

Clinical Relevance

Context, Connections and Collaboration

FDA/PQRI Conference
March 22, 2017

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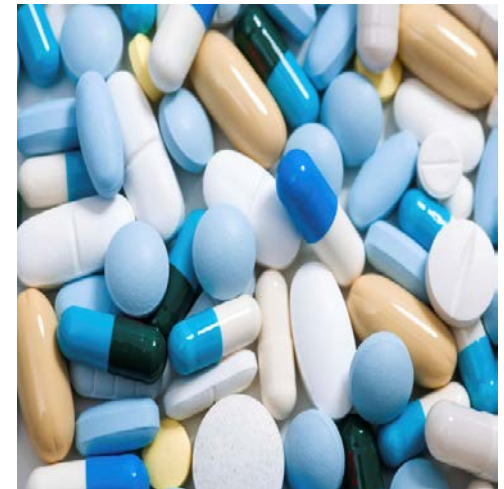
CDER's Office of Pharmaceutical Quality (OPQ)

January 11, 2015

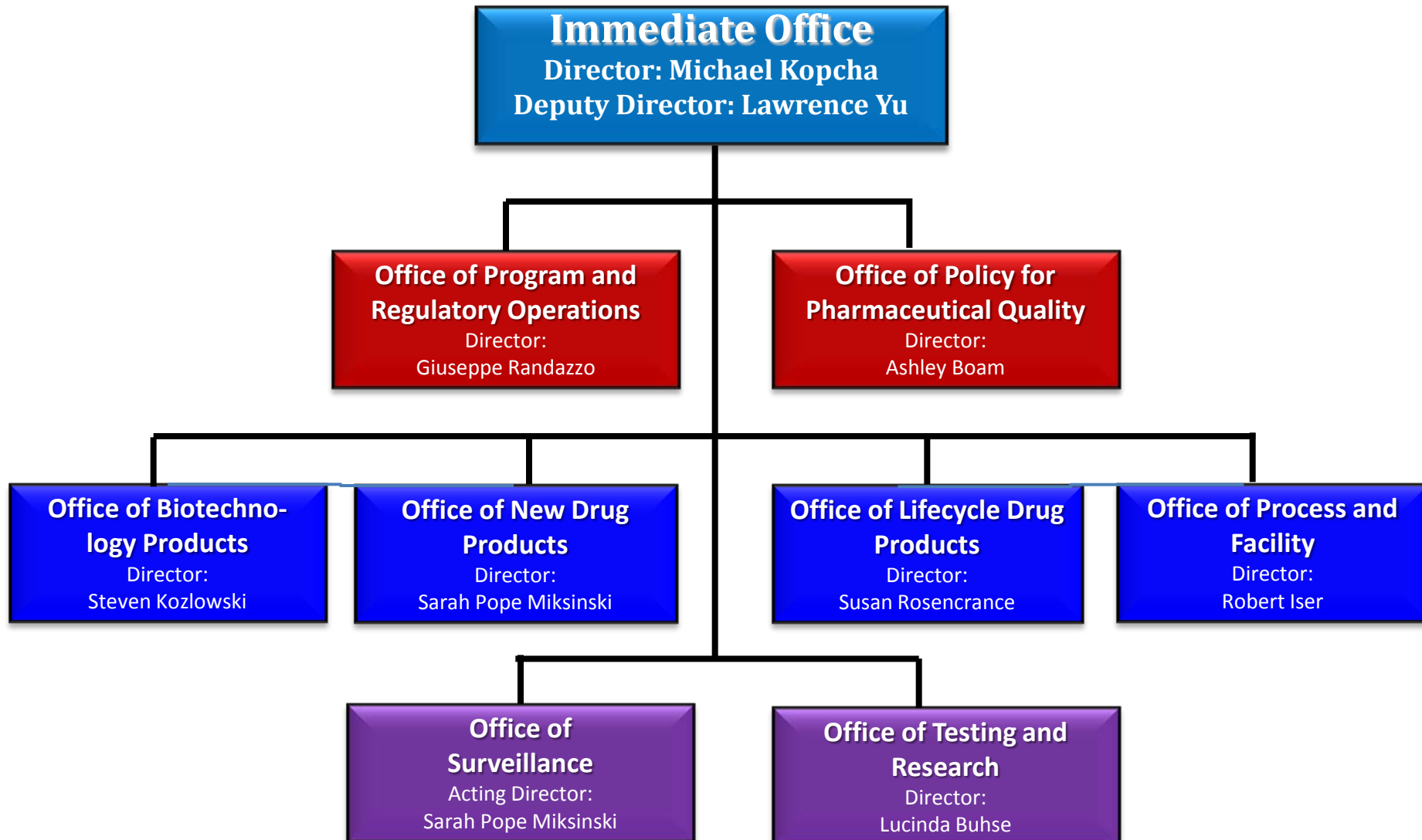
Advances FDA's Quality Initiative to the next level



The link to the patient/consumer...

