EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

ICMRA
INTERNATIONAL COALITION OF MEDICINES REGULATORY AUTHORITIES

3.4 ICMRA PQKMS- update on activities

November 2023

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Sep 2019

FDA reflection paper

Sep 2020

ICMRA convened topic group

Jun 2021

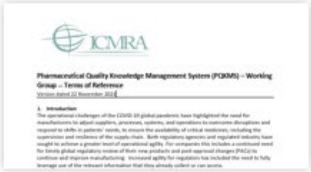
ICMRA Strategic Vision

Jul 2021

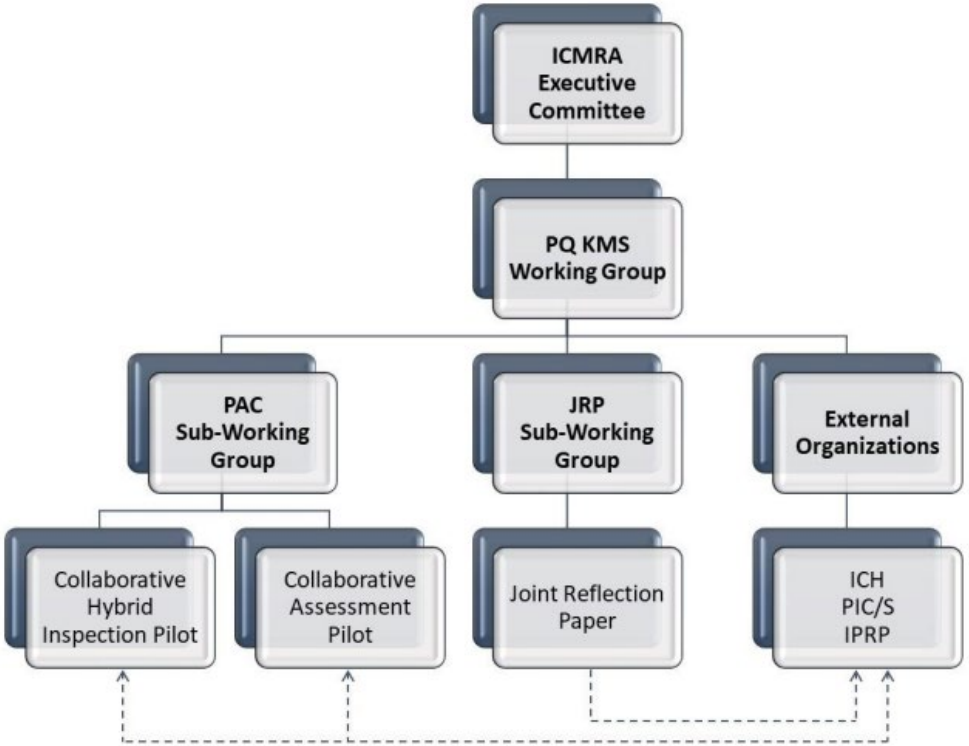
ICMRA-industry workshop

Sep 2021

Establishment of PQ KMS working group



The ICMRA PQKMS working group



Aims to

- Enhance **regulatory reliance and agility**
- Enhance **regulatory effectiveness and efficiency**

  through harmonised data submissions,

  expectations, assessments, and inspections
- **Enhance availability of quality medicines for patients**

Origins of the PQ KMS Concept and Working Group

ICMRA-Industry Workshop: Enabling Manufacturing Capacity in the COVID-19 Pandemic

Main Workshop Summary:

- Opportunity for an ***exchange of views between regulators and the pharmaceutical industry*** on the regulatory flexibilities introduced to enhance the manufacturing capacity of COVID-19 products

- ***Identification of key enablers and bottlenecks*** limiting the use of regulatory flexibilities, in addition to the most effective mechanisms that enabled increased manufacturing capacity

- Workshop will serve as a ***catalyst…leading to greater convergence and further efficiencies*** in global CMC assessment and inspection activities

https://www.icmra.info/drupal/sites/default/files/2021-10/covid-19_manufacturing_capacity_ws_report.pdf

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

ICMRA

ICH harmonisation for better health

PIC/S

IPRP International Pharmaceutical Regulators Programme

Development of a reflection paper on technological solutions to support a PQKMS

Publication of a Joint Reflection Paper on PQKMS

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

Ongoing and future work - PQKMS

Continue to gain further experience with the pilots

Collaborative Pilot Update

16 December 2022

Background

In July 2022, ICMRA initiated two pilot programs focusing on i) collaborative assessment of chemistry, manufacturing, and control (CMC) related post-approval changes (PACs) and ii) collaborative hybrid inspections to inform CMC assessment. In addition to maximising resources and facilitating more effective and efficient reviews, the overarching goal of each collaborative pilot is the identification of misalignments, differences, and potential areas for alignment or harmonization in assessment and inspection activities across participating regulatory regions in the context of manufacturing lifecycle management. A better understanding of areas of potential alignment and difference is an important first step to harmonising specific CMC- and inspection-related regulatory procedures to facilitate the timely implementation of appropriate regulatory actions across different regions. In the interests of transparency and openness, ICMRA will provide regular updates on the status of each collaborative pilot and include further information on the types of applications received and selected for each pilot to help industry take advantage of this opportunity to participate.

