

ICMRA efforts to achieve Regulatory Convergence and Reliance – A Progress Report on the Collaborative Assessment and Hybrid Inspection Pilots

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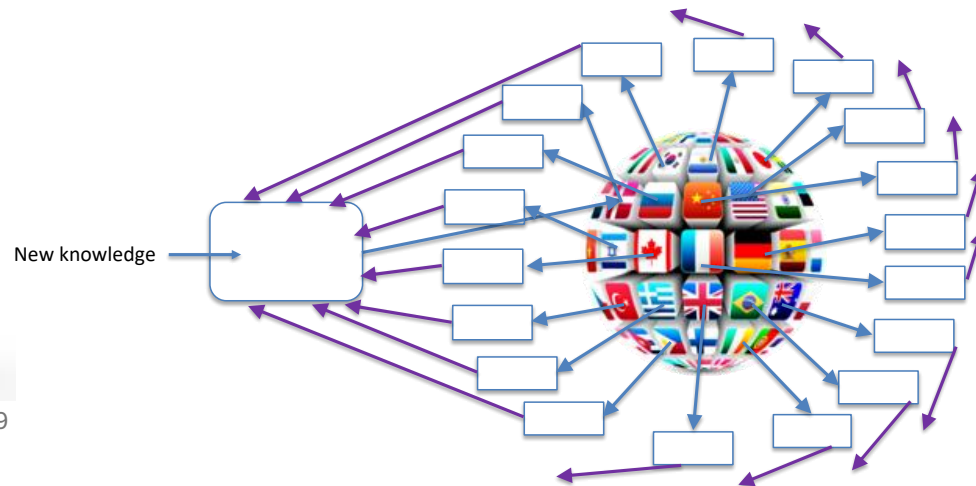
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Post Approval Changes (PACs) – A Complex Regulatory Pathway

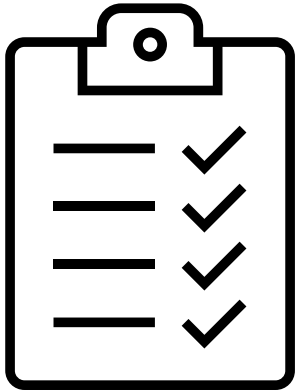
- ▶ Today -- PACs require separate prior approvals, reviews and inspections by RAs
- ▶ Regulatory complexity, cost, and delay in implementing changes and managing quality
- ▶ Greater reliance among regulators can reduce effort by all involved and accelerate supply chain resilience and faster access to critical medicines globally



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Key Enablers of Regulatory Reliance



- ✓ Harmonized **regulatory requirements** across regions
- ✓ **Comparable/convergent** basis for making **regulatory assessments**
- ✓ **Accessible and usable “reports”** for reference by other regulators
- ✓ Assure **non-disclosure** of confidential trade secret information
- ✓ Regulators reviewing **same product & quality dossier**
- ✓ **IT tool(s)** to facilitate review and collaboration
- ✓ Alignment of regional **laws and regulations**

ICMRA working with ICH, PIC/S and IPRP to coordinate work to address these key enablers

Enabler	Efforts under way
<p>Harmonized regulatory requirements across regions</p>	<p>ICH Q GLs; Q12, M4Q(R2), SPQS (<i>expected start 11/24</i>)</p> 
<p>Comparable/convergent basis for making regulatory assessments; reports</p>	<p>ICMRA PQKM--PACMP and CHIP collaboration pilots IPRP QWG & surveys</p>  
<p>Readily accessible and usable “reports” for reference by other regulators</p>	<p>ICH PQKM Task Force PIC/S – more structured data in inspection reports</p>  
<p>Assure non-disclosure of confidential trade secret information</p>	<p>ICMRA PQKM pilot design ICH PQKM Task Force</p>  
<p>Regulators reviewing same product, quality dossier, PAC-related submissions, etc.</p>	<p>ICMRA PQKM WG on Identifiers to enable greater reliance</p> 

ICMRA Collaborative Assessment Pilot (CAP)