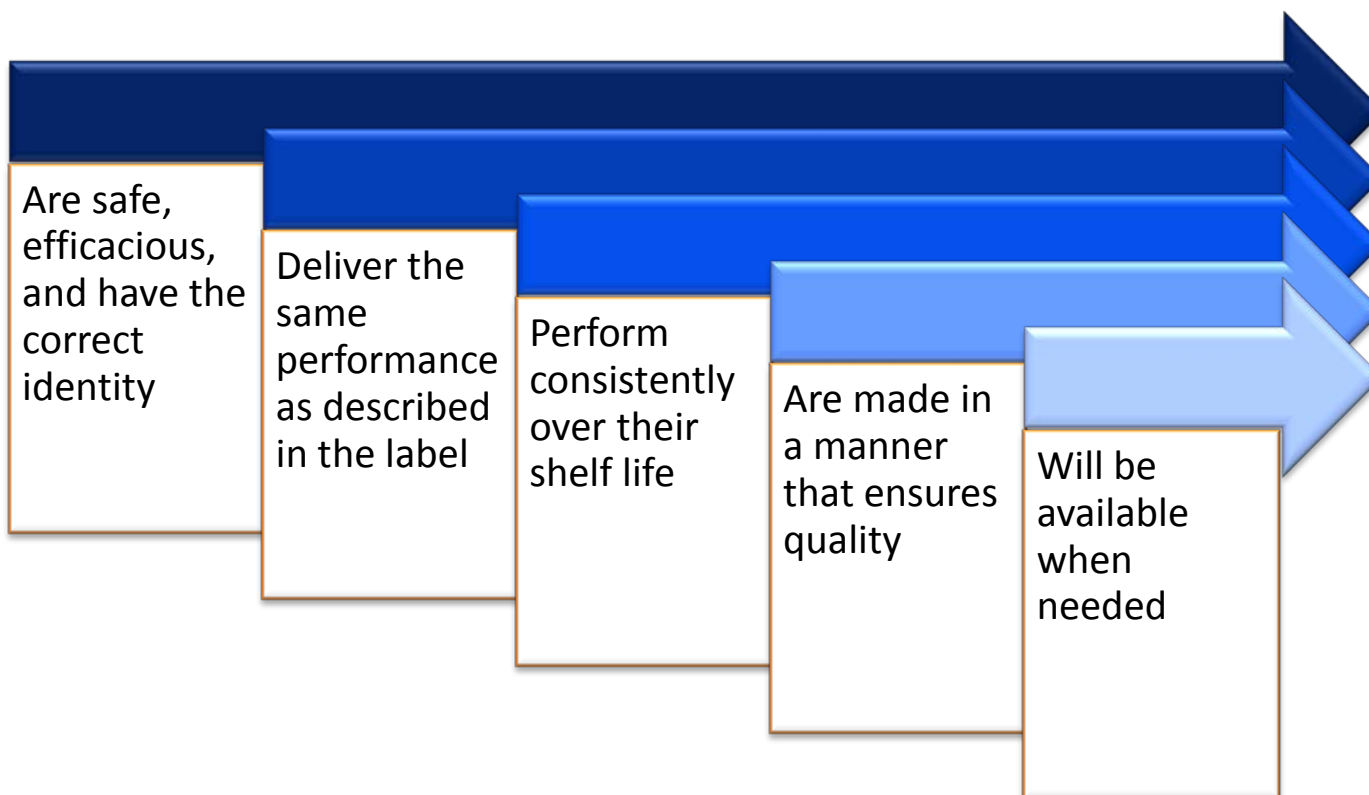


Office of Pharmaceutical Quality



Expectations for Quality

Patients and caregivers assume that their drugs:



