CASSS CMC Strategy Forum Europe 2023

Collaborative CMC Assessment of Post-Approval Change Management Protocols: A Regulatory Health Authority-Perspective

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FDA U.S. FOOD & DRUG ADMINISTRATION

DISCLAIMER

This presentation reflects the views of the presenter and should not be construed to represent FDA's views or policies.


Everyone deserves confidence in their *next* dose of medicine.
Pharmaceutical quality assures the availability, safety, and efficacy of *every* dose.

OVERVIEW

1. Rationale for Collaborative Assessment of Post-Approval CMC Changes
2. ICMRA Collaborative Assessment Pilot Program
3. Collaborative Assessment Challenges
4. Collaborative Assessment Achievements & Future Directions

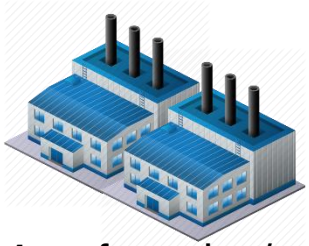
1. RATIONALE FOR COLLABORATIVE ASSESSMENT OF POST-APPROVAL CMC CHANGES

CMC Product Lifecycle Management

- CMC development does not end upon approval of an original application
- Post-approval CMC changes are critical to ensure the continued global availability of medicines to patients

Original Drug Application Approval

Post-approval CMC Changes



Manufacturing/ Testing Site & Scale-up

Analytical Methods

Raw Materials

Continued Global Drug Availability

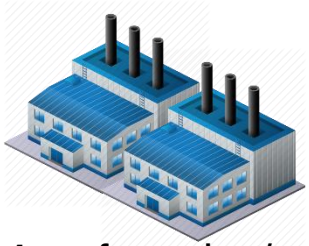
Global CMC Regulatory Challenges

- Submission/maintenance of CMC dossiers to multiple Health Authorities
- Compliance with region-specific regulatory requirements/expectations
- Varying region-specific regulatory processes/ timelines

Original Drug Application Approval

FDA

Post-approval CMC Changes



Manufacturing/ Testing Site & Scale-up

Analytical Methods

Raw Materials

Continued Global Drug Availability

Overcoming Global CMC Regulatory Challenges

- Facilitate harmonization of quality dossier submissions, regulatory expectations, and review processes/ timelines
- Improve timely approval and implementation of CMC changes for global market

Collaborative CMC Assessment Across Health Authorities

2. ICMRA COLLABORATIVE ASSESSMENT PILOT PROGRAM

International Coalition of Medicines Regulatory Authorities (ICMRA)

- July 2022, initiated two pilot programs
- Overall goal to identify misalignments and potential areas for alignment in assessment and inspectional activities across regulatory regions

ICMRA Collaborative Pilot Programs:

1. Collaborative Assessment of CMC-Related Post-Approval Changes (PACs) and Post-Approval Change Management Protocols (PACMPs)

2. Collaborative Hybrid Inspections (CHIPs) to Inform CMC Assessment

International Coalition of Medicines Regulatory Authorities (ICMRA)

- Strive for single outcome between Lead and Participating Authorities, notwithstanding region-specific requirements
- No additional regulatory burden to Applicants; no delay in approval timeline

ICMRA Collaborative Pilot Programs:

1. Collaborative Assessment of CMC-Related Post-Approval Changes (PACs) and Post-Approval Change Management Protocols (PACMPs)
2. Collaborative Hybrid Inspections (CHIPs) to Inform CMC Assessment

International Coalition of Medicines Regulatory Authorities (ICMRA)

- Identify areas where International Regulatory Authorities need to focus collaboration efforts in the future to facilitate maximum benefit to patients

ICMRA Collaborative Pilot Programs:

* 1. Collaborative Assessment of CMC-Related Post-Approval Changes (PACs) and Post-Approval Change Management Protocols (PACMPs)

2. Collaborative Hybrid Inspections (CHIPs) to Inform CMC Assessment

Focus of today's presentation

International Coalition of Medicines Regulatory Authorities (ICMRA)

1. Collaborative Assessment of CMC-Related Post-Approval Changes (PACs) and Post-Approval Change Management Protocols (PACMPs)