Exploring the potential use of unique identifiers in a PQ KMS

Development of JRP-cited work plans

ICH harmonisation for better health

1. M4Q (R2): Common Technical Document on Quality Guideline
2. New guideline on structure product quality submissions

IPRP International Pharmaceutical Regulators Programme

1. IPRP quality assessment tools and best practices
2. Convergence of quality post-approval changes/variations
3. Implementation of ICH Q12

PIC/S

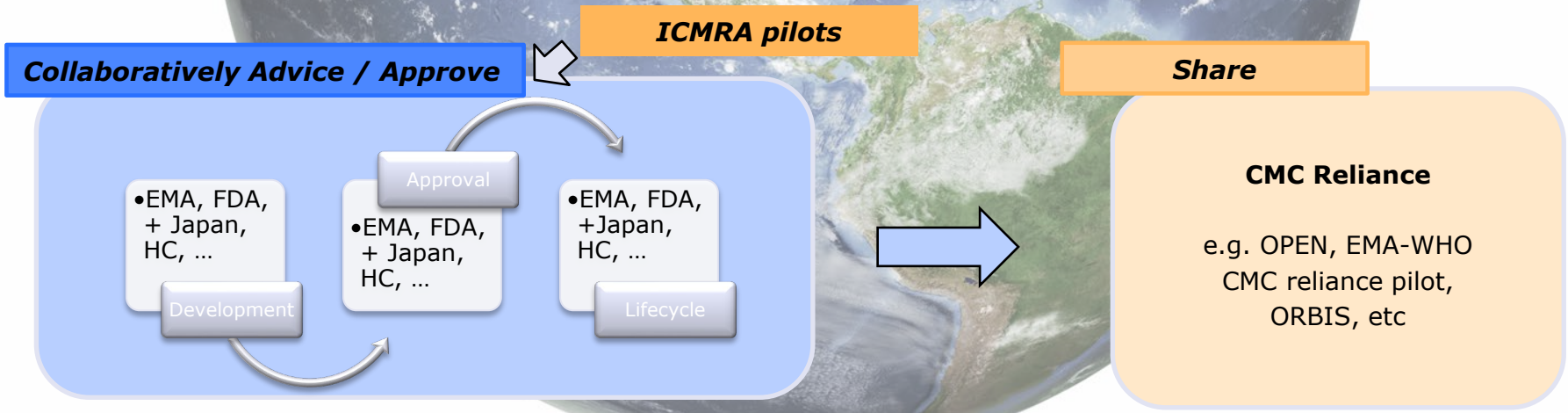
1. Structured data format for inspection reports
2. Tools and templates for PQS assessment for inspectors and associated training
3. Promotion of use and reliance on GMP inspectional information

ICMRA pilots - update

Thinking globally…

Advice / Approve collaboratively and share

- Use collaborative ICMRA pathways (incl Insp) for consultative advices and approval (either in the initial MAA or as a variation)
- Then build on existing regional initiatives like ORBIS, OPEN, EMA- WHO CMC reliance pilot to allow other Regulators to onboard this journey and facilitate approvals in different regions so more patients can benefit