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

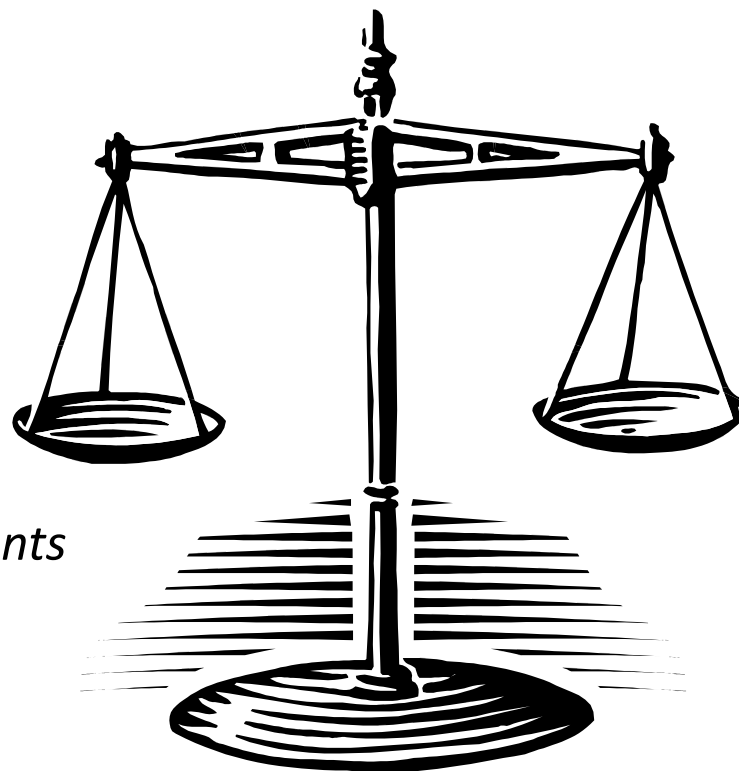
Clinical Relevance - The Continuing Dialog

- 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

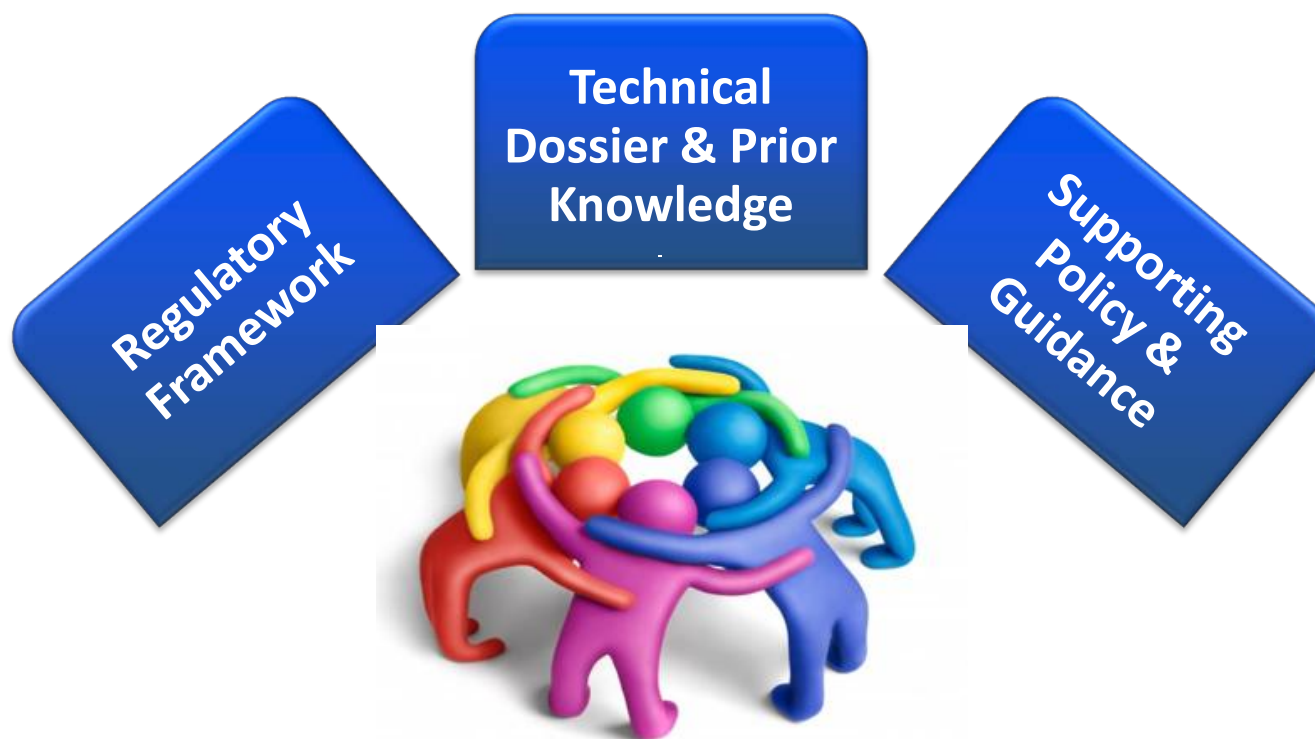
Clinical Relevance – Context

- 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



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

Clinical Relevance – Selected Initiatives

- Breakthrough Therapies – lessons learned
- Quality Overall Summary
 - Risk communication
 - Review efficiency
- Review process innovations
- Product Quality Benefit Risk Framework
 - Started in 2014
 - Developed framework for consideration of quality deficiencies within clinical context of proposed product

