Emerging Stability Expectations in OGD An Update

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Dr. Radhika Rajagopalan delivered a presentation on Emerging Stability Expectations in OGD. In this presentation, she indicated that OGD was investigating the implementation of ICH Q1A for drug products.

What led us to this situation?

Current Status

- OGD does not have a formal published Stability Guidance. Therefore OGD has had to rely on other Guidances.
  - 1987 Stability Guidance
  - Draft 1998 Stability Guidance
  - ICH documents
- Questions are currently addressed on a case by case basis.

Field Alert Reports

- Search of Field Alert Reports (FARs) since January, 2011 show >20% are for stability failures. These include:
  - Out of Specification (OOS) for known degradants
  - OOS for unidentified degradants
  - OOS for Total degradants
  - Dissolution rate failures
  - Reduced expiry dating
- OGD continues to receive supplements to reduce expiry dating due to stability failure.

OGD Stability Work Group

- WG consists of Drs. Upinder Atwal, Suhas Patankar, Raman Murali and Radhika Rajagopalan.
- Make an evaluation of where OGD is and where OGD should be.
- OGD specific Guidance vs. utilize existing tools.
- Practices in the Office of New Drugs that may provide insight.
- Identify areas needing training, change of culture and time frames.

Available Tools

- MAPP 5016.1 Applying ICH Q8(R2), Q9, and Q10 Principles to CMC Review.
- Q1A (R2) Stability Testing of New Drug Substances and Products*
- Q1B Photostability Testing of New Drug Substances and Products
- [Q1C Stability Testing for New Dosage Forms]
- Q1D Bracketing and Matrixing Designs for Stability Testing of New Drug Substances and Products
- Q1E Evaluation of Stability Data- statistical analysis

Observations

- Office of New Drug Quality Assessment (ONDQA) has adopted ICH Q1A
- OGD has successfully adopted ICH Q1A for Drug Substances
- The logical extension is to adopt ICH Q1A for ANDA Drug Products.

What are the major changes?

Current Requirements

- One lot of drug product which is at least 10% of the intended market batch size or 100,000 dosage units, whichever is greater.
- Three months accelerated stability data at 40 C 2 C/75% RH 5% RH and,
- Three months long term stability data at 25 C 2 C/60% RH 5% RH.
- Note that the size of the exhibit lot may vary upon consultation with the Office.

New Stability Conditions

- Long Term
  - 25 C 2 C/60% RH 5% RH - 12 months or
  - 30 C 2 C/65% RH 5% RH - 12 months
    and,
- Intermediate
  - 30 C 2 C/65% RH 5% RH - 12 months
    and,
- Accelerated
  - 40 C 2 C/75% RH 5% RH - 6 months

New Batch Requirements

- Stability data should be supplied on at least three primary batches of drug product.
  - Same formulation, manufacturing process and specifications as those for market.
  - Same container/closure system as proposed for market.
  - 2 of the 3 batches should be at least pilot scale.
  - Different lots of API where possible.

Pros and Cons

- Industry will have to revise their scheduling to accommodate new filing requirements.
- Industry and OGD will have a single consistent standard.
- Increased knowledge of product consistent with QbD paradigm.
- Increased performance data should reduce FARs for stability and therefore the loss of resources to failure investigations and recalls.

Emerging Stability Expectations

- The working group has completed a draft of a Guidance and is currently obtaining clearance for posting.
- Industry will have the opportunity to provide comments.
- After evaluation of comments and revision as necessary, the guidance will be posted.
- During the evaluation, an implementation strategy will be formulated and after final posting executed

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