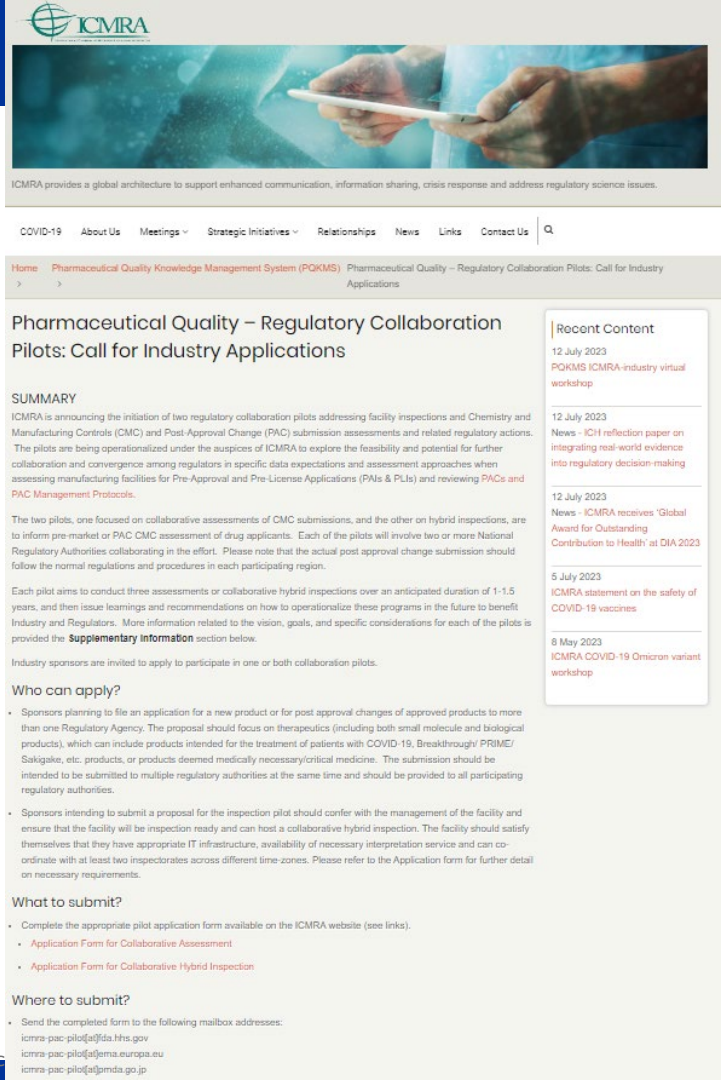


ICMRA pilots

Support to Global convergence and alignment

- Collaborative assessment (*PACMP*)
- Collaborative Hybrid Inspections (*CHIP*)

[Pharmaceutical Quality – Regulatory Collaboration Pilots: Call for Industry Applications | International Coalition of Medicines Regulatory Authorities (ICMRA)]



ICMRA

ICMRA provides a global architecture to support enhanced communication, information sharing, crisis response and address regulatory science issues.

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Home › Pharmaceutical Quality Knowledge Management System (PQKMS) › Pharmaceutical Quality – Regulatory Collaboration Pilots: Call for Industry Applications

Pharmaceutical Quality – Regulatory Collaboration Pilots: Call for Industry Applications

SUMMARY

ICMRA is announcing the initiation of two regulatory collaboration pilots addressing facility inspections and Chemistry and Manufacturing Controls (CMC) and Post-Approval Change (PAC) submission assessments and related regulatory actions. The pilots are being operationalized under the auspices of ICMRA to explore the feasibility and potential for further collaboration and convergence among regulators in specific data expectations and assessment approaches when assessing manufacturing facilities for Pre-Approval and Pre-License Applications (PAIs & PLIs) and reviewing PACs and PAC Management Protocols.

The two pilots, one focused on collaborative assessments of CMC submissions, and the other on hybrid inspections, are to inform pre-market or PAC CMC assessment of drug applicants. Each of the pilots will involve two or more National Regulatory Authorities collaborating in the effort. Please note that the actual post approval change submission should follow the normal regulations and procedures in each participating region.

Each pilot aims to conduct three assessments or collaborative hybrid inspections over an anticipated duration of 1-1.5 years, and then issue learnings and recommendations on how to operationalize these programs in the future to benefit Industry and Regulators. More information related to the vision, goals, and specific considerations for each of the pilots is provided the **Supplementary Information** section below.

Industry sponsors are invited to apply to participate in one or both collaboration pilots.

Who can apply?

- Sponsors planning to file an application for a new product or for post approval changes of approved products to more than one Regulatory Agency. The proposal should focus on therapeutics (including both small molecule and biological products), which can include products intended for the treatment of patients with COVID-19, Breakthrough/ PRIME/ Sakigake, etc. products, or products deemed medically necessary/critical medicine. The submission should be intended to be submitted to multiple regulatory authorities at the same time and should be provided to all participating regulatory authorities.
- Sponsors intending to submit a proposal for the inspection pilot should confer with the management of the facility and ensure that the facility will be inspection ready and can host a collaborative hybrid inspection. The facility should satisfy themselves that they have appropriate IT infrastructure, availability of necessary interpretation service and can co-ordinate with at least two inspectorates across different time-zones. Please refer to the Application form for further detail on necessary requirements.

What to submit?

- Complete the appropriate pilot application form available on the ICMRA website (see links).
  - Application Form for Collaborative Assessment
  - Application Form for Collaborative Hybrid Inspection

Where to submit?

