Generic Drug Product Quality Assessment

Robert Berendt, PhD
Branch Chief

Office of Lifecycle Drug Products
Office of Pharmaceutical Quality
CDER/FDA

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Generic Drug Product Quality

Overview

- Team-based quality assessment
- Key considerations
- Drug product quality assessment
  - Drug substance
  - Drug product
  - Labeling
- Major deficiencies
- Take-away message

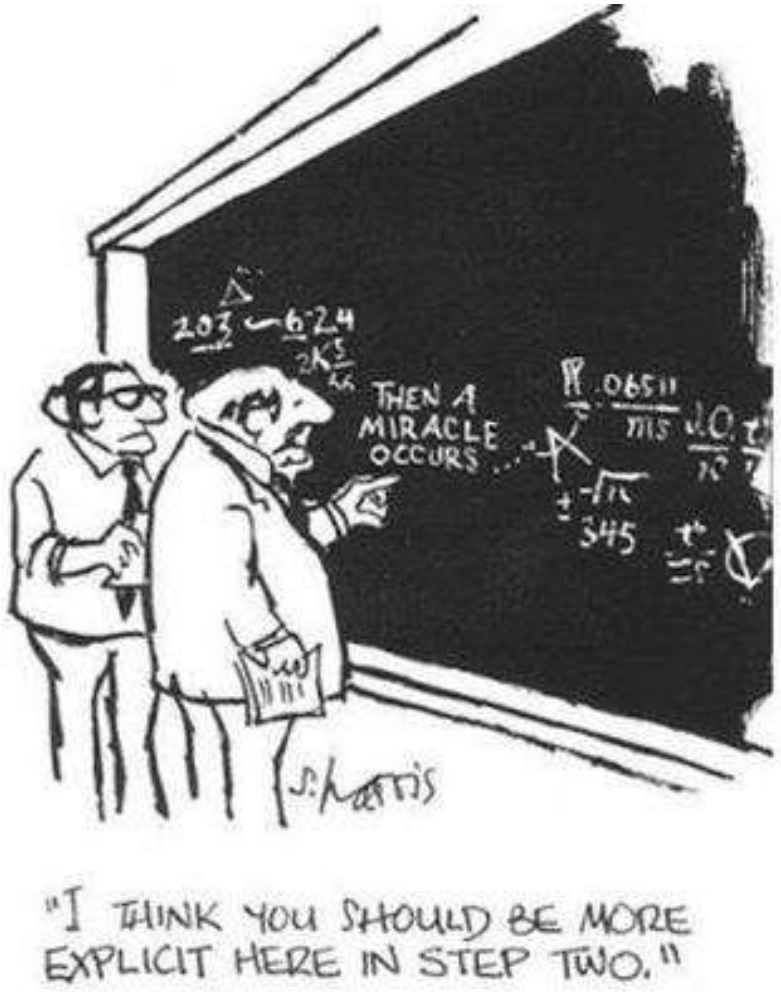
ANDA Quality Assessment (Team-Based)

• Drug Substance* • Drug Product • Labeling	Office of Lifecycle Drug Products (OLDP) **Drug Product Quality Assessment**
• Process • Facilities • Microbiology	Office of Process and Facilities (OPF)
• Biopharmaceutics	Office of New Drug Products (ONDP)*

*Review of Drug Substance also involves ONDP's Division of Lifecycle API

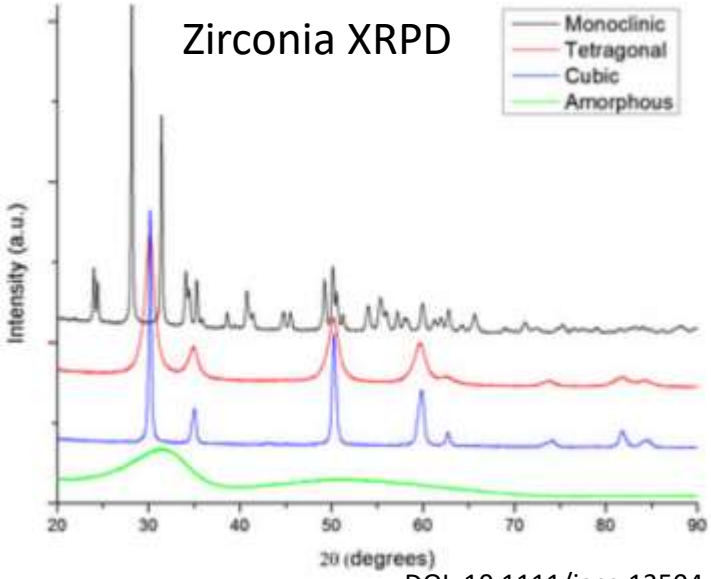
Key Considerations: Your application should…

- ☆ Meet all regulatory requirements
- ☆ Demonstrate product understanding (CQAs)
- ☆ Mitigate risks
- ☆ Provide supporting data



Drug Substance

- Typical drug substance CQAs
  - Polymorphism
  - Particle size
  - Solubility (pH dependence)
  - Chemical stability
- Differences among suppliers
- Risks to drug product quality
  - Solution for injection?
  - Modified-release tablet?



