ICMRA-ICH-IPRP-PICS Joint Work Plan for Harmonisation and Convergence Work to Advance Development of a Regulatory Pharmaceutical Quality Knowledge Management Capability

September 2024

Introduction

The International Coalition of Medicines Regulatory Authorities (ICMRA), International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), International Pharmaceutical Regulators Programme (IPRP), and Pharmaceutical Inspection Co-operation Scheme (PIC/S) are aligning efforts to build the data infrastructure to support a global regulatory Pharmaceutical Quality Knowledge Management (PQKM) capability to ultimately enable better availability of high-quality medicines. The shared vision of the four organisations for the development of this global capability was outlined in a Joint Reflection Paper published in July 2022. The paper outlined the coordinated, multi-stakeholder approach to harmonisation work required to support the development of a regulatory PQKM capability. It is envisaged that such work can strengthen international collaboration to support global development, manufacture, and supply, ultimately resulting in timely access to safe, effective, high-quality medicines, and thereby assuring public health.

Working collaboratively, ICMRA, ICH, IPRP and PIC/S identified areas of regulatory harmonisation or convergence-related work that each organisation intends to undertake to support the development of a PQKM capability, to be coordinated through the ICMRA PQKM Joint Reflection Paper (JRP) Sub-Working Group. The focus areas identified are as follows:

- ICH proposed to undertake work primarily focused on further specification or clarification of harmonised requirements for the quality sections of the electronic common technical document (CTD) and the data elements and data standards related to those CTD module 2 and 3 submissions.
- IPRP proposed to undertake work on convergence of regulatory expectations among regulators regarding quality assessments for new applications and in relation to post-approval changes (PACs), taking into consideration available harmonised technical guidelines.
- PIC/S proposed to carry out work focused revisions to the PIC/S inspection report template to enable a structured data format to facilitate electronic data exchange, and continued work to develop tools and templates for pharmaceutical quality system (PQS) assessment for inspectors and work on related inspector training modules.
- Additionally, it was proposed that as part of the overall ICMRA PQKM project, the PQKM WG would progress work to:
    - Assess the need for internationally harmonised unique identifiers to enable the envisioned PQKM capabilities supporting regulatory collaboration and reliance, and
    - Explore approaches to establishment and governance of a secure standardized technology platform for PQKM.

Within the joint reflection paper, ICMRA, ICH, IPRP and PIC/S committed to developing a multi-year work plan. The work plan, presented below, identifies the specific harmonisation or convergence topics/projects that the four organisations will undertake in a coordinated and prioritised manner, focussing on work to be initiated in the period 2023 to 2027.

Joint work plan
Identified areas of harmonisation work

The following section provides an overview of the harmonisation work to be undertaken by each of the four organisations that will contribute to the development of a Pharmaceutical Quality Knowledge Management System (PQKMS).

ICH – Data elements and standards

1. M4Q(R2): Common Technical Document and Quality Guidance

The M4Q(R2) Expert Working Group (EWG) will focus on the revision of Common Technical Document (CTD) quality sections in modules 2 and 3 to capture quality information for the registration and lifecycle management of pharmaceuticals for human use.

2. New Guideline on Structured Product Quality Submissions

This project will seek to identify existing common quality information within electronic Common Technical Document (eCTD) module 3 for which structured information standardisation will benefit business processes or public health and the development, where appropriate, of structured data models, including elements, vocabulary, and ontologies for quality information (the content standard).

IPRP – Alignment of regulatory assessment and expectations

1. Survey of IPRP members and observers and analysis of the implementation of the IPRP Quality Assessment Tools

A suite of four Quality Assessment tools were developed to share best practices and promote convergence of expectations and procedures for the assessment of quality information in registration applications and active substance master files / drug master files. The work could facilitate information and work sharing among regulators.

A survey on the status of the implementation of some of these Quality Assessment tools was conducted in 2020. Since that time, there have been several developments within the work of the IPRP Quality Working Group (QWG) (e.g., documents reaching finalisation, additional members joining the QWG, further progress on implementation by some of the regulators). An updated survey is intended to obtain recent information on the statuses of the implementation of these four documents and any recommendations for enhancements to these documents that may further support the objectives of the QWG.

2. Survey of Industry and IPRP members and observers for analysis of similarities and differences and for identification of potential opportunities for convergence for quality post-approval changes and variations

This project aims to identify potential areas to promote convergence of regulatory expectations among participating regulators regarding quality post-approval changes (PACs)/variations, by analysing the current situation, with a goal of enhancing predictability and transparency, facilitating convergence, enabling collaborative assessment, and ultimately promoting more reliance on assessment of PACs/variations.