Collaborative Assessment Pilot

- ▶ Multi-agency collaborative assessment of Post Approval Change Management Protocols (PACMPs)
- ▶ 14 applications received - prioritized based on impact to supply of **critical medicines**, potential for **agreed regulatory approach**
- ▶ Five proposals accepted:
 - New DS & DP manufacturing sites, new QC testing sites, changes to the DS manufacturing process
 - 2 x small molecules, 2 x mAbs, 1 x ADC
- ▶ Identical submission sent to all participating agencies
- ▶ All 5 collaborative assessments completed successfully

Global Assessment Teams

Lead Authority	Participating Authorities	Observer Authorities
<ul style="list-style-type: none"> • Assess application • Propose IRs • Coordinate all activities • Lead on project calls • Consolidates IRs • Applicants' main contact 	<ul style="list-style-type: none"> • Conduct independent assessment • Participate in discussion meetings • Propose IRs 	<ul style="list-style-type: none"> • Participate in discussion meetings • Cannot raise IRs

Applicant	Lead Authority	Participating Authorities	Observers
Roche	EMA	FDA	PMDA
AstraZeneca	FDA	EMA	PMDA, Health Canada, HSA, ANVISA
Merck Healthcare KGaA	PMDA	FDA, EMA, MHRA, Swiss Medic	HSA, Health Canada, TGA
Gilead	FDA	EMA, MHRA, Swiss Medic	Health Canada
MSD	EMA	FDA, PMDA, Health Canada	HSA, Swiss Medic

Anticipated Timeline

Activity	timeline
Submission – receipt date	Day 0
Project start	Day 1
Regulatory Authorities specific steps ¹	Day 1-105
Assessment teams internal meetings	Day 20 - 105
Information Requests (IR) to Sponsor ²	Day 20 - 105
Sponsor meeting ³	TBD
Regulatory Authorities specific steps ¹	D105 - 113
Draft Quality assessment by Lead regulatory Authority	Day 106
Decision making ¹	Day 113 – 120
Project end	Day 120

¹ Due to different legal frameworks each Authority needs to meet internal regulatory milestones, e.g. FDA: initial filling/ completeness assessment, complete filing review; EMA: validation, developing AR for CHMP comments/ adoption, etc.

² There may be multiple IR throughout this period

³ Flexibility based on the needs of the participating authorities

Assessment Process & IRs

Harmonization of IRs was achieved across the entire Module 3

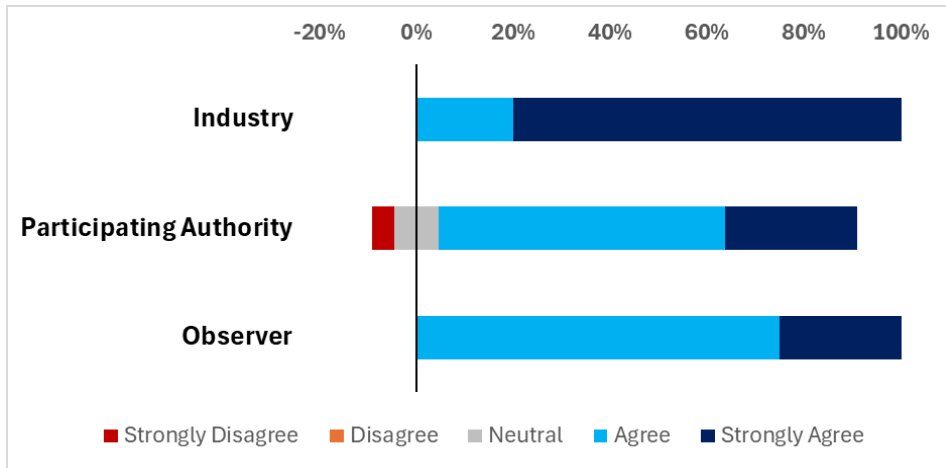
Question area	No. harmonised IRs
Comparability	26
Reporting category	7
Stability	5
Control strategy	4
Analytical methods & validation	3
Process validation	3
Viral safety	3
Impurities	2
Manufacturing site details	2
Method transfer	2
Batch traceability	1
Container closure	1
Equipment details	1
Extractables & <u>leachables</u>	1
Sterility assurance	1
Transport validation	1