Risk Communication

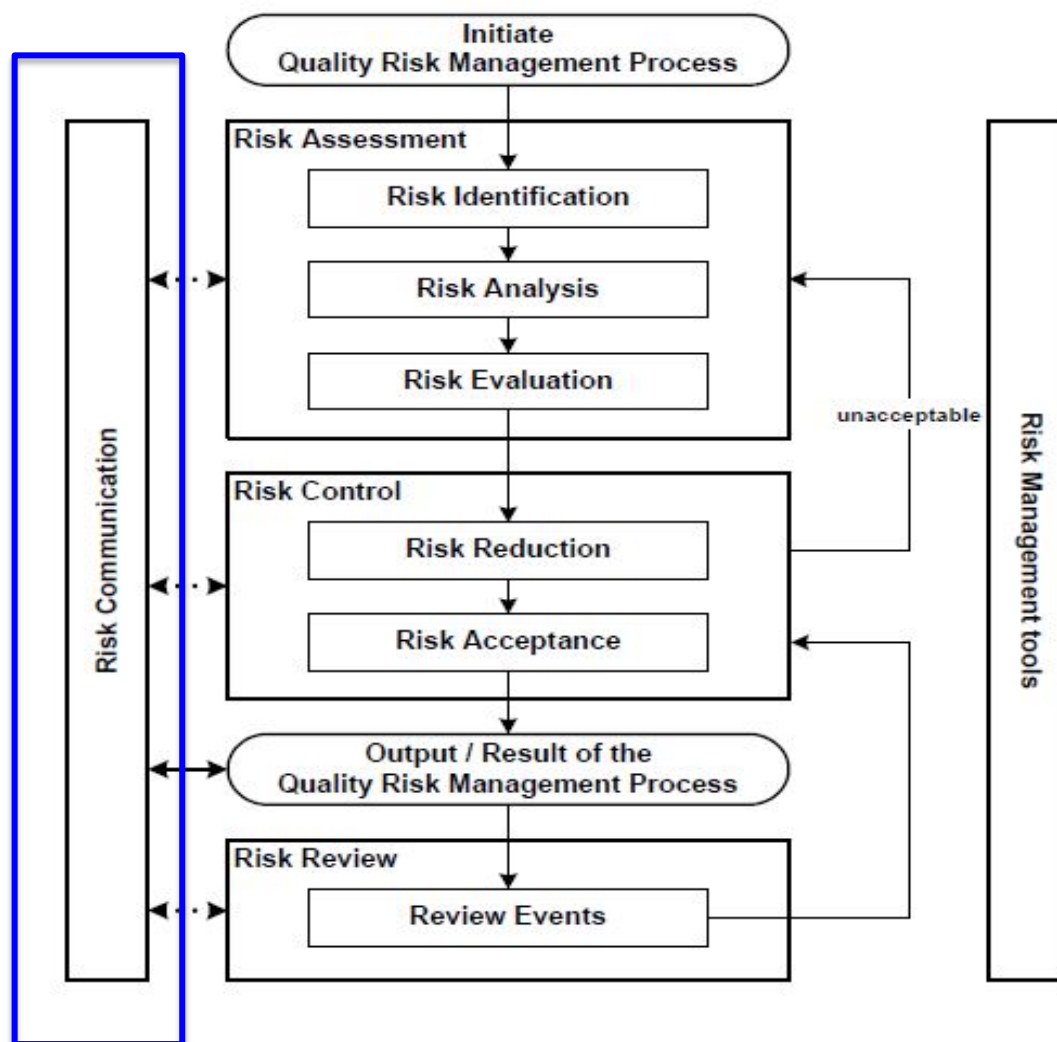
Excerpts from ICH Q9

“...*risk* is defined as the combination of the probability of occurrence of *harm* and the *severity* of that harm.

However, achieving a shared understanding of the application of risk management among diverse stakeholders is difficult because each stakeholder might perceive different potential harms, place a different probability on each harm occurring and attribute different severities to each harm.

...there are a variety of stakeholders...the protection of the patient by managing the risk to quality should be considered of prime importance.”