3. Survey of IPRP members and observers and analysis of the implementation of ICH Q12

The purpose of this survey is to understand and analyse the status and challenges regarding the implementation of the ICH Q12 guideline for the IPRP members and observers, focusing mainly on the following essential items:

a. Categorisation of quality PACs
b. Post-Approval Change Management Protocol (PACMP)
c. Established Conditions (ECs).

PIC/S – Inspections

1. Propose revisions to the PIC/S inspection report template

A PIC/S Working Group will review and propose revisions to the PIC/S inspection report template to enable a structured data format to facilitate electronic data exchange.

2. Develop tools and templates for PQS assessment for inspectors and associated training

PIC/S will continue its work to develop tools and templates for PQS assessment for inspectors and work on related inspector training modules in the PIC/S Inspectorates' Academy (PIA). This is an ongoing activity that is subject to routine work of PIC/S and review under annual and multiyear work plans, which are subject to change.

3. Promotion of use and reliance on good manufacturing practice inspectional information

PIC/S will continue its work on promoting use and reliance on good manufacturing practice (GMP) inspectional information. This is an ongoing activity that is subject to routine work of PIC/S and review under annual workplans.

ICMRA PQKM WG - Cross-organisational collaboration – Unique identifiers

Assessing need for internationally harmonized unique identifiers to enable PQ KM capability

The ICMRA PQKM Working Group established a sub-working group to assess and confirm the minimum requirements for identification of products, facilities, marketing applications, marketing application holders, and any other key information components needed to conduct regulatory inspections or assessments related to pharmaceutical quality oversight—that would be needed to support the envisioned PQKM capability. To fortify this joint effort under ICMRA, the PIC/S Working Group on Unique Facility Identifiers has been provided with a wider mandate to engage with IPRP, ICH and ICMRA to share recommended approaches in application of geo-coordinates and collaborate in adoption of a common approach to unique facility identifiers. The assessments and recommendations from this sub-working group including regulatory authorities will be further advanced through subsequent engagement with industry and other external expert stakeholders to consider existing global standards and assess the degree to which these can meet the PQKM needs.

ICMRA PQKM WG - Cross-organisational collaboration – Secure Standardized Technology Platform

Exploring approaches to establishment and governance of a secure standardized technology platform for PQKM.

The PQKMS Working Group additionally established a sub-working group to address approaches for building a PQKMS technology solution. This group has engaged in initial exploration of the issues and approach(es) for establishing and supporting a technology platform solution to support PQKM including considerations related to technical capability, data and system security, governance, and financing. Their general approach has been to identify key questions related to these considerations and develop a reflection paper to propose an approach to further address the identified issues and include engagement of industry stakeholders in that further work.

Key actions and estimated timelines

Further details on the key actions to be completed in the context of the above-mentioned projects are presented below in Table 1. It is important to note that the estimated timelines and expected completion dates are subject to change. ICMRA, ICH, IPRP and, PIC/S will routinely review the progress and status of the projects and actions listed in the work plan and will update this document accordingly.

Table 1 - Key actions and estimated timelines of identified areas of harmonisation work

ICH - M4Q(R2): Common Technical Document and Quality Guidance	
Expected Future Completion Date	**Milestone**
May 2020	*Establishment of the Expert Working Group (EWG)*
May 2025	*Step 2 Sign-off, first draft guideline available*
June 2026	*Step 3 Sign-off and Step 4*
2024 Update	*The M4Q(R2) draft Technical Document was shared with the M4Q(R2) Plenary Working Party (PWP) in April 2024 ahead of Step 1 sign-off. Steps 1 and 2a/b are now expected by May 2025.*
ICH - New Guideline on Structured Product Quality Submissions	
Expected Future Completion Date	**Milestone**
May 2020	*Endorsement of the new topic proposal by the ICH Assembly*
TBD	*Start /establishment of an informal Working Group for this new guideline work is anticipated when ICH M4Q(R2) achieves Step 2a/2b which is currently foreseen May 2025*

2024 Update	*Given the anticipated delays for ICH M4Q(R2), the Working Group will start its work in Q1/Q2 of 2025*

Technology Platform Task Force

The ICH Pharmaceutical Quality Knowledge Management (PQKM) Technology Platform Task Force was established in January 2024 and is tasked with addressing the following key areas over a period not to exceed 18 months:

- *Lead and develop an effective end-to-end strategy, approach, and technological solution to support the PQKM vision*
- *Formulate a technology governance model*
- *Identify the data and technology capabilities required to support PQKM objectives*
- *Fully align with applicable data and system security requirements, legal and regulatory guidelines, and privacy policies across participating jurisdictions*
- *Develop a sustainable financial and procurement model*
- *Encourage key stakeholder outreach and engagement*

IPRP - Survey of IPRP members and observers and analysis of the implementation of the IPRP Quality Assessment Tools

