veterinary medicine: AMR which will be published early in 2023.
- Publication of a signal report: Health horizons: Future trends and technologies from the European Medicines Agency's horizon scanning collaborations.

Conclusion and next steps

As outlined in the introduction this report set out to provide an overview of main achievements, from March 2020 to December 2022 structured along the strategic goals presented in the original RSS to 2025 strategy as they apply to both human and veterinary areas.

It is a challenging compilation exercise in itself in view of the various delivery workstreams that were established to enable its implementation primarily the multiannual work programme of the EMA and its various Committees and working parties and a strong interconnection with the wider EMRN strategy to 2025.

Upon establishing the RSS to 2025 concerns were raised by stakeholders as to whether the Agency and the network had sufficient resources with which to deliver it and this was even before the COVID-19 pandemic impacted the system. What is remarkable about this report is to reflect on what has actually been achieved during this immensely challenging period for the European Regulatory Network and how far the strategic goals and underlying recommendations have been progressed. Far from blocking such progress COVID-19 appears to have acted as a catalyst for change in the European system enabling these parallel developments to take place.

Despite this notable progress the work must and does continue at pace through 2023-2025 to deliver the strategic goals to their fullest potential. As 2023 marks the third year of the COVID-19 pandemic, EMA will gradually lift its business continuity status and will refocus its efforts to address the strategic goals set out in the RSS to 2025 to an even greater extent throughout the remaining 2023-2025 period.

It is considered essential to succeed in this objective to further evolve the networks operational capability now building on a strong investment in regulatory science and preparing to further adapt to and benefit from the legislative changes foreseen in the following years.

List of acronyms

ACE - EMA's Analytics Centre of Excellence

AI - Artificial Intelligence

AMR - Antimicrobial Resistance

ATMP - Advanced Therapy Medicinal Product

BR - Benefit-risk

CODEX - Codex Alimentarius

CQA - Critical Quality Attribute

CVMP - Committee for Veterinary Medicinal Products (EMA)

DigiLab - EMA's Digital Innovation Lab

DG RTD - European Commission Directorate General for Research and Innovation

DG AGRI - European Commission Directorate General for Agriculture and Rural Development

DG JRC - European Commission Directorate General Joint Research Centre

DG SANTE - European Commission Directorate General for Health and Food Safety

EC - European Commission

ECHA - European Chemicals Agency

EEA - European Economic Area

EFSA - European Food Safety Authority

EMA - European Medicines Agency

EMRN - European Medicines Regulatory Network, the EU network

ePI - electronic Product Information

ERA - Environmental Risk Assessment

ETF – EMA Pandemic Task Force

FDA - Food and Drug Administration (USA)

FIM - First-In-Man

GCP - Good Clinical Practice

GMP - Good Manufacturing Practice

HMA - Heads of Medicine Agencies

HTA - Health Technology Assessment body

ICDRA - International Coalition of Drug Regulatory Authorities

ICH - International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use

ICMRA - International Coalition of Medicines Regulatory Authorities

IMI - Innovative Medicines Initiative

iSPOC – Industry Single Points of Contract

IVDR - EU In Vitro Diagnostic Regulation (2017/746)

JEFCA - Joint FAO/WHO Expert Committee on Food Additives

MAA - Marketing Authorisation Application

MDR - EU Medical Device Regulation (2017/745)

MRL - Maximum Residue Limit

MSSG – Executive Steering Group on Shortages Safety and Medicinal Products

NAMs - New Approach Methodologies

NITAG - National Immunisation Technical Advisory Group

OECD - Organisation for Economic Co-operation and Development

OIE - World Organisation for Animal Health

PI - Product Information

PIC/S - Pharmaceutical Inspection Collaboration Scheme

PK/PD - Pharmacokinetics/Pharmacodynamics

PMDA - Pharmaceuticals and Medical Devices Agency (Japan)

PRIME - Priority Medicines Scheme

PRO - Patient-Reported Outcome

PROM - Patient-Reported Outcome Measure

RWD - Real World Data

SciCoBo - Scientific Coordination Board

SEND - Standard for Exchange of Nonclinical Data

SME - Small or Medium-sized Enterprise

SPOC – Single Points of Contact

STAMP - Commission Group on Safe and Timely Access to Medicines for Patients

VICH - Veterinary International Conference on Harmonization

WHO - World Health Organization