Discussion meetings resulted in **~25% reduction** in #IRs

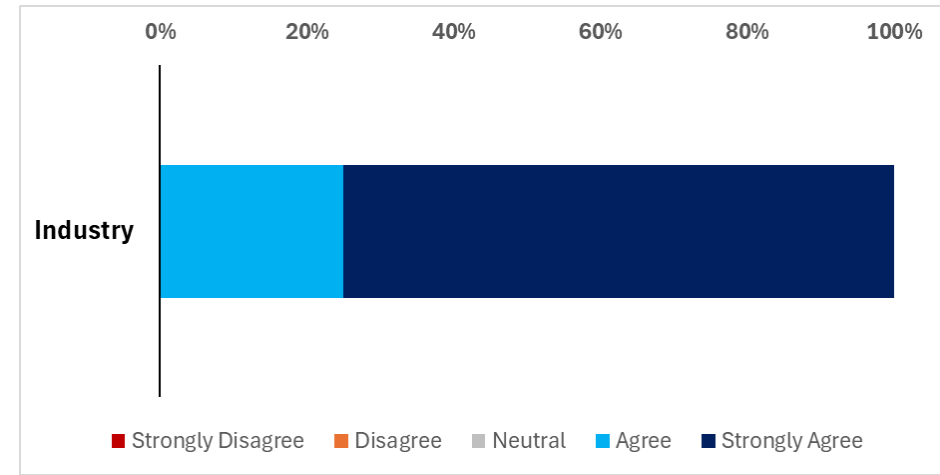
- ▶ 88% of all assessment IRs were harmonized
- ▶ Required discussion among regulators to reach a consensus
- ▶ Some regional specific IRs, e.g. method transfer data, requirement for certain validation reports
- ▶ A small number of region-specific administrative questions, e.g. applicant forms, GMP documentation

Positive outcome based on survey results

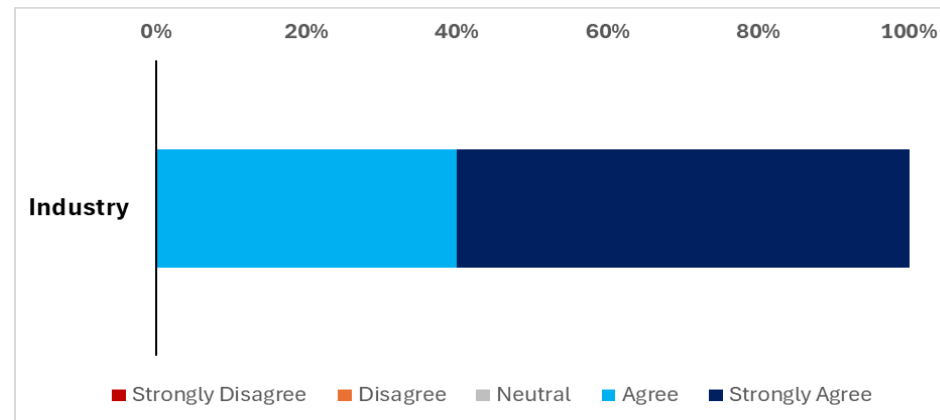
Overall experience and support its operationalisation into a global regulatory program



