EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMA perspectives on international convergence and collaboration for CMC submissions

CASSS CMC strategy forum

Presented by Klara Tiitso on 18 October 2023
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EMA in the global environment

All Divisions/Departments are concerned and the exchange of information with international regulatory authorities is **part of EMA's daily work**.

International collaboration is **key** to:

- **Facilitate alignment** of regulatory approaches between international authorities
- **Speed up patient access** to new and/or affordable medicines
- **Avoid duplication** of work
- **Release scarce resources** for more critical areas
- **Support regulators** outside the EU who may lack resources and/or specific competence

Mechanisms for international collaboration

Bilateral relations

Argentina, Australia, Brazil, Canada, Chile, China, Colombia, Dominican Republic, Israel, Japan, New Zealand, Peru, Republic of Korea, Saudi Arabia, Singapore, South Africa, Switzerland, Taiwan, United Kingdom, United States of America, EDQM, WHO

International Liaison Officers

Confidentiality Arrangements (CA)

Ad Hoc CA

Mutual Recognition Agreements (MRA)

Multilateral relations

ICH harmonisation for better health

OPEN

PIC/S

IPA project

ICMRA

EU-M4all

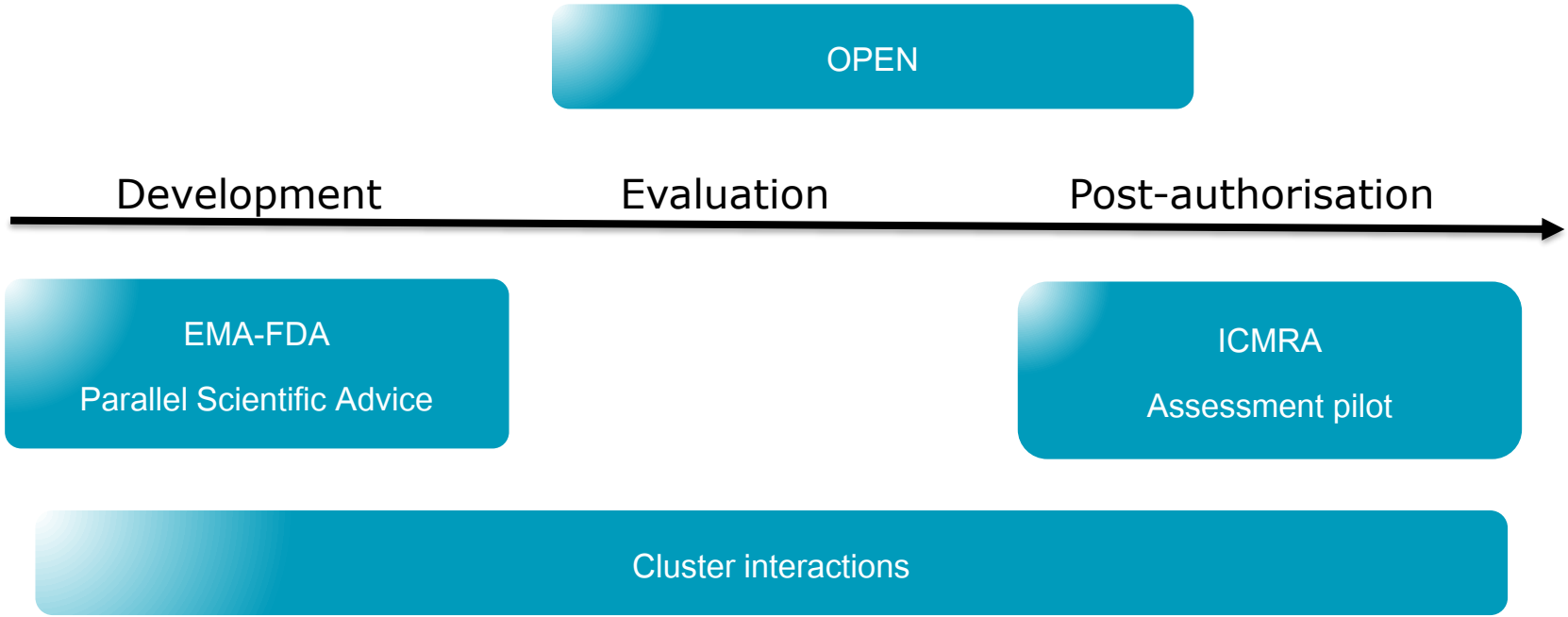
IPRP International Pharmaceutical Regulators Programme

