U.S. FOOD & DRUG ADMINISTRATION

Stability – Why do we care?/Justifying your product!

Frank Holcombe, Jr., PhD
Advisor
IO/OLDP/OPQ/CDER/FDA

Outline

Introduction
Expectations
Considerations
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Guidance Content
Final Thoughts

Why Do We Care?

- Product Release Status — Acceptable
- Time — ?
- Environment — ?
- Patient Use Product Status — ?

- Stability Program – A Rationally Designed Data Collection Program
- Data Describing Product Characteristics Over Time
- Result Is A Stability Profile
- Can Be Considered A Product Quality Measure

Expectations

- Rational Design To Allow Evaluation
- What Changes Occur Or Can Be Expected To Occur
- What Is Important
  Efficacy, Safety, Quality (Performance)

Expectations

What Is Important?

- Efficacy - Drug Substance Content
- Safety - Degradation Products
- Performance (Quality)-
  - Drug Substance Availability
  - Physicochemical Properties

Expectations

What Is Important May Be Product Specific

- Physicochemical Properties
  - Tablet Hardness – Chewable Tablets
  - pH – Unbuffered Solution
  - Viscosity – Ophthalmic Solutions

Expectations

- ICH Q1 Guidance Recommendations Will Be Followed
- Other ICH Guidance May Be Applicable
- USP/NF Requirements Are Applicable
- Relevant FDA Guidance Is Applicable

Considerations

What Might Affect the Important Product Properties?

- Formulation/Component Interactions
- Light
- Temperature
- Chemical Degradation

Considerations

- Analytical Capability
- What Change Is Expected
- What Should Be Tested For
- Sample Generation
- Valid/Appropriate Test Methods

Guidance

ICH Q1A(R2)	Stability Testing of New drug Substances and Products
ICH Q1B	Stability Testing: Photostability Testing of New Drug Substances and Products
ICH Q1C	Stability Testing for New Dosage Forms
ICH Q1D	Bracketing and Matrixing Designs of New Drug Substances and Products

Guidance

ICH Q1E Evaluation of Stability Data

Guidance for Industry

ANDAs: Stability Testing of Drug Substances and Drug Products Questions and Answers

United States Pharmacopeia/National Formulary

Guidance

SUPAC-IR Immediate Release Solid Oral Dosage Forms Scale Up and Postapproval Changes: Chemistry, Manufacturing and Controls; In Vitro Dissolution Testing, and In Vivo Bioequivalence Documentation

SUPAC-MR Modified Release Solid Oral Dosage Forms Scale Up and Postapproval Changes

SUPAC-SS Nonsterile Semisolid Dosage Forms Scale Up and Postapproval Changes

- Product Criteria

  ICH Q3A – Q3E Impurities

  ICH Q6A – Q6B Specifications

Guidance Content

ICH Q1A(R2) - The Basic Guidance

Batch Recommendations - Multiple, Scale

Storage Conditions - Standard Conditions Across Regions

Study Commitment - Relate Market Product to Application Data

Test Frequency - Time Intervals

Guidance Content

ICH Q1B Photostability Testing

- Provides Standard Conditions for Testing
- Guide for Packaging Considerations

Guidance Content

ICH Q1C New Dosage Forms

- Applies to Owner of Existing Application
- Follow Principles of Q1A
- Potential for Reduced Database on Submission

Guidance Content

ICH Q1D Bracketing and Matrixing

Reduced Design
Reduction Extent of Testing

- Bracketing – Exclusion of Samples
- Matrixing – Elimination of Testing at Selected Time Points

Guidance Content

ICH Q1E Data Evaluation

- Discussion of Determination of Retest Period or Shelf-Life Estimation
- Based on Accelerated, Intermediate, Long Term Study Results
- Treatment of Multiple Batches, Variable Data, Statistical Models

Guidance Content

SUPAC-IR, SUPAC-MR, SUPAC-SS

Recommendations for Product Data and Submission Categories for Certain Postapproval Changes

Stability –

- Batch Scale
- Number of Batches
- Study Length, Conditions
- Study Commitment

Final Thoughts

- Use The Available Guidance
- Justify Deviations
- Identify Relevant Product Characteristics
- Maintain The Protocol