Had a measurable impact on public health and/or availability of medicines

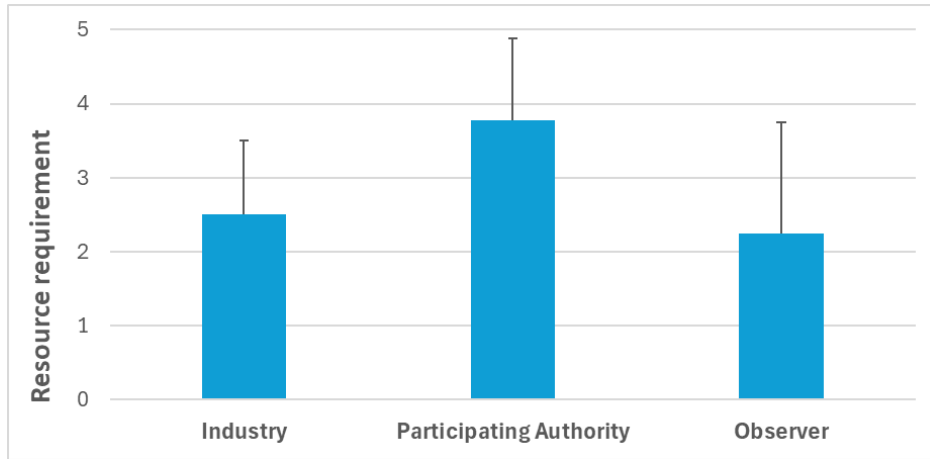


Participation did not impact standard approval times



Impact on resources & areas of further development

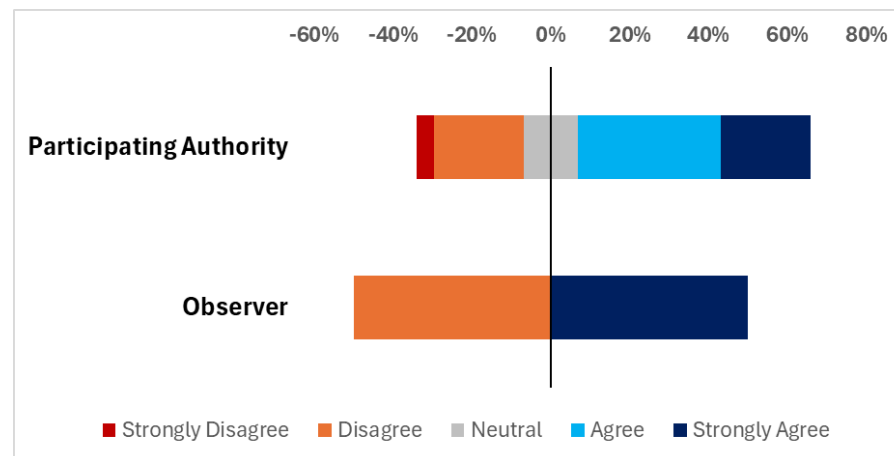
Resource impact 0 = no additional resources and
5 = Significantly more additional resources



Did the benefits outweigh any additional resource requirements?

	% Respondents who answered yes
Industry	100%
Participating Authority	95%
Observer	100%

It was possible to use a single IT platform



Developing a dedicated shared IT platform is a priority

Achievements & Lessons Learned

- ▶ Positive and productive collaborations
- ▶ Agreed process with standard 120-day timetable
- ▶ Agreement on data requirements across numerous areas of CMC
- ▶ Authorities approved applications within days of each other
- ▶ Positive feedback from industry participants
- ▶ Resource-intensive exercise to achieve aligned decisions
- ▶ Identified areas of further development and improvement

Future directions

- ▶ Pilot results support further **development** of a **global** collaborative assessment **pathway**
- ▶ Ongoing activities:
 - Summary Report & Propose an Operationalisation Framework by end of 2024
 - Develop a dedicated globally shared secure **IT platform** (under ICH)
- ▶ The collaborative assessment process can be a key enabler of global regulatory convergence and reliance in conjunction with other global programmes such as OPEN, Orbis, PIC/S, Access Consortium, parallel scientific advice etc.
- ▶ First steps toward the ultimate goal of **one submission = one global approval**

ICMRA Collaborative Hybrid Inspection Pilot



Collaborative Hybrid Inspection Pilot (CHIP)

- ▶ Three proposals submitted for collaborative hybrid inspection pilot (CHIP)
 - Planned to accept three proposals
 - Two proposal accepted; third CHIP was a reinspection
 - One proposal withdrawn

- ▶ Three collaborative hybrid inspections completed without technical difficulties

- ▶ Post inspection feedback is being collected via survey

- ▶ Efforts are ongoing to develop recommendations on next steps

CHP Inspections

▶ **1st and 3rd collaborative hybrid inspections**

- Addition of a new DP manufacturing site located in USA
- Initial inspection completed successfully in Sept. 2023
- Reinspection completed successfully in May 2024

▶ **2nd collaborative hybrid inspection**

- Addition of a DS manufacturing/analytical testing site located in Switzerland
- Completed successfully in February 2024