SRA CRP

AMA project

VICH International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products

Opportunities for collaborative assessment



What is EMA-FDA parallel scientific advice (PSA)?

A mechanism where EMA and FDA concurrently exchange their views on scientific issues with the sponsor

- Opportunity for engagement with both regulatory agencies
- Avoid duplication of work
- '*Both agencies will strive to provide PSA responses that are convergent*' *(PSA General Principles)*
- Common approach where feasible or better understanding of the reasons for potentially remaining divergences

Conducted under Confidentiality Agreements

Scope of PSA

PSA is a useful and efficient way to align complex global development programmes

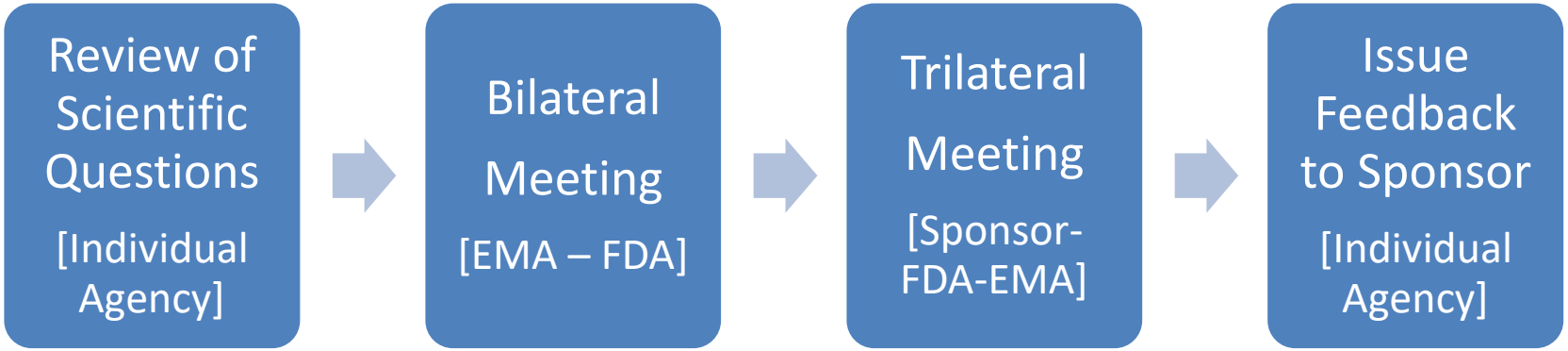
- Innovative products
- Areas with lacking/diverging regulatory guidance
- Products targeting challenging populations
- Products with significant clinical safety, animal toxicology, or unique manufacturing concerns

Scientific advice can be provided on **any scientific question**

Encouraged in areas of innovation, e.g. advanced manufacturing, ATMPs

~70% of PSA requests accepted

PSA - Overview of collaboration



Overall process aligned with CHMP Scientific Advice (SA) procedure (70-day timeline) and timeline for Type B Meeting at FDA

PSA - More information/contact

A single “Request for PSA” letter sent to both FDA and EMA

- Email: emainternational@ema.europa.eu
- Email: US-FDA-EUR@fda.hhs.gov

PSA General Principles

https://www.ema.europa.eu/en/documents/other/general-principles-european-medicines-agency-food-drug-administration-parallel-scientific-advice_en.pdf

Opening our **P**rocedures at **E**MA to **N**on-EU authorities

OPEN is **an international collaboration framework** of near-concurrent review among international regulators.