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Product Design and Formulation

- Design and formulation differences from innovator product (RLD)
  - May be allowed (21 CFR 314.94)
  - But may increase risk
- Demonstrate that differences do not affect safety
- Consider size, shape, and visual differences
- Consider patient and administration

Control of Excipients

- USP-NF monograph testing = minimum requirement
- Communicate with the supplier to ensure understanding of your raw materials
- Additional control strategies/tests may be warranted
  - Particle size distribution
  - Polymer viscosity range
  - BSE/TSE
  - Melamine contamination
  - Impurities

Control of Drug Product

- Finished product testing alone should not be relied upon to ensure quality
- Impurities
  - Refer to MAPP 5017.2 and ICH guidance (ICH Q3A-Q3D, M7)
  - Caution: Submission of pharm/tox data in an amendment may significantly alter the assessment timeline
- Analytical methods
  - Provide the standard test procedure (STP) for all testing
  - Provide validation/verification/transfer reports
  - Referencing compendia or DMF alone is insufficient
- Assay – drug substance and critical excipients

Container Closure System

- Appropriate to ensure quality over proposed shelf life?
- Safety, function, performance, compatibility
  - Chemical stability? (oxygen scavengers, desiccant, nitrogen gas, etc.)
  - Physical stability? (desiccant, structural protection, etc.)
  - Compatibility and protection from contamination (glass delamination, extractable/leachable assessment, etc.)
  - Consider in-use stability issues that may require additional data

Container Closure System

Finished Product Stability

- Poor stability often a result of lack of product understanding
- Accelerated and long-term (6 months at filing)
- Photostability
- In-use stability
- Test results per final specification to support the shelf life
  - Examples of missing testing/results
    - Physical stability (polymorphism, phase changes)
    - In vitro release testing (dissolution)

Labeling

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing infor listed.

Major Deficiencies – Drug Product Quality

(list not comprehensive)

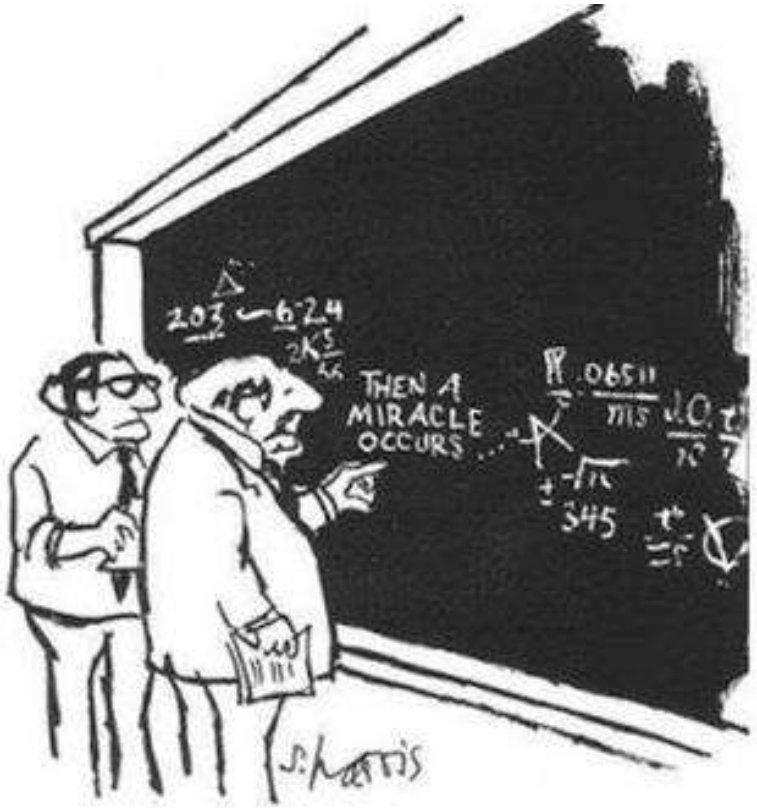
- Missing toxicological studies to qualify an unqualified impurity
- Unacceptable physical properties for drug product
- Need full-term stability data to establish expiration dating
- Failure to identify or include CQAs or methods for controlling them
- Insufficient data to support use-related risk analysis and any human factors studies associated with the proposed product
- Insufficient data to support drug/device compatibility
- Lack of safety assessment of extractables and leachables, inadequate assessment of extractables and leachables, or submission of that assessment in an unsolicited amendment

Notable FDA Documents

Topic	Resource Title
Related substance impurities	FDA MAPP 5017.2: Establishing Impurity Acceptance Criteria As Part of Specifications for NDAs, ANDAs, and BLAs Based on Clinical Relevance (January 2018)
Polymorphism	FDA Guidance for Industry: ANDAs: Pharmaceutical Solid Polymorphism (July 2007)
Product design	FDA Guidance for Industry: Size, Shape, and Other Physical Attributes of Generic Tablets and Capsules (June 2015)
Product design	FDA Guidance for Industry: Tablet Scoring: Nomenclature, Labeling, and Data for Evaluation (March 2013)
Raw materials/ Excipients	Pharmaceutical Components at Risk for Melamine Contamination (August 2009)
Major deficiencies	FDA Guidance for Industry: ANDA Submissions — Amendments to Abbreviated New Drug Applications Under GDUFA (October 2017)

Generic Drug Product Quality Assessment

- We share a common goal
- Ensure that your product can deliver the therapeutic benefit



"I THINK YOU SHOULD BE MORE EXPLICIT HERE IN STEP TWO."

Acknowledgements

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Thank you


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