CHIP - Proposals Accepted and Regulatory Authorities

Applicant	Lead 'Onsite' Authority	Remote Authority	Observers
Roche	Swissmedic	FDA	EMA and Health Canada
Gilead*	FDA	Health Canada	PMDA, Swissmedic, MHRA, MoH Israel, EMA, HPRA

* using a CMO

CHIP Achievements

- ▶ Positive and productive collaborations with supporting tools developed
 - Regulators - Joint Inspection Protocol w/ agreed timetable for inspections
 - Sponsors & Facilities – Industry Expectations Guidance and timely communication and response to deficiencies.
 - Sponsors achieved approvals w/ sites securing CGMP Compliance Status.

- ▶ Lead and Remote Regulatory Authorities aligned on inspection procedure and findings
 - Agreement on deficiencies, significance and post-inspection activities.
 - Harmonized approach towards unfavourable compliance status in participating regions with no supply from facility pending resolution. Achieved in different ways.

- ▶ Continuous communication among the RAs
 - Use of IT platform to securely share information between participating inspectorates before, during and post inspection.

CHIP Anticipated Timeline

Activity	Timeline (calendar days)
Pre-inspection planning between RAs	30 - 60 days before the start of the inspection
Communication with the facility to test IT and communication capabilities	7 - 14 days prior to the inspection
Start of the inspection	0
Close-out meeting to provide the firm with a consolidated list of observations	5 - 8 days after initiating the inspection
RAs receive CAPAs	30 days after close-out meeting
Engagement with facility to clarify CAPA plan(s), if necessary	10 days post receipt of CAPAs from the facility
Preliminary inspection report reviewed by the RAs	60 days post inspection
Final inspection report(s) sent by RAs (GMP certificate or equivalent issued/ or statement of GMP Non-Compliance, if applicable) to facility	90 days post inspection

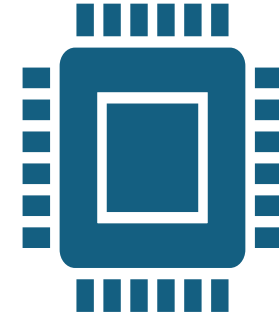
CHIP Preliminary Survey Outcomes



Good completion rate for questionnaires, representative of all participants in the Pilot



Majority found that sufficient guidance was provided in the preparation of the inspection.

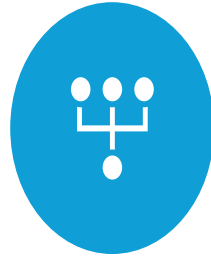


Majority found that material on ICMRA website was found to be a helpful resource.

CHIP Preliminary Specific Findings



Mixed view of Communication and information sharing during the inspection. Authorities agreed, but industry disagreed.



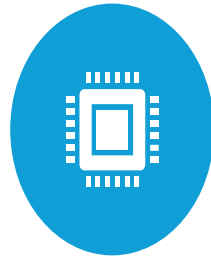
Authorities agreed there was active communication to achieve consensus, and single list of deficiencies.



Divided view amongst authority respondents on benefits versus resource commitment. Industry more favorable view.



Majority of respondents have positive view of participation experience and majority would consider participation in future initiative.



Majority agree that the CHIP could be operationalized and deployed in the future.

CHIP Preliminary Specific Findings



Majority authorities and companies indicated CHIP required significant extra resources.



Participating authorities and companies agreed there was observable impact on public health.

CHIP Lessons Learned

- ▶ Expectations document posted on the ICMRA website on 31-Aug-2023 very helpful to Industry

- ▶ A lot of effort taken to align regulatory processes, clarify roles and requirements to enable collaboration of different RAs and to facilitate communication with company (joint report, one voice for all, one CAPA)
 - Balance of different Regulatory Commitments

- ▶ Need to consider in which cases this regulatory tool would be of value in the future (output of the pilot)
 - How to Initiate (Sponsor, Regulator)
 - How to combine with dossier review decision-making and timelines
 - Inspection Types

