International collaboration to facilitate medicines availability
Global assessment / Inspection pathways

Update on ICMRA pilots

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ICMRA collaborative assessment pilot- Update
ICMRA Collaborative Assessment pilot

- Multi-agency collaborative assessment of Post Approval Change Management Protocols (PACMP) introducing changes important to supply of critical or high priority medicines
- 14 applications received; 5 cases were selected based on impact to supply and have been reviewed collaboratively
  - 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
- **Same submission** submitted to all Authorities
- No of participating Reg Authorities up to 4; No of Observers up to 4

Pilot still open for limited number of applications till we transition to a new phase
### Global Assessment Teams

#### Lead Authority
- Assess application
- Propose IRs
- Coordinate all activities
- Lead on project calls
- Consolidates IRs
- Applicants’ main contact

#### Participating Authorities
- Conduct independent assessment
- Participate in discussion meetings
- Propose IRs

#### Observer Authorities
- Participate in discussion meetings
- Cannot raise IRs

<table>
<thead>
<tr>
<th>Applicant</th>
<th>Lead Authority</th>
<th>Participating Authorities</th>
<th>Observers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Roche</td>
<td>EMA</td>
<td>FDA</td>
<td>PMDA</td>
</tr>
<tr>
<td>AstraZeneca</td>
<td>FDA</td>
<td>EMA</td>
<td>PMDA, Health Canada, HSA, ANVISA</td>
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<tr>
<td>Merck Healthcare KGaA</td>
<td>PMDA</td>
<td>FDA, EMA, MHRA, Swiss Medic</td>
<td>HSA, Health Canada, TGA</td>
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<tr>
<td>Gilead</td>
<td>FDA</td>
<td>EMA, MHRA, Swiss Medic</td>
<td>Health Canada</td>
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<tr>
<td>MSD</td>
<td>EMA</td>
<td>FDA, PMDA, Health Canada</td>
<td>HSA, Swiss Medic</td>
</tr>
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ICMRA Collaborative Assessment pilot

Outcomes

• **Synchronised** approval across multiple regulatory regions **within 120d**
• **Harmonised technical assessments** with limited regional specific considerations
  • 88% of all assessment IRs were harmonized;
  • Discussion meetings resulted in **~25% reduction** in #IRs
• No additional regulatory burden as a result of the pilot
• Resource intensive for Regulators
• **Step towards single submission single outcome**
Positive outcome based on survey results

The overall experience was positive and support its operationalisation into a global regulatory program.

Participation in the pilot had a measurable impact on public health and/or availability of medicines.

Participation in the pilot did not impact standard approval times.

<table>
<thead>
<tr>
<th>Overall duration (days)</th>
<th>Max difference in approval dates between participating authorities</th>
</tr>
</thead>
<tbody>
<tr>
<td>115</td>
<td>0</td>
</tr>
<tr>
<td>118</td>
<td>0</td>
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<tr>
<td>105</td>
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<td>122</td>
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</tr>
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<td>119</td>
<td>12</td>
</tr>
</tbody>
</table>
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?

<table>
<thead>
<tr>
<th>% Respondents who answered yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Industry</td>
</tr>
<tr>
<td>Participating Authority</td>
</tr>
<tr>
<td>Observer</td>
</tr>
</tbody>
</table>

It was possible to use a single IT platform

Developing a dedicated shared IT platform is a priority
Future directions

• First steps toward the ultimate goal of **one submission = one global approval**
• Pilot results support further development of a global collaborative assessment pathway. ICMRA proposal to be shared via report on pilots by end of Q4 2024
• Ongoing activities:
  - Develop governance structure and dedicated project management capability
  - Refine collaborative assessment process with harmonized milestone dates, standard templates etc.
  - Target increased participation by additional ICMRA member agencies.
  - Target optimal use of reg. resources to maximize patient benefit e.g. innovative manufacturing technologies; Post approval changes which impact supply
• Consider use of ICMRA pilots in conjunction with other ongoing programmes supporting reliance
Leveraging international collaboration to support medicines supply globally
ICMRA Collaborative Inspection Pilot - Update
Collaborative Hybrid Inspection Pilot (CHIP)

- Three collaborative hybrid inspections completed without technical difficulties
- Ready to collect post inspection feedback via survey
- Efforts are ongoing to develop recommendations on next steps (by end of 2024)
- CHIP is still open for pilot applications
CHIP

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

<table>
<thead>
<tr>
<th>Applicant</th>
<th>Lead ‘Onsite’ Authority</th>
<th>Remote Authority</th>
<th>Observers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Roche</td>
<td>Swissmedic</td>
<td>FDA</td>
<td>EMA and Health Canada</td>
</tr>
<tr>
<td>Gilead*</td>
<td>FDA</td>
<td>Health Canada</td>
<td>PMDA, Swissmedic, MHRA, MoH, Israel, EMA, HPRA</td>
</tr>
</tbody>
</table>
Achievements

• Positive and productive collaborations with supporting tools developed
  o Regulators - Joint Inspection Protocol w/ agreed timetable for inspections

• Lead and Remote Regulatory Authorities aligned on inspection procedure and findings
  o Agreement on deficiencies, significance and post-inspection activities.
  o 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
  o Use of IT platform to securely share information between participating inspectorates before, during and post inspection.
Lessons Learned

• Need to clarify expectations for industry in hosting a collaborative hybrid inspection
  – Expectations document posted on the ICMRA website on 31-Aug-2023

• 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 Platform
For more information about the ICMRA PQKM project, scan the QR code or visit: https://www.icmra.info/drupal/en/strategic-initiatives/pqkms