Collaborative CMC Assessment Team

Lead Regulatory Authority

Participating Regulatory Authority(ies)

Observing Regulatory Authority(ies)

International Coalition of Medicines Regulatory Authorities (ICMRA)

1. Collaborative Assessment of CMC-Related Post-Approval Changes (PACs) and Post-Approval Change Management Protocols (PACMPs)

Objectives

- Scope initially focused on COVID-19 therapeutics and was further expanded to other product types
- Identify best practices and standards in quality assessment
- Identify misalignments, differences, and potential areas for harmonization across regions

International Coalition of Medicines Regulatory Authorities (ICMRA)

1. Collaborative Assessment of CMC-Related Post-Approval Changes (PACs) and Post-Approval Change Management Protocols (PACMPs)

Objectives

- Share and discuss information requests across Health Authorities prior to external communication with Applicant
- Share and discuss Applicant's response to information requests to reach alignment on deficiency resolution
- Build and improve the communication and collaboration framework between Health Authorities

International Coalition of Medicines Regulatory Authorities (ICMRA)

1. Collaborative Assessment of CMC-Related Post-Approval Changes (PACs) and Post-Approval Change Management Protocols (PACMPs)

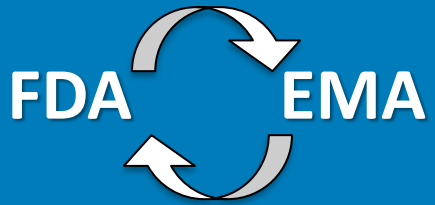
Objectives

Concurrent action taken on application across Lead and Participating Authorities

3. COLLABORATIVE ASSESSMENT CHALLENGES FROM A HEALTH AUTHORITY-PERSPECTIVE

Logistical & Administrative Challenges

1st Collaborative Assessment of PACMPs to support the transfer of drug substance and drug product manufacturing and testing sites



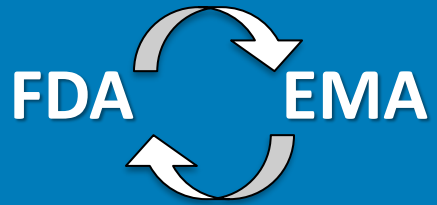
Document Sharing

FDA

- Facilitate sharing and alignment of information requests and assessments
- Need for the Lead, Participating, and Observing Authorities to gain and maintain access to a common document sharing platform
- Compatibility of document sharing platform with internal Information Technology (IT) systems; Agency-specific IT support

Logistical & Administrative Challenges

1st Collaborative Assessment of PACMPs to support the transfer of drug substance and drug product manufacturing and testing sites

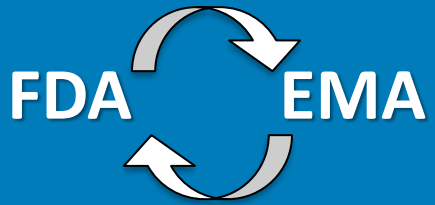


Regulatory Review Process

- **Inherent differences in regulatory review processes/milestones across Health Authorities:**
  - ❑ **Timing for conveying information requests throughout review cycle**
  - ❑ **Single review memo (FDA) versus Rapporteur Assessment Reports for CHMP adoption throughout review cycle (EMA)**
  - ❑ **Region-specific assessment goal dates and procedures**

Logistical & Administrative Challenges

1st Collaborative Assessment of PACMPs to support the transfer of drug substance and drug product manufacturing and testing sites



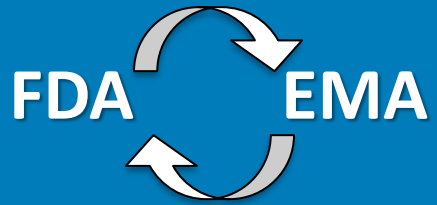
Regulatory Review Process

ACTIVITY	TIMELINE
Submission Receipt Date	Day 0
Project Start	Day 3
Initial Filing/Completeness Assessment	Day 10
Sponsor Meeting[1]	TBD
Information requests to Sponsor[2]	Day 20-60
Complete Filing Review	Day 60 or earlier *Note: EMA*[3]
Information requests to Sponsor[4]	After Day 60
Draft Quality Assessment by Lead Regulatory Authority	Day 106
Complete Quality Review	Day 113
Final/Action Letter Issued	Day 120

[1] There is flexibility within the timeline to schedule Sponsor meetings based on the needs of the Participating Regulatory Authorities.
[2] There may be multiple Information Requests throughout this time frame.
[3] Due to EMA and HC's legal framework, internally, they will need to meet regulatory milestones such as developing final AR for adoption by CHMP and Screening date, respectively. EMA and HC's timeframes will be incorporated into the timeline and its associated milestones document agreed upon by the Participating Regulatory Authorities.
[4] There may be multiple Information Requests throughout this time frame.

