Regulatory Reliance in LCM: A Reality, Not Just a Dream?

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Agenda

- Problem statement
- Regulatory reliance
- ICH involvement
- AZ case studies; early learnings
- Change ambassadors

Challenges with PACs – A different perspective

Regulatory Authority Perspective

Single set of reporting categories / documentation requirements / approval timelines.

Single approval

3-5 years before all approvals received

Industry Perspective

Different reporting categories / documentation requirements / approval timelines.

90 approvals

Challenges with PACs

Path Forward to Optimise Post Approval Change Management and Facilitate Continuous Supply of Medicines and Vaccines of High Quality and Worldwide; Joint Position from EFPIA, IFPMA, VE. Deavin et al.

Regulatory Divergence - Example

- Many markets have different requirements leading to customised submissions for each market
- For example, requests for CoA's from different markets for different components and specific requirements demonstrates the lack of regulatory convergence
- A single set of regulatory requirements would greatly enhance efficient use of resources

CoA	Country																						
	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T	U	V	W	X
Drug Substance	y	y	y	n	n	n	n	y	y	y	y	n	y	y	y	y	y	y	n	y	y	y	n	n
Drug Product	y	y	y	y	y	y	y	y	y	y	y	y	y	y	y	y	y	y	y	y	y	y	y	y
Excipients	y	y	n	n	y	y	n	y	y	y	n	n	y	y	y	y	y	n	n	y	y	y	n	n
Reference Standard	y	n	n	n	n	n	n	n	n	n	n	n	n	n	n	n	n	n	n	n	y	n	n	n
Primary Pack Materials	n	n	n	n	n	n	n	n	n	n	n	n	y	n	n	n	n	n	n	n	y	n	n	n
Additional notes:		1			2			3			4						4	5				6		

Notes:

1. Should match samples provided
2. DP CoA to match samples provided; 1 x excipient CoA from each supplier.
3. DS CoA required from DS & DP manufacturer
4. Wet ink signature & stamped
5. Should include testing of ID/assay API by approved lab after import
6. DP CoA should match sample pack.

A simple change can lead to significant complexity…

- Change of name for a packaging site for a biological product…a very simple change!
  - Packaging site purchased by a new company, and name of the site changed
  - Impact assessment includes changes to Module 3.2.P.3.1, but also to PIL, Cartons and Prescriber Information (SPC)
- Global impact, but 15 markets share the same pack
  - Shortest approval time: **notification**, so implementation could be immediate
  - Longest approval time: **18 months**, so implementation is delayed for 18 months

Reliance

WHO Definition

*"**Reliance:** The act whereby the regulatory authority in one jurisdiction **takes into account and gives significant weight to assessments performed by another regulatory authority** or trusted institution, or to any other authoritative information, **in reaching its own decision**. The relying authority remains independent, responsible and accountable for the decisions taken, even when it relies on the decisions, assessments and information of others"*

ICH PQKM Task Force

Background

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 support a global regulatory Pharmaceutical Quality Knowledge Management (PQKM) capability for chemistry, manufacturing, and controls (CMC) related post approval changes (PACs) submissions, products, and facilities. 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 in the ICMRA PQKMS Joint Reflection Paper (JRP) published July 2022. Such work is intended to 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. As work progressed, needs emerged relating to the establishment and operation of a secure technology platform to operationalise the envisioned PQKM capability. To address this need, ICH agreed to establish a PQKM Technology Platform Task Force aimed at understanding the foundation needed to establish and govern a secure standardised technology platform for PQKM.

Overview

The Pharmaceutical Quality Knowledge Management (PQKM) Technology Platform Task Force 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;
- Be fully aligned 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.

PQKM News

Prospective RFI Announcement

Prospective ICH Pharmaceutical Quality Knowledge Management (PQKM) Task Force Request for Information (RFI)

7 August 2024

The ICH is announcing that it will be releasing a Request for Information (RFI) expected in October to determine interest and potential approaches to support the ICH Pharmaceutical Quality Knowledge Management (PQKM) Task Force's initial assessment for a secure standardised regulatory platform.

In March of 2024, ICH formed the ICH PQKM Task Force to begin exploring what it would take to establish and govern a secure, standardised technology platform to both enable the PQKM vision and make it scalable to other collaborative regulatory use cases. (Official press releases about the ICH PQKM Task Force and related efforts and pilots can be seen HERE and HERE). The PQKM vision is to align efforts to support a global regulatory capability for chemistry, manufacturing, and control (CMC) related post approval change (PAC) submissions supporting products and facilities. The ICH PQKM Task Force has been assessing multiple requirements for operating a secure standardised platform including potential governance and operating models; alignment with relevant privacy, legal and regulatory guidelines across jurisdictions; and data security and technology capabilities needed within the platform. Anticipated capabilities and third-party provisioning services needed to establish and govern the technology platform will be incorporated in an RFI.