- Send the completed form to the following mailbox addresses:
  icmra-pac-pilot[at]fda.hhs.gov
  icmra-pac-pilot[at]ema.europa.eu
  icmra-pac-pilot[at]pmda.go.jp

Recent Content

12 July 2023
PQKMS ICMRA-industry virtual workshop

12 July 2023
News - ICH reflection paper on integrating real-world evidence into regulatory decision-making

12 July 2023
News - ICMRA receives 'Global Award for Outstanding Contribution to Health' at DIA 2023

5 July 2023
ICMRA statement on the safety of COVID-19 vaccines

8 May 2023
ICMRA COVID-19 Omicron variant workshop

ICMRA Pilots - Scope

Therapeutic area

1. Products intended for the treatment of patients with COVID-19, or changes necessitated by COVID-19, e.g. supply chain changes
    - ***Vaccines are excluded (may be considered in the future if pilot extended)***
2. Breakthrough/ PRIME/ Sakigake, etc. products
3. Products deemed medically necessary/critical medicine

Product types

- Therapeutics, including small molecules and biologicals
- Vaccines are excluded from the pilot (however, they may be considered in the future if the pilot is extended)

Anticipated duration of pilot 1-1.5 years

ICMRA Collaborative Assessment Pilot: Aim

Develop a framework that allows **multiple** regulatory **agencies** to participate in a **collaborative assessment** of post-approval CMC changes **reaching a harmonised outcome at the same time**

A stated goal of the pilot is to **identify** misalignments, differences, and potential areas for further **convergence** or harmonization across regions ->**predictability**

Regulators to develop **best practices** in the quality assessment of CMC post-approval changes and share learnings aiming ultimately towards a common approach to the application assessment and decision making

No delays in approval; No additional regulatory burden, as a result of participation in the pilot

ICMRA Collaborative Assessment Pilot: Status update

- Call to industry open since June 2022, now CLOSED
- 14 proposals submitted
- 5 were selected
- 2 ongoing under assessment
- 2 completed

Participating Authorities:

- First pilot: EMA led– FDA participating authority, (observer: Japan) - completed
- Second pilot: FDA led – EMA participating authority (observers: Japan, Singapore, Brazil, Canada) - completed
- Third pilot: FDA leads – EMA, MHRA (UK), SwissMedic participating authorities (observers: Brazil, Canada) - ongoing
- Fourth pilot: PMDA leads – EMA, FDA, MHRA (UK), SwissMedic participating authorities (observers: Brazil, Singapore, Canada, Australia) - ongoing

1st Pilot observations

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- Strong commitment of all parties
- Good collaborative spirit, goal oriented
- Informative, constructive discussions
- Procedural flexibility - resource intensive as it is
- **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 **!**

Inspection Pilot (CHIP): Status update

- Open call to Industry since June 2022 for participation.
- Three proposals submitted for CHIP so far.
- Two proposals have been accepted & are proceeding.
- One proposal was accepted but was subsequently withdrawn by the company.
- The first collaborative hybrid inspection was finalised in November 2023
- The second one in 1st quarter 2024.
- CHIP is still seeking new proposals to meet the target of 3 inspections (at least).

Pilots – Update on **Inspection Pilot**

Participating Authorities:

- **First pilot:** FDA (lead Inspector) & Health Canada participating authority, UK, HPRA, Swissmedic, Israel, Observer authorities)
- **Second pilot:** Swissmedic (lead inspector) & FDA participating authority (UK, EMA Observer Authorities)

Pilots – July 2023 ICMRA –IFPMA **Workshop Update**

Very positive feedback on the pilots during both days of workshop. Praise for the collaborative efforts, the increased engagement and transparency in the process – very positive experiences.

Full support for strategic vision, direction of travel and goals of the pilots.

- Industry see great potential for further convergence and harmonisation.
- Regulators see great potential for reliance, capacity building, opportunities for innovative regulatory approaches.
- All see Pilots as leading to increasing predictability of regulatory outcomes.

Feedback that still a learning exercise and appreciate that regulators flexing as much as possible to prevent emergence of new barriers.

Some apprehension of inspection still there.

ICMRA pilots - What's next

- Finalisation of the ongoing activities
- Lesson learnt report with recommendations for operationalisation of the pilots to be presented at a 3rd IFPMA/ ICMRA workshop paving the path for a cross regional collaborative assessment pathway

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(FDA)

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PQ KMS Working Group

Canada, Health Canada
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Ireland, HPRA
Japan, MHLW/PMDA
Nigeria, NAFDAC
Singapore, HSA
Spain AEMPS
UK, MHRA
US, FDA
WHO (Observer)

PAC Working Group

HPRA
EMA
FDA
MHLW
PMDA