ICH Q12: Perspectives on Post-approval

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This presentation does not necessarily reflect the policies and views of Anvisa.
• Introduction;
• Perceived problem;
• Intentions;
• Lifecycle:
  o Risk Management;
  o Established Conditions.
• Challenges.
Introduction

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ICH Q8: Pharmaceutical Development

Application of scientific approaches and quality risk management

Greater understanding of pharmaceutical and manufacturing sciences

Basis for flexible regulatory approaches

Innovation and continual improvement

ICH Q10: Pharmaceutical Quality System (PQS)

ICH Q9: Quality Risk Management
Introduction

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Review timeline

Post-approval regulation

Stability requirements

Dossier format
Introduction

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Perceived problem

lack of a harmonized approach on lifecycle management

confusion on the necessary information and level of detail in the dossier

post-approval flexibility not achieved

hinder innovation and continual improvement

post-approval tools
Intention

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ICH Q12

- Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management

SCOPE

- Pharmaceutical products, including currently marketed chemical, biotechnological and biological products

APPLICABILITY

- Lifecycle of the product, focusing particularly on the Commercial Manufacturing phase
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lack of a harmonised approach on lifecycle management
classification on the necessary information and level of detail in the dossier
post-approval flexibility not achieved
post-approval tools
hinder innovation and continual improvement

Intention

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Intention

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ICH Q12 Lifecycle Management

ICH Q8: Pharmaceutical Development

ICH Q10: Pharmaceutical Quality System (PQS)

ICH Q9: Quality Risk Management

Innovation and continual improvement

Application of scientific approaches and quality risk management

Greater understanding of pharmaceutical and manufacturing sciences

Basis for flexible regulatory approaches
**Intention**

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**ICH Q12 Lifecycle Management**

*Issues to be Resolved*

**Regulatory Dossier**
- Development of a harmonized approach to “regulatory commitments”
- Delineate the appropriate level of detail and in the dossier

**PQS**
- Establish criteria for a harmonized risk-based change management system
- Clarify expectations and reinforce the need to maintain a knowledge management system

**Post-Approval Change Management**
- Proactively identify post-approval changes
- Mechanism to submit and assess these changes by regulatory authorities
- Establish criteria for post-approval tools that can be adopted by the ICH regions
Intention

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ICH Q12 Lifecycle Management

Desired Outcomes

• Complement the existing ICH Q8 to Q11 Guidelines
• Facilitate the management of post-approval CMC changes in a more predictable and efficient manner across the product lifecycle
• Promote innovation and continual improvement
Lifecycle

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Definition

All phases in the life of a product from the initial development through marketing until the product’s discontinuation.

(ICH Q8)
Lifecycle

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- Drug substance development;
- Formulation development;
- Manufacturing process development;
- Analytical method development.

- From Development to Manufacturing;
- Transfers within or between manufacturing sites

- Acquisition and control of materials;
- Provision of facilities, utilities and equipment;
- Production;
- Quality control and assurance.

Based on ICH Q10
<table>
<thead>
<tr>
<th>Aspect</th>
<th>Minimal Approaches</th>
<th>Enhanced, Quality by Design Approaches</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall Pharmaceutical Development</td>
<td>Mainly empirical&lt;br&gt;Developmental research often conducted one variable at a time</td>
<td>Systematic, relating mechanistic understanding of material attributes and process parameters to drug product CQAs &lt;br&gt; Multivariate experiments to understand product and process &lt;br&gt; Establishment of design space &lt;br&gt; PAT tools utilised</td>
</tr>
<tr>
<td>Manufacturing Process</td>
<td>Fixed&lt;br&gt;Validation primarily based on initial full-scale batches&lt;br&gt;Focus on optimisation and reproducibility</td>
<td>Adjustable within design space&lt;br&gt;Lifecycle approach to validation and, ideally, continuous process verification&lt;br&gt;Focus on control strategy and robustness&lt;br&gt;Use of statistical process control methods</td>
</tr>
<tr>
<td>Process Controls</td>
<td>In-process tests primarily for go/no go decisions&lt;br&gt;Off-line analysis</td>
<td>PAT tools utilised with appropriate feed forward and feedback controls&lt;br&gt;Process operations tracked and trended to support continual improvement efforts post-approval</td>
</tr>
<tr>
<td>Product Specifications</td>
<td>Primary means of control&lt;br&gt;Based on batch data available at time of registration</td>
<td>Part of the overall quality control strategy&lt;br&gt;Based on desired product performance with relevant supportive data</td>
</tr>
<tr>
<td>Control Strategy</td>
<td>Drug product quality controlled primarily by intermediates (in-process materials) and end product testing</td>
<td>Drug product quality ensured by risk-based control strategy for well understood product and process&lt;br&gt;Quality controls shifted upstream, with the possibility of real-time release testing or reduced end-product testing</td>
</tr>
<tr>
<td>Lifecycle Management</td>
<td>Reactive (i.e., problem solving and corrective action)</td>
<td>Preventive action&lt;br&gt;Continual improvement facilitated</td>
</tr>
</tbody>
</table>

Differing Approaches to Pharmaceutical Development

ICH Q8, Appendix I
Lifecycle: Established Conditions

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Critical elements which assure process performance and product quality across the lifecycle

Legally binding information

Proposed in the Application

Approved by Regulator

Changes are reported using relevant post-approval submission
Lifecycle: Established Conditions

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PQS

Scientific- Risk-based

• Established Conditions

   • Risk-based regulatory decisions
   • Adjustment within design space
   • Reduction of post-approval submissions

Pharmaceutical Development

Manufacturing Experience

CQA

Specifications

Design Space

Manufacturing Controls

Product Quality

Process Performance

PRODUCT PERFORMANCE

Established Conditions

process parameters

material attributes
Lifecycle: Established Conditions

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Science Based

Product Understanding

CMC

EC

non-EC

Post-approval Regulatory Submission (different reporting levels)

Solely in PQS
Challenges

• Harmonization among different countries and regulatory contexts
• Application to small and large molecules
• Application to currently marketed products
• Measurement of PQS effectiveness
• Regulatory flexibility tools through non-ICH members
• Product-by-product science- and risk-based approach
• Definition of EC within CMC elements and location in the dossier
• Assessment of EC
• Different ECs approved in different regions
Thank you for your attention!

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