Expected Future Completion Date	**Milestone**
December 2024	*Survey of IPRP members and observers and analysis of the implementation of the IPRP Quality Assessment Tools, notably,* • *Guidance for Quality Assessors – Drug Substance* • *Guidance for Quality Assessors – Drug Product* • *Quality Assessment Report (QAR) template for ASMFs/DMFs* • *Quality Assessment Report (QAR) template – Full Dossier*
December 2024	*Review existing IPRP Quality Assessment tools for potential updates and improvements*

IPRP - Survey of Industry and IPRP members and observers for analysis of similarities and differences and for identification of potential opportunities for convergence for quality post-approval changes and variations

Expected Future Completion Date	**Milestone**
February 2024	*Design and conduct the survey for industry and IPRP members and observers related to Quality PACs/variations*
September 2024	*Analyse and discuss survey responses to identify similarities, differences, and challenges*
December 2024	*Summarise findings and recommendations, including potential areas to promote convergence; close of the project*
December 2024	*Conduct literature review of recent PAC related publication from Industry.* *Summarize findings from Industry publications review.*

	*The outcome of the review's available data will be used to determine whether a survey for industry should be performed***
March 2025	*** (If needed) the group will design and conduct a survey for industry and analyse and discuss the survey responses.*
June 2025	*Summarize findings and recommendations, including potential areas to promote convergence.* *Close of the project.*

IPRP - Survey of IPRP members and observers and analysis of the implementation of ICH Q12	
Expected Future Completion Date	**Milestone**
December 2023	*Elaboration of survey questions*
March 2024	*Launch of the survey*
July 2024	*Collection of answers from the survey*
December 2024	*Analysis of the answers and prepare a report of the survey*

PIC/S - Propose revisions to the PIC/S inspection report template	
Expected Future Completion Date	**Milestone**
March 2023	*Establishment of the PIC/S Working Group to Propose Revision to the PIC/S Inspection Report Format with an agreed mandate between ICMRA and PIC/S*
November 2024	*Draft recommendations on the revision to the PIC/S Inspection Report Format for consultation within PIC/S within the Committee of Officials-*
November 2025	*Final recommendations on the revision to the PIC/S Inspection Report Format for endorsement by PIC/S by the Committee of Officials*
2024 Update	*As of mid-2024, the PIC/S Working Group will propose revisions to the PIC/S Inspection Report Format. The group has been actively advancing the mandate and is currently on track to complete its set milestones.*

PIC/S - Develop tools and templates for PQS assessment for inspectors and associated training	
Expected Future Completion Date	**Milestone**
January 2021	*Publication of the PIC/S Aide-memoire on Assessment of Quality Risk Management Implementation.*
July 2021	*Publication of the PIC/S Recommendations on How to Evaluate and Demonstrate the Effectiveness of a Pharmaceutical Quality System in relation to Risk-based Change Management.*
March 2022	*PIC/S Expert Circle on Quality Risk Management (QRM) Webinar Training Event and Meeting, hosted by UK / MHRA.* *Published for On-Demand Training on the PIA in March 2023.*
October 2022	*PIC/S Seminar Inspecting the Pharmaceutical Quality System, hosted by Ireland/HPRA.*

November 2022	*PIC/S Expert Circle on Quality Risk Management (QRM) Advanced Training Event and Meeting, hosted by Brazil/ANVISA. Published for On-Demand Access on the PIA in 2024.*
March 2023	*Publication of a PIA e-module for Inspectors training on ICH Q9 Quality Risk Management.*
March 2023	*Publication of a PIA e-module for Inspectors training on ICH Q12 Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management.*
2023	*Proposed initiation of a revision process to the Publication of the PIC/S Aide-memoire on Assessment of Quality Risk Management Implementation to reflect revisions to ICH Q9 (under a separate project plan).*
2023-24	*Initiate multiyear plan to update PIC/S e-module for Inspectors training on ICH Q9 Quality Risk Management to reflect revisions to ICH Q9 (under a separate project plan).*
2023-24	*ICH Q10: Proposed delivery of e-module (PQS and key responsibilities).*
2023-24	*ICH Q12: Proposed update of e-module (introduction to ICH Q12).*
2024	*ICH Q9: Proposed status report on preparatory work for e-module (advanced) & Update of e-module (introduction to QRM).*
2024	*ICH Q10: Proposed preparatory work for e-module (PQS / GMP and basic principles) & Update of e-module (introduction to PQS).*
2024	*ICH Q12: Proposed status report on preparatory work for e-module(s) advanced including tools developed by PIC/S WG on ICH Q12 Training Materials & Update of e-module (introduction to ICH Q12).*
2025	*ICH Q9: Proposed delivery of e-module (advanced).*
2025	*ICH Q10: Proposed preparatory work for e-module (PQS / GMP and basic principles)*
2025	*ICH Q12: Proposed status report on preparatory work for e-module(s) advanced including tools developed by PIC/S WG on ICH Q12 Training Materials & Update of e-module (introduction to ICH Q12).*
2026-27	*ICH Q9: Proposed update of e-module (advanced).*
2026-27	*ICH Q10: Proposed update of e-modules (PQS and key responsibilities) & (PQS / GMP and basic principles).*
2026-27	*ICH Q12: Proposed update of e-module advanced including tools developed by PIC/S WG on ICH Q12 Training Materials & Update of e-module (introduction to ICH Q12) and advanced e-module.*
2024 Update	*As of mid 2024, PIC/S has been actively working to deliver upon commitments for key milestones to support development of tools and templates for PQS assessment for inspectors and associated training. Time frames and proposed goals remaining in effect at this time.*
PIC/S - Promotion of use and reliance on good manufacturing practice inspectional information	
Expected Future Completion Date	**Milestone**

