Industry Perspectives on OINDP Regulatory Challenges in Global Environment

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Overview

• Introduction
• OINDP and Guidelines
• OINDP and QbD
• Challenges and Opportunities
• Conclusions
Introduction

• Previously, heard about:
  • Public collaboration between Canada and Europe to produce a joint guideline on OINDP.
  • New regulatory initiatives and how these impact OINDPs.

• This presentation will focus on:
  • The challenges and opportunities ahead for OINDP manufacturers in preparing global submissions.

OINDP and Guidelines
**OINDP Quality Guidelines**

- All the ICH quality guidelines apply to OINDP.

- Devices guidance, ISO standards, CFR, pharmacopoeias, national guidances, etc.

- Specific OINDP guidance:
  - Pharmaceutical Quality of Inhalation and Nasal Products (Health Canada and EU, Final 2006).
  - Metered Dose Inhaler (MDI) and Dry Powder Inhaler (DPI) Drug Products (FDA, Draft 1998).

- No Japan OINDP specific guidance.

**OINDP-Specific Guidelines**

- Outline expectations for various sections of the application, notably:
  - Pharmaceutical Development
    - Product characterization
    - Labelling support
  - Product Specifications
    - Tests to be considered.
    - Reflect pre-QbD approach.

- Scope for further guideline revision or harmonisation, beyond that started by Europe and Canada.
  - But OINDP-specific guidelines don’t stand alone.
OINDP and QbD

Quality by Design

• ‘It is important to recognize that quality cannot be tested into products; i.e., quality should be built in by design.’ (ICH Q8)

• QbD builds on existing expectations.
  • EU regulatory systems required information on the pharmaceutical development of the medicinal product.

• More focus on product knowledge and enhanced process understanding:
  • Impact of raw materials and process parameters on product quality.
  • Identify and control sources of process variability.
  • Appropriate control strategies!
    • Less emphasis on end-product testing.
    • More reliance on process control and in-process monitoring.
ICH Guidelines

- Guidelines simplifying regulatory implementation of the cGMPs for the 21st Century initiative:
  - ICH Q8 Pharmaceutical Development
  - ICH Q9 Quality Risk Management
  - ICH Q10 Pharmaceutical Quality Systems
  - Guidelines for a global environment that encourage development of science based and risk based approaches to quality.

- ICH Q6A and OINDP guidelines:
  - Don’t reflect current QbD approach.
  - But quality targets based on safety and efficacy.

OINDP and QbD

- ICH Q8:
  - ‘At a minimum, those aspects of drug substances, excipients, container closure systems, and manufacturing processes that are critical to product quality should be determined and control strategies justified.’

- OINDP are combination products of drug formulation and device.
  - Drug(s)
  - Excipient(s)
  - Container Closure System

- OINDPs ideal candidates for QbD approach.
What does it all mean for Industry?

- Paradigm shift
  - From:
    - “Confirm the proposed product and processes are suitable for manufacture.”
  - To:
    - “What suite of studies, DoE, multivariate analyses, etc, is needed to establish product understanding, design space, etc?”

- Benefits include better product and process understanding, leading to more predictable approvals and greater regulatory flexibility.

One Successful Science and Risk Based Approach

- Leachables and extractables for p-MDIs.
  - Subject has progressed to the benefit of Industry and Regulators.
  - IPAC-RS has dedicated much time working with OINDP suppliers to better understand extractables and their potential to become leachables.
  - Through the Product Quality Research Institute (PQRI), IPAC-RS, OINDP Suppliers, FDA, and other industry groups have worked together to successfully advance the idea of safety threshold levels for leachables.
  - The idea of control on extractables at the component level rather than on leachables at the product level is well accepted.
Challenges and Opportunities

Challenges

- Changing mindset:
  - ‘That’s not how we did it with the ark?’
  - Data ≠ knowledge or understanding.

- Move away from yesterday’s thinking on specifications.
  - Non-prescriptive, fit for purpose ‘specifications.’
  - Science and patient based control strategies.
    - Focus on what is critical to safety and efficacy.
    - Critical not Nice to Have Quality Attributes!

- Demonstrating comprehensive understanding of the product and manufacturing process in the original marketing application comes at a considerable cost for Industry.
Opportunities

• From enhanced product knowledge and process understanding.
  • “Real time” quality assurance with less dependence on end-product testing.
  • Facilitation of innovation and continuous improvement throughout product life cycle.
  • Increased manufacturing efficiency
    • Waste minimisation.
    • Less product recalls and batch failures.
  • Increased post-approval regulatory flexibility.
    • Proposed by applicant, approved by regulator.
    • Fewer post-approval submissions.

• Applicant decides when to invest!!

Global Scene

• It’s not an homogeneous regulatory landscape.
  • ICH is not the world.
  • ICH vs nonICH vs ASEAN vs SADC etc
  • Mechanisms for post-approval change.

• Requirements are not harmonised.
  • QbD to be worked into Regional guidances as overarching philosophy.
  • Challenge - need to develop products via QbD but recognise that concepts not fully assimilated in some countries.
Further Harmonization?

• Further harmonization and updating of CMC requirements may be required.
  • Updating OINDP specific guidelines and other regional guidelines to incorporate ICH Q8, Q9 and Q10 principles.
  • Update ICH Q6 with key aspects of QbD, e.g. PAT.

• Benefits of any harmonization may be:
  • More economical use of resources for industry and regulators.
  • More streamlined development process and more predictable approvals for industry.
  • Elimination of unnecessary delay in the global development and availability of new medicines to patients.

Conclusions
Conclusions

- Most OINDP producers seek to operate in more than one region
  - Global acceptance of QbD concepts will facilitate global developments.

- Through QbD:
  - Emphasis on enhanced product and process understanding
  - Control strategies based on understanding.
  - Less emphasis on end-product testing.
  - More reliance on process control and in-process monitoring.

Conclusions (Cont’d)

- At this time, the potential benefits of QbD to Industry are unproven for OINDP
  - Challenges should also be seen as opportunities for industry.
  - Application of QbD in the development of OINDP will help set a sound scientific basis for controls, based on greater understanding.

- Industry and Regulators can collaborate to achieve a win-win situation
  - L/E work is an excellent example.

- Need for open and sharing applicant/regulator interactions.
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