OPEN Pilot (December 2020 – May 2023)

Goal: Sharing scientific expertise to tackle common challenges on COVID-19 vaccines and therapeutics

Approach: Participating non-EU experts invited to **attend and contribute** to **ETF and CHMP evaluation**

OPEN experts follow **similar requirements** as the EU experts *(e.g., confidentiality, absence of conflict of interests).*

OPEN regulators

EMA, Health Canada, Swissmedic, TGA, MHLW/PMDA, WHO

All participating under the terms of their Confidentiality Arrangement with the EU.

OPEN products

All the COVID-19 vaccines and therapeutics evaluated since the launch of the pilot.

Implementation:

- **EMA conducted a full review** of applications but shared and discussed assessments in real-time with OPEN experts
- OPEN experts **participated actively** in Emergency Task Force (ETF) and CHMP meetings
- OPEN experts **exchanged comments and reviews** with EMA product leads and assessment teams.
- All Regulators kept full scientific and regulatory **independence.**

Scope for extension of OPEN

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Expand to identified areas

1. **Antimicrobial resistance** (AMR) *global threat where progress requires a collective effort for human and veterinary products*
2. Priority medicines designated under the **PRIME scheme (temporarily not including ATMPs products)** and products which **address high unmet need** (e.g. RSV, Alzheimer, ALS)
3. Medicinal products responding to health threats or **public health emergencies**

Consolidate the pilot's operation

- Engaged with all OPEN partners to:
  - **Define terms of reference that promote RECIPROCITY and more active** participation
  - Increase the initiative **visibility** with more **systematic and coordinated communication** by all OPEN participants

OPEN framework – High level process

OPEN regulators

Selection criteria for OPEN products

- CHMP and min. 1 OPEN partner interested in collaboration
- Alignment of dossier content/claimed indication, submission date

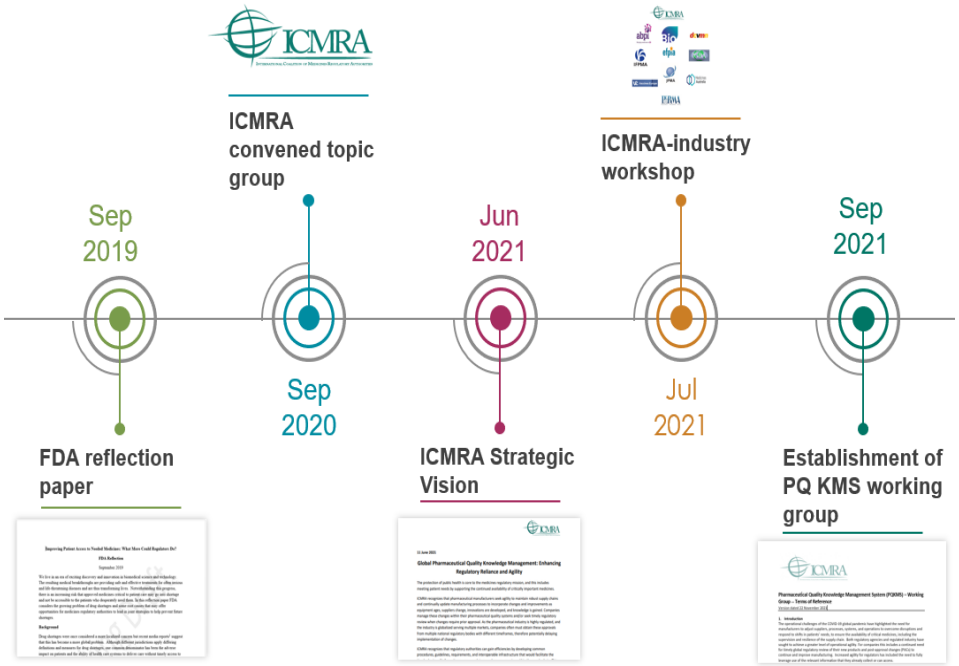
Principles/procedure

- Early Selection of OPEN products (allowing OPEN partners to discuss timing of submissions with their applicants)
- OPEN experts invited to comment during the CHMP evaluation as any other EU Member State
- OPEN experts participate in ETF (when applicable) and CHMP meetings
- OPEN experts are not contributing to CHMP conclusions during the final benefit-risk decision