- ▶ Need for a common secure IT Framework

Next Steps – Future Directions

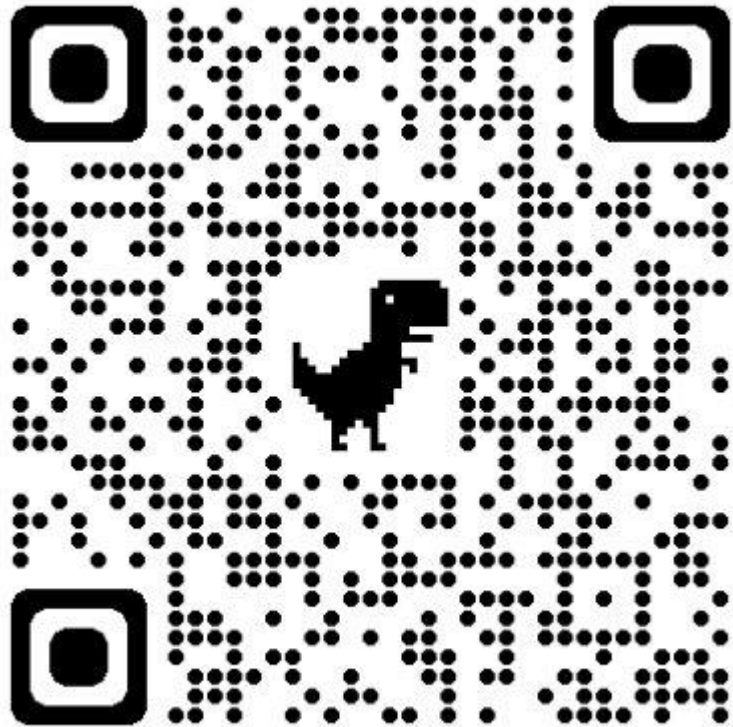
- ▶ Feedback from participating sponsors, Sites and Regulators is being collected
 - Target to issue a summary report by end of December 2024

- ▶ The CHIP continues to accept applications. For information on how to apply refer to ICMRA's webpage (next Slide).

- ▶ Incorporate the CHIP into the Operational Plan being prepared for CAP noted earlier.
 - One dedicated globally shared secure **IT platform**
 - Set of directions & supportive documents for planning, executing and reporting CHIP inspections
 - Requirements for Global Authorities to be part of CHIP

- ▶ First steps toward the ultimate goal of **one submission = one inspection (when necessary) = one global approval**

Collaborative Pilots: Pharmaceutical Quality Knowledge Management System (PQ KMS) Website



Scan the 2D barcode using your phone for all information needed concerning the collaborative pilots



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 Knowledge Management System (PQKMS)

17 July 2024

Identifiers to enable a pharmaceutical quality knowledge management capability

A key challenge that must be addressed in establishing a pharmaceutical quality knowledge management (PQKM) capability is the ability to identify or confirm that it is the same product under assessment by different regulatory authorities in parallel or at different times. Although some authorities use national or regional identifiers, a common and interoperable limited set of identifiers for manufacturing facilities, pharmaceutical products, substances, marketing applications, and/or marketing application holders is not currently endorsed. As part of the PQKM project, a group composed of representatives from multiple regulatory authorities was convened to consider relevant standards and identifiers. This progress report provides an overview of the initial activities and work undertaken by the group, alongside relevant international developments and high-level proposals for next steps.

[Progress report \[PDF\]](#)

Update: 12 June 2024

PQ KMS Pilot Updates

In the interests of transparency and to ensure key stakeholders are informed, the pages below will provide regular updates on the current status of each collaborative pilot. Further information will also be provided on the rationale for choosing specific applications to participate in each pilot.

[Collaborative Pilot Update: 12 June 2024](#)

[Collaborative Pilot Update: 16 December 2022](#)

Recent Content

17 July 2024

[Identifiers to enable a pharmaceutical quality knowledge management capability](#)

12 June 2024

[Update - PQKMS Collaborative Pilot Update](#)

17 April 2024

[ICMRA-WHO COVID-19 vaccine strain update workshop report](#)

17 April 2024

[10th ICMRA Teleconference Minutes COVID-19 Real-World Evidence observational studies Working Group](#)

12 April 2024

[ICMRA Summit 2023 Melbourne Meeting Report](#)

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ICMRA CAP & CHIP Pilot Organizing RAs