June 2018	*Publication and Entry into Force of the PIC/S Guidance on GMP Inspection Reliance initially drafted by the International Coalition of Medicines Regulatory Authorities (ICMRA) GMP Inspection Reliance Framework and taken over by PIC/S at the request of ICMRA.*
December 2020	*Establishment of the PIC/S Working Group on Inspection Reliance.*
August 2022	*PIC/S Working Group on Inspection Reliance launch of a PIC/S survey, addressed to all PIC/S Participating Authorities (PA), to get a better understanding on the inspection reliance framework and existence of potential barriers preventing a PA.*
2023	*PIC/S Working Group on Inspection Reliance report on survey findings.*
2024 and beyond	*Further actions to be defined in promoting use and reliance on GMP inspection information.*
2024 Update	*As of mid-2024, PIC/S is advancing new project plans within the PIC/S Working Group on Inspection Reliance with short to medium term plans to:* - *Update the PIC/S GMP Inspection Reliance Guidance PI-048 incorporating inspection reliance definitions and feedback received from the inspection reliance survey,* - *Develop an aide-memoire to assist regulators performing inspections intended to be used for inspection reliance,* - *Development of a centralised live contact list for PIC/S Participating Authority inspection reliance contacts,* - *Establish a small pilot to explore a PIC/S Single Inspection Program (SIP),* - *Develop case-study/arrange a presentation on confidence building practices & how active inspection reliance works,* - *Establish specific operational PIC/S forums on Inspection planning to promote greater inspection reliance.*

ICMRA PQKM WG - Cross-organisational collaboration – Unique identifiers
Assessing need for internationally harmonized unique identifiers to enable PQ KM capability

Expected Future Completion Date	**Milestone**
May 2024	*Phase 1 effort by regulators to address which items or entities referred to in regulatory submissions or information collected need to be confirmed to be the same, for regulators to work collaboratively/jointly on an assessment and inspection, or to rely on the assessment report or inspection report of another regulator. This would include confirming whether, for example, a unique ID is needed for: the marketing authorization holder, marketing authorization application, drug product, drug substance, facility or other components or entities.*
June 2024	*Identifiers to Enable Pharmaceutical Quality Knowledge Management (PQ KM) – a Progress Report was developed to capture the identifier working group efforts over the last year and was published on the following ICMRA Website.*
September 2024	*Phase 2 effort to assess the degree to which currently available [and accessible, affordable] identifiers and standards meet the needs identified*

	in Phase 1. This work would be undertaken by the ICMRA sub-working group engaging their technical experts in informatics and electronic data standards who are likely best able to identify all potential candidates from available standards and do this assessment. This phase is also anticipated to include a broader set of other technical expert stakeholders through a few "virtual workshop" teleconferences to include pharmaceutical industry stakeholders.
ICMRA PQKM WG - Cross-organisational collaboration – Secure Standardized Technology Platform: Exploring approaches to establishment and governance of a secure standardized technology platform for PQKM.	
Expected Future Completion Date	**Milestone**
August 2023	*Developed an ICMRA Sub-working group jointly authored Reflection Paper on "Exploring the establishment and governance of a secure standardized technology platform for regulatory PQKM"*
September 2023	*Transmission of the Reflection Paper to the ICH Management Committee for ICH consideration for further exploration and the assessment of potential approaches and related requirements and feasibility.*
January 2024	*Platform work transferred to newly established ICH PQKM Tech Platform Task Force Under ICH. See ICH PQKM Task Force for further details.*

Next Steps

This ICMRA-ICH-IPRP-PIC/S work plan reflects current plans and time frames anticipated for these tasks by the respective organizations to advance the development of the envisioned PQKM capability. It may be noted that the identified tasks and estimated timelines are subject to change as the work evolves and additional contributory efforts may be identified. Going forward the ICMRA PQKM Working Group will update this workplan document as needed.