Risk Communication (ICH Q9)



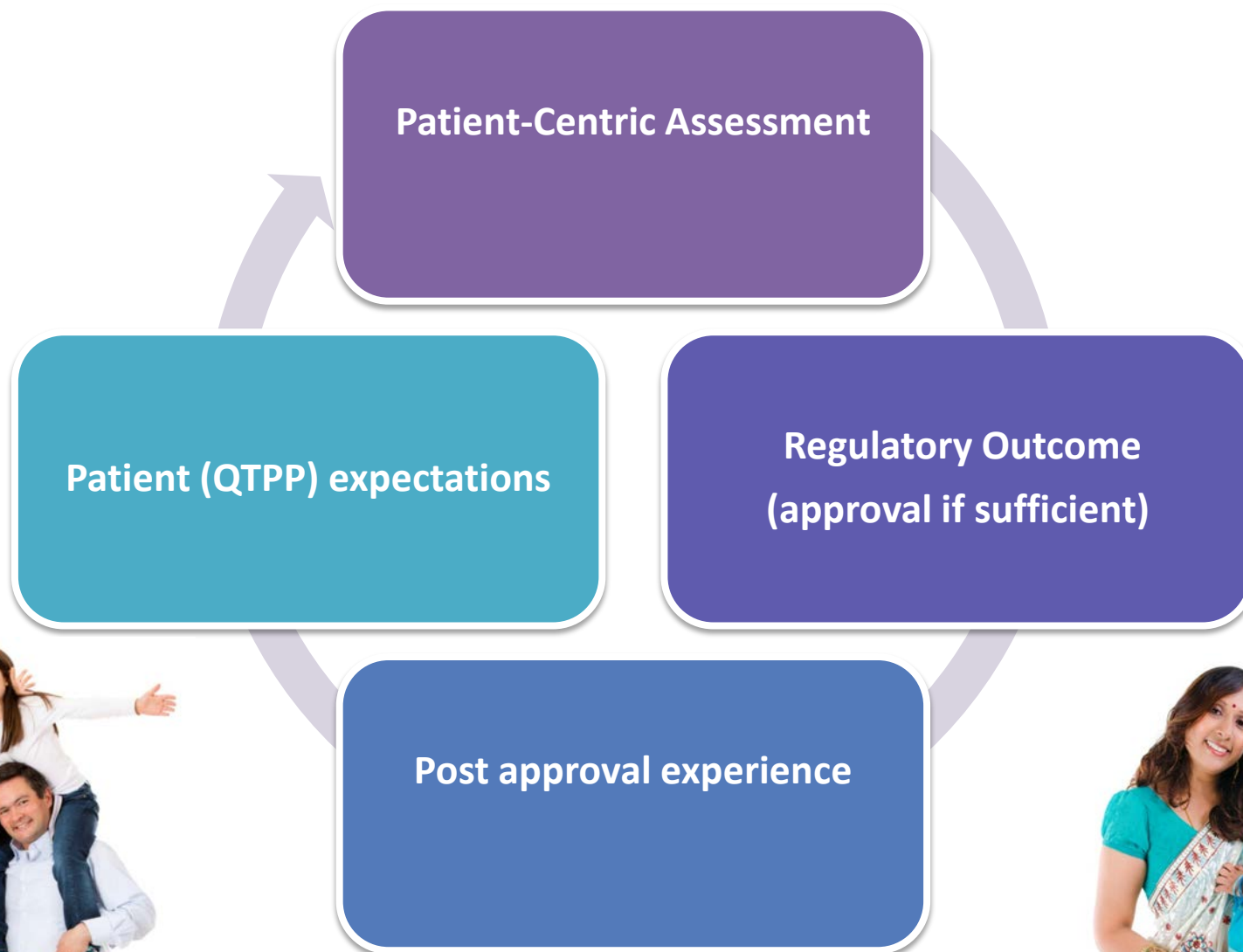
Risk Communication/General

- Frequent interfaces of risk communication in all stages of quality risk management
- Similarly true for various stages of review and assessment
- Various types of risk communication
 - Dossier
 - Dialog
 - Information available on site
- From a practical standpoint (e.g.)
 - Risk identification and assessment
 - Risk communication

Effective Risk Communication

- Confirms high-level alignment first
- Builds common understanding
- Considers the needs of parties in discussion
 - What happens after the discussion?
- Balances technical debates with overall goals
- Timeframes – “Right conversation, right time”
- Allows time for idea generation and/or information digestion
- Considers the intended output of the dialog

Clinical Relevance - A Lifecycle Approach



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!