Technical Challenges

1st Collaborative Assessment of PACMPs to support the transfer of drug substance and drug product manufacturing and testing sites



Collaborative Documentation

- Need for a common document template for Lead and Participating Authority to capture identified deficiencies, rationale for deficiencies, and recommended information request language
- Need for common document template for consolidating and revising aligned information requests

Technical Challenges

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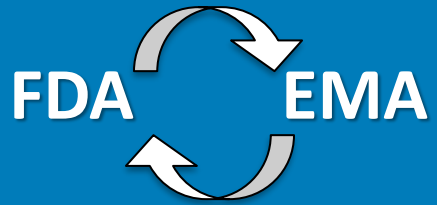
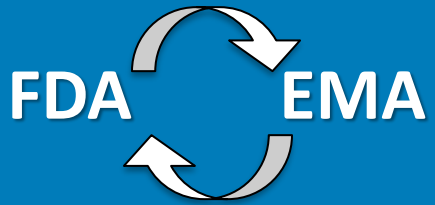


Regulatory Alignment

- Goal to reach alignment in regulatory decisions and information requests
- Misalignments may occur when Health Authorities must adhere to region-specific regulatory requirements (e.g., statute, CFR), Guidance, and general expectations
- Need for Region-Specific Information Requests

Technical Challenges

1st Collaborative Assessment of PACMPs to support the transfer of drug substance and drug product manufacturing and testing sites



Resource Limitations

- **Collaborative assessment is a very resource-intensive exercise for Health Authorities in order to achieve aligned regulatory decisions.**

- **Need for Health Authorities to consider which applications (e.g., product class, disease indication, PAC type) to invest limited work capacity in order to maximize benefit to patients**

4. COLLABORATIVE ASSESSMENT ACHIEVEMENTS & FUTURE DIRECTIONS FROM A HEALTH AUTHORITY-PERSPECTIVE

Achievements

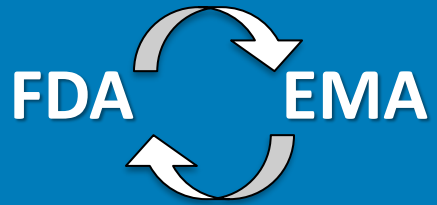
1st Collaborative Assessment of PACMPs to support the transfer of drug substance and drug product manufacturing and testing sites

FDA ⇄ EMA

- **Majority of information requests conveyed to Applicant were aligned across Lead and Participating Health Authorities; limited region-specific comments**
- **PACMPs were essentially approved on same day by Lead and Participating Health Authorities**

Lessons Learned/ Future Directions

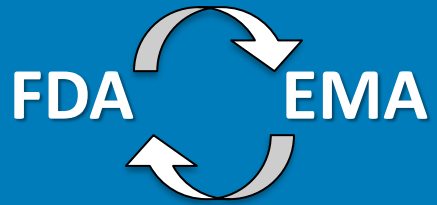
1st Collaborative Assessment of PACMPs to support the transfer of drug substance and drug product manufacturing and testing sites



- Establish a globally shared secure document sharing platform with streamlined instructions for Health Authorities to gain and maintain access
- Establish a global collaborative assessment process with harmonized milestone dates and flexibility to accommodate region-specific requirements

Lessons Learned/ Future Directions

1st Collaborative Assessment of PACMPs to support the transfer of drug substance and drug product manufacturing and testing sites



- **Establish standardized template documents for:**
  - ❑ **Capturing draft information requests from each Health Authority with comment sections to expand on rationale and to confirm alignment**
  - ❑ **Compiling all draft aligned and region-specific information requests for final concurrence**

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