Clinical Relevance

Seeing the Big Picture

M-CERSI Conference
May 15, 2017

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January 11, 2015

Advances FDA’s Quality Initiative to the next level
The link to the patient/consumer...
Expectations for Quality

Patients and caregivers assume that their drugs:

- Are safe, efficacious, and have the correct identity
- Deliver the same performance as described in the label
- Perform consistently over their shelf life
- Are made in a manner that ensures quality
- Will be available when needed
Clinical Relevance

• Product quality is the foundation upon which the clinical safety and efficacy assessment rests

• A product is “fit for use” if it meets the established quality attributes
  – purity, potency/strength, identity, bioavailability/delivery, labeling/packaging, performance, etc.

• Strive to establish appropriate correlations between quality attributes and clinical performance

Adapted from M. Nasr’s “Setting Specifications in the 21st Century”/PQRI Workshop, March 16, 2005
Applying Clinical Relevance to Quality

• A high quality drug product is a product that reproducibly delivers the therapeutic benefit to the patient/consumer as stated in the label, is free of defects, and presents no undeclared risk (e.g., is not contaminated)

• **Attributes**
  – Beginning with the end in mind – designing the product to meet patients’ needs and the intended product performance
  – Developing the Quality Target Product Profile (QTPP)
    • A prospective summary of the quality characteristics of a drug product that ideally will be achieved to ensure the desired quality, taking into account safety and efficacy of the drug product (ICH Q8 (R2))
    – Identifying “clinically relevant” CQAs – those characteristics having an impact on product quality

• **Specifications**, such as:
  – Dissolution, Impurities, Size/Shape/Delivery/Design
Clinical Relevance - The Continuing Dialog

- How much is enough?
- Need to know vs want to know
- Risk communication
- Uncertainty/Risk-Informed
- Multidisciplinary interactions
- Efficiency of interactions/discussions
- Stakeholder feedback
- Timeframes (including expedited)
- Seeing the “big picture”
Clinical Relevance – Specific Discussions

• Clinically relevant specifications
  – Impurities
  – Dissolution, IVRT
  – …

• Emerging technologies

• Effective risk communication

• Policy/guidance development

• Benefit-Risk

• Breakthrough Therapies
  • …
The Risk/Benefit Balance...

Availability to patients

Risks to Quality
Clinical Relevance – Context

• Clinical relevance is not only about clinical data
  – Patient/consumer-focused
  – Links quality to clinical performance
  – Involves pertinent multidisciplinary data/dialog
  – Helps to ensure that drug products will perform as indicated in the label

• Clinical relevance is more than specifications
  – More than dissolution or IVIVC
  – CRS are just part of clinical relevance
  – Clinical relevance is not owned by a single discipline
  – Not a “cookie-cutter” approach
Clinical Relevance – Connections

• Clinical relevance is just as much about what we don’t know vs what we do know
  – Risk involves uncertainty
  – Need to know vs want to know in our communication to stakeholders
  – Timely engagement of internal and external stakeholders

• Clinical relevance is a balanced conversation
  – Not a “magic bullet”
  – Balanced within quality, multidisciplinary, and/or Agency/industry
A Balanced Conversation

- Technical Dossier & Prior Knowledge
- Regulatory Framework
- Supporting Policy & Guidance
Clinical Relevance – Collaboration

• Clinical relevance is just as much about HOW we work vs WHAT we do
  – More than a single discipline/not owned by any single discipline
  – Based on robust internal/external discussions and solid collaboration
  – Based on concept of building mutual understanding and benefit/risk-based decision making
  – Striving to identify potential efficiencies and continuous improvement
ONDP Strategic Priorities (2016-21)

- Enhance the team-based review process
- Proactively support continuous improvement – review quality
- Proactively support continuous improvement – review efficiency
- Facilitate effective, transparent and risk-based communication
- Enhance robust discussions linking quality to clinical performance
- Achieve excellence through a skilled, knowledgeable and collaborative workforce
Clinical Relevance - A Lifecycle Approach

Patient-Centric Assessment

Patient (QTPP) expectations

Regulatory Outcome (approval if sufficient)

Post approval experience
Moving Forward…

- Our primary stakeholder – the patient/consumer
- Supporting OPQ organizational constructs and initiatives
- Various objectives in 2017 heavily support clinical relevance, effective risk communication, and enhanced collaboration/integration
- Additional opportunities may exist to align objectives with meaningful outcomes for industry
- Appropriate context, robust connections, and effective collaboration are crucial to progress
Thank You!