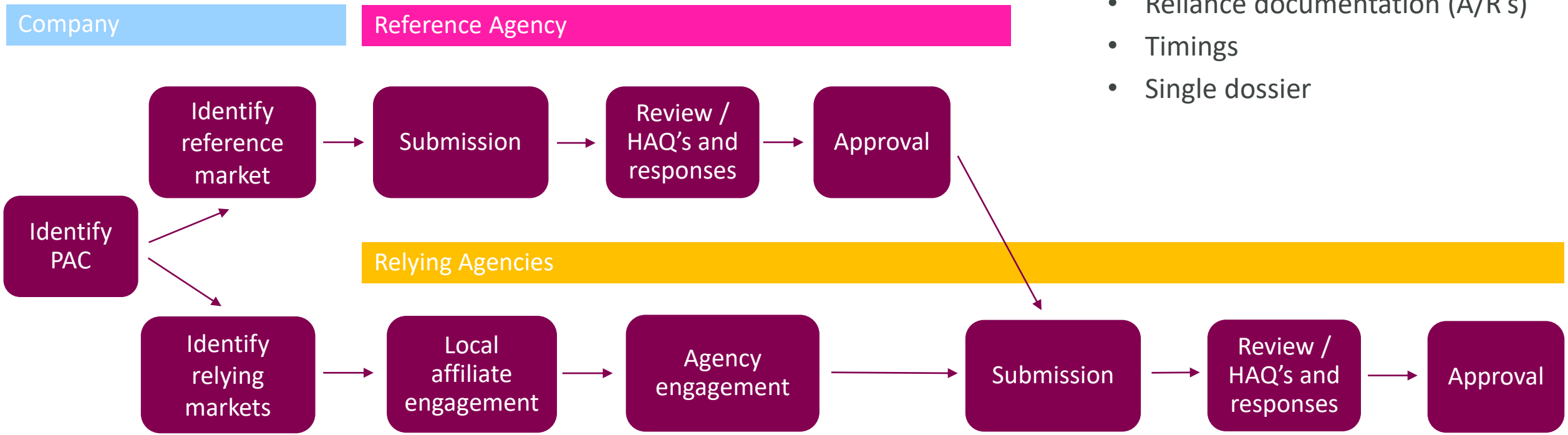
The RFI will focus on gaining vendor feedback to the ICH PQKM Task Force's initial findings and approach, understanding vendor capabilities, and eliciting high-level vendor solutions. The RFI is planned to be released in October of calendar year 2024 and additional instructions will be provided at that time for an interactive vendor session. Parties interested in participating in the RFI process are asked to send notification along with contact information to PQKMtaskforce@ich.org.

AZ Pilots

- Two pilots in progress
  - Biologicals
  - Grouped variations
  - Relying agencies submission planned for 4Q
- Issues
  - Need for a standardised process (AZ/Industry)
  - Shorter approval timelines
  - Alignment of dossiers
  - Divergence in classifications
  - Agency and Company (internal stakeholders) engagement

Process Flow

- Key discussion points during development of process
  - Question and answer document
  - EMA engagement
  - Reliance documentation (A/R's)
  - Timings
  - Single dossier



Reliance Parameters

AZ have initiated a PAC CMC reliance pilot using predetermined reliance parameters.

Core Package

Based on the EU Package.

No market specific requirements.

No local testing.

Dossier Transparency

Use of the IFPMA Template of Differences.

Reliance Documentation

Reference Agency Approval Letter.

Reference Agency Assessment Report.

Reference Agency HAQ / Responses.

Reference Agency engagement letter

One Timeline

All relying Agencies work to the same predefined timeline

Online Platform

Provide reliance documentation transparency

Agency collaboration

Timelines

- EMA selected as the reference agency
- Multiple relying agencies selected; regional representation; EU following markets.
- Complex variations

- Simple variations (TBC)

Local Timelines

- Variable local approval timelines
- Alignment required to support single implementation
- Some predicted to be earlier than proposed and therefore have questioned the need to be included
- Resolution:
  - Timing is not the only advantage
  - Single data package, and transparency of HAQ's are additional advantages.
  - Therefore, Agencies that would normally approve earlier than the proposed timelines to be included in the pilot; earlier approvals can be accommodated.

Alignment of Dossiers

- PAC's are dependent on what has already been registered
- Divergent dossiers in each market, e.g.
  - Inclusion / exclusion of brand names
  - Changes during MAA to IPC's
  - DS manufacturing process details
- PAC's in these pilots only impact certain parts of a CTD and not all of it
- Resolved by aligning only those changes, and not the whole CTD component
  - Avoids re-review of whole CTD component by relying Agency
  - Complies with the principles of reliance – single data set

Classification Divergences

- All changes classified according to the EU variations guideline
- Variety of classifications:
  - Some of the changes are not considered variations in some of the markets
  - Some of the changes are notifications
  - Some of the changes require approvals
- Resolution: Apply EMA position and apply a single submission package for all changes to all markets

Engagement

- Internal stakeholders
- Reference agency – EMA
- Marketing companies, local operating companies, affiliates
- Relying agencies
  - Previous experience of reliance pilots: assume involvement
  - New to reliance pilots: Agency engagement

Change Ambassadors

The pandemic highlighted the need for reliance / regulatory convergence in order to accelerate submissions and approvals.

“Patients are waiting for us to make this change.”

Take the message back to your organisations (Agency and Industry), and drive the changes needed.