The Case for a New Framework for Regulating Drug Quality

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Mike Ward
International Programs Division
Therapeutic Products Directorate

Purpose of Presentation

- To initiate Progressive Licensing discussions with stakeholders on the design of a new regulatory model for drug quality

What is Quality?

Within the pharmaceutical context:

- Suitability of a drug substance or the subsequent drug product for its intended use; includes attributes of identity, purity and strength **(- ICH Q6A)**
- An acceptably low risk of failing to achieve the desired clinical attribute **(- Janet Woodcock, FDA 2004)**
- All definitions embody principles of consistency in producing product of intended performance, attributes and composition.

Why is a Change Necessary?

- **Quality of drugs marketed in Canada generally very good based on low level of recalls/complaints**
- **Sites involved in the manufacture of drugs generally in compliance with GMP**
- **By these measures, current system has worked well, *but* at what cost?**
  - **Are resources being used effectively by both industry and Health Canada?**
  - **Does the current system position us well to handle future challenges?**

Consider the Current State

- Pharmaceutical sector one of the most heavily regulated – and most resistant to change
  - "procrustean" state (J. **B**erridge, Pfizer, UK)
- Widening regulatory workload/resource gap due to steady rise in the number of marketing applications and site inspections; expected to worsen given:
  - number of post-approval changes that typically follow initial product authorization
  - growing complexity of products
  - increasing number of activities to be undertaken by Inspectorate
- Drug manufacturing more global than ever and with it dramatic rise in sourcing of drug substances and products from non-ICH countries

At Same Time, Opportunities Exist to Design a Better Approach

Drivers/enablers:

1. International developments:
   - ICH guidances Q8/Q9/Q10
     - foundation for a modern science and risk-based approach to PD and manufacturing
     - also creates conditions for reduced regulatory oversight
   - MOUs with key regulatory counterparts
     - All regulators facing same pressures
     - Recognition that no regulatory authority can ‘go it alone’ and that enhanced regulatory cooperation offers a more strategic solution
     - Pharmaceutical quality area particularly well-suited for cooperation

At Same Time, Opportunities Exist to Design a Better Approach (2)

2. Progressive Licensing
   - "Quality" an essential element of an acceptable drug - and of PL
   - Quality objectives align well with PL themes, in particular:
     - Life-cycle, evidence-based approach
     - Good planning
     - Accountability

Must seize the opportunity for change!

Life-cycle Management

- Knowledge gained over life-cycle allows for process and product improvement
- Quality by Design (QbD), risk management and quality system important enablers
- Regulatory flexibility conditional on knowledge transfer
- Will also require common understanding and better coordination between reviewers and inspectors

Good Planning

- Planning essential element of QbD:

  "*Deliberative design effort from product conception through commercialization*" (M. Nasr, FDA, 2007)

- Drug quality considerations form part of proposed life-cycle management plan
- Importance of early communication:
  - Provides regulator with a better understanding of proposed strategy
  - Reduces risk of comments at submission evaluation stage

Accountability

- Responsibility for producing drugs of suitable quality ultimately rests with industry
- Demonstration of enhanced product combined with implementation of a effective quality management system, makes possible greater shift in ‘ownership’ of post-approval changes to industry
- ***Not de-regulation*** – same obligation to comply with regulatory requirements

Accountability (2)

- Health Canada also accountable to Canadians by virtue of regulatory mandate
- Accordingly, risk management and quality systems should also be hallmark of a modern regulator, thereby enabling sound decision-making, use of resources and continual improvement

Build upon Best Practices

Examples:

- Submission review:
  - long-established request to file pharmaceutical development information
  - Use of QOS as review template; CPID as basis for documenting ‘regulatory agreement’
- Leveraging international cooperation:
  - Effective use of MRAs, PIC/S
  - contribution and adherence to ICH guidances
  - Recent MOU with EDQM
- Risked-based approach to lot release (biologics)

Elements of A Desired State

- Manufacturers (and regulators) have extensive knowledge about critical product and process parameters and quality attributes
- Manufacturers strive for continuous improvement
- Regulator's role:
  - initial verification, subsequent audit
  - creating a regulatory environment conducive to innovation, continuous improvement…and ultimately, access to high quality medicines

Elements of a Desired State (2)

- Regulatory oversight commensurate with risk and product knowledge
- Effective internal, national and international cooperation

Implementation Considerations

- Maintaining more than one approach: traditional and QbD (and hybrid of the two)
  - Implications with respect to regulatory guidance, transparency, predictability, etc.
- Regulatory and industry preparedness
  - Training: common understanding of concepts – between and within companies and regulatory authorities
  - Requisite resources/expertise

Implementation (2)

- Regulatory and industry preparedness (cont'd)
  - Better coordination of pre-/post-market programs; establish specialized team(s)?
  - More/earlier communication
  - Guidance/policy work
  - ***Trust and commitment***
- Regulatory flexibility
  - Regulations must provide necessary flexibility
  - Regulatory 'mindset' and philosophy equally important

Implementation (4)

- More *strategic and effective* International regulatory cooperation

Points to Consider

- Does support exist for a differentiated approach to regulation whereby level of regulatory oversight commensurate with risk and product knowledge/control?
- What might qualify for a reduction in regulatory oversight? Potential scope of Design Space and supportive data?
- How to best document ‘regulatory agreement’ for specific product: CPID? Do regulations currently support?

Points to Consider (2)

- Special considerations: biologics, legacy products
- How might product evaluation and inspection programs be aligned to provide for a more effective regulatory system?
- Need for advisory committee on pharmaceutical science?

Points to Consider (3)

- New vision, desired state and perhaps definition of ‘Quality’
- NB - New regulatory framework needs to address ***all*** drugs, including vast majority that are not ‘new drugs’ or for which traditional approach followed
- What’s missing?

Next Steps

- Posting of concept paper and selected Quality discussion papers for comment on PL website
- Proposed one day PL session on new framework for pharmaceutical quality to be held on June 28, 2007 in Ottawa
- Development of implementation plan that covers near, medium and long term
- Integrate feedback received into PL framework

We need to work together to succeed in defining and implementing the Quality component of the PL framework - your input is welcome!

Thank you!