

Quality Standards for Medicines, Supplements, and Food Ingredients throughout the World

# USP PANCRELIPASE UPDATE (Monograph Revision)

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# History of Pancreatin/Pancrelipase Monographs

- Pancreatin Monograph published in USP IX (1916)
- Revised in USP XI (1936)
- Transferred from USP XIV to NF (1947)
- Revised and published in its current state in NF XIV (1975), lipase assay added. Pancrelipase monographs added.
- Transferred from National Formulary Official in USP since July 1, 1980



# The need for revision of the monographs

- Monograph tests are outdated
- Issues remain with assays and specifications
- Interchangeability issues
- Colonopathy, caused by overdosing observed in Cystic Fibrosis patients
- Change of regulatory approach by FDA



# Monograph Revision Approach

- Ad Hoc Advisory Panel was created by Biologics & Biotechnology: Proteins and Polysaccharides Expert Committee
- Issues with the monograph are discussed and the revision directions recommended to the Expert Committee



# Colipase Issue

- Purified pancreatin lipase is colipase sensitive
- Experiments were done to check if colipase addition is necessary for USP Pancreatin Lipase Reference standard
- Conclusions:
  - Current Reference Standard, and all commercially available lots studied are not colipase-sensitive
  - The test for colipase still may be needed (Input welcome!)



# Tightening of the Assay Range

- Current lipase assay calls for 8-16 units of lipase activity per ml in assay, both for RS and sample solution.
- The given conditions may yield up to 100% difference in lipase activity between sample and standard solution
- It was suggested to tighten this range to be not more than +/- 30%

# Reagent Considerations

- There are currently no Olive Oil and Acacia USP Reference Standards for use in Lipase assay
- Both substances are natural and hard to characterize fully
- There is Olive Oil Authentic Substance, available from USP, but its suitability for use in the lipase assay has not yet been established
- Further directions
  - USP may consider to develop Olive Oil RS for Lipase Assay
  - The development of Acacia RS is unlikely, unless the reliable characterization methods can be obtained (Input welcome!)



# Microbial Testing Issues

- Current monographs require compliance with <61> and <62> for the absence of *Salmonella* species and *E. coli*
- Following tests are suggested to be added
  - Total Aerobic Count and Yeast Mold Count
  - Absence of *P. aeruginosa* (method established)
  - Absence of *B. cepacia* (no current method established, input welcome!)
  - Porcine Endogenous Retrovirus (PERV)

# Dissolution Tests For Delayed-Release Products

- Single Unit Testing (current test uses 10 capsules) is will be developed for the Delayed-Release products monographs
- The issues to decide
  - Type of apparatus
  - The readout method (lipase activity vs. optical absorbance, absorbance wavelength)
- Separate gastric resistance test is required if absorbance readout is adopted



# Purity and Identity Tests

- There are no purity and identity tests in current USP monographs
- FDA recommends analytical Identity test (HPLC, PAGE, IEF etc.) for current NDAs
- FDA recommends procedures for estimating impurities
- The main challenge is the inherent variability of the animal origin material and reproducibility of results
- Input welcome from stakeholders

# Specification

- Current specifications for Pancrelipase Drug Products call for 90-150% of labeled enzyme
- Overages are the main concern with Pancrelipase products
- Current FDA recommendations calls for 100% formulation

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*Thank you*

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