Expected benefits for industry and global health

- Alignment of dossiers to improve regulatory convergence within OPEN partner countries
- Potential faster overall global approval through leveraging existing or ongoing assessments and expertise beyond the EU regulatory network (e.g. fewer questions for industry)
- Potential to align also the post-approval lifecycle management for major changes and/or also using reliance mechanism
- Promoting capacity optimisation and convergence of assessment standards
- Possibility to engage with EMA in a discussion to harmonise global standards of submissions

The ICMRA Pharmaceutical Quality Knowledge Management System (PQKMS) project



Aims of the PQKMS strategy:

- Transitioning to harmonised structured and standardised electronic formats using unique facility identifiers.
- Sharing of information about manufacturing facilities, among multiple regulators.
- Developing a framework that can support harmonisation of data requirements and facilitate management of PACs.
- Enabling more mutual reliance among regulators.

PQKMS working group - achievements to date

Commencement of two pilot programmes

PQKMS Collaborative Pilot Information and Application Forms

Following the July 2021 ICMRA-Industry virtual workshop on enabling manufacturing capacity in the COVID-19 pandemic, ICMRA is commencing two pilot programs focusing on i) collaborative assessment with initial focus on chemistry, manufacturing, and control (CMC) post-approval changes and ii) collaborative hybrid inspections. The overall aim of these pilots is to improve manufacturing capacity for production of critical medicines and facilitate collaborative assessments and inspections by multiple regulatory authorities (see links for further information).

Call for Applications to PQ Pilots

Application Form for Collaborative Assessment

Application Form for Collaborative Hybrid Inspection

Overview of Collaborative Assessment

Overall Plan for Collaborative Assessment

Overview of Hybrid Inspection

Overall Plan for Hybrid Inspection

Publication of a joint Reflection Paper

Version Dated: 21 July 2022

A Regulatory Pharmaceutical Quality Knowledge Management System (PQ KMS) to Enhance the Availability of Quality Medicines

ICMRA-ICH-PIC/S-IPRP Joint Reflection Paper

Background and Rationale

Changes to pharmaceutical manufacturing processes, technological innovations, and altered supply chains are just some examples of the many issues requiring operational agility that affect the availability of medicines required to meet patient needs. Whether pursuing continuing improvement in manufacturing a novel therapeutic based on post approval experience, or routine updates to operations, equipment, suppliers, and other post approval changes (PACs) later in a product life cycle, manufacturers are expected to proactively manage pharmaceutical quality using existing frameworks outlined in the internationally harmonized guidelines. Specifically, this includes ICH Q10 Pharmaceutical Quality System[1], building on the guidance in ICH Q8 Pharmaceutical Development[2], while applying the principles in ICH Q9 Quality Risk Management[3], and utilizing the enablers and tools outlined in the ICH Q12 guideline on Lifecycle Management[4].

While companies manage these PACs within their pharmaceutical quality systems (PQS), the current operating environment requires prior approval by the regulatory authority of each region and country individually. For a product to be globally available to patients, this can translate to numerous and often duplicative regulatory review processes and time frames. This presents regulatory complexity that can significantly constrain manufacturer agility in addressing

Aim of the ICMRA Collaborative Assessment Pilot

- Provide a platform for multiple regulatory agencies to participate in a **collaborative assessment of post-approval CMC changes** including post-approval change management protocols (PACMPs)
- Deliver a **single list of questions** to the applicant wherever possible, and **identify** misalignments, differences, and potential **areas for further convergence** or harmonisation across regions
- Regulators to work towards a **common approach** to the application assessment and decision making
- Develop **best practices** in the quality assessment of CMC post-approval changes and share learnings to build further collaborations in assessment

Collaborative Assessment Pilot – Status update

- ✓ Call to industry is open since June 2022 → 14 proposals submitted
- ✓ One procedure completed: EMA lead, FDA participating authority, PMDA observer
- ✓ Two procedures ongoing: FDA lead
- ✓ Two further procedures accepted for the pilot (October/November 2023 submissions)

Collaborative Assessment Pilot – observations from first pilot

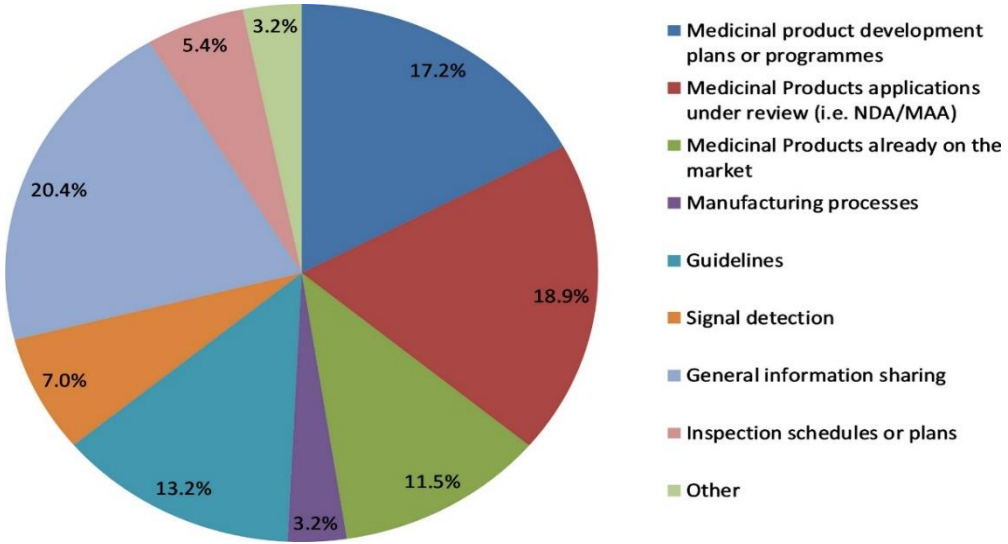
- Strong commitment of all parties
- Good collaborative spirit, goal oriented
- Informative, constructive discussions
- Procedural flexibility - resource intensive
- Successful in achieving harmonised outcome
- Successful in providing valuable lessons
- Positive uptake by regulators - positive feedback from Industry

Decision to **expand the number of applications** in the pilot

Cluster interactions

- Regular interactions between core groups of topic experts
- Around 30 different clusters
- Facilitate timely information exchange

Areas of discussion:



Source: "Are the European Medicines Agency, US Food and Drug Administration, and Other International Regulators Talking to Each Other?", Clinical Pharmacology & Therapeutics, Volume: 107, Issue: 3, Pages: 507-513, First published: 26 August 2019, DOI: (10.1002/cpt.1617).

Cluster interactions for biologicals

Biosimilars Est. 2011
3 meetings per year
EMA, FDA, Health Canada, PMDA, Swissmedic

Advanced Therapies Est. 2008
5-6 meetings per year
EMA, FDA, Health Canada

Vaccines Est. 2005
4 meetings per year
EMA, FDA, Health Canada

Blood products Est. 2010
3 meetings per year
EMA, FDA, Health Canada

+ ad-hoc product- or issue-related meetings

Outlook

- Strengthening of international collaboration is an important objective for quality domain including the newly established QIG

  https://www.ema.europa.eu/en/committees/working-parties-other-groups/chmp/quality-innovation-group

- Convergence (e.g. ICH guidelines) important enabler for efficient collaboration/reliance
- Applicants encouraged to make further use of available tools
- Need to consider how to maximise benefit to patients in view of capacity constraints

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Any questions?

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