Positron Emission Tomography Drugs Workshop

PET: Product Lifecycle

Presented by: Ramesh Raghavachari, PhD, Chief, Branch I/DPMA I/
Office of Lifecycle Drug Products/OPQ/CDER

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The Lifecycle

New Drug

Post Approval

Generic Drug

Post-Approval of a Generic Drug
Why Post-Approval CMC Changes?

- Continuous improvement
  - Product Optimization
  - Incorporating new technologies
  - Process improvement (based on historical knowledge)
- Regulatory Requirements/Commitments
- Product quality issues
- Business Reasons
  - Supply & Demand

Types of Supplements

- Efficacy supplements
  - New Indication
  - Changes in the dosing regimen
  - Safety Changes (precautionary statements/Blackbox warning/new contraindications)
  - Addition of dosing information for special population
- Labeling supplements
  - Changes in the approved labeling, including prescribing information, immediate container and carton labels, medication guide, etc.
- CMC Supplements
  - Changes in the drug substance and/or drug product manufacturing, analytical changes, site changes etc.
Typical Post-Approval CMC Changes

• Drug Substance - Changes to:
  – New manufacturing site (including for the kits)
  – New supplier for regulatory starting materials
  – Route/Method of synthesis
  – Manufacturing process
  – In-process controls and/or drug substance specifications
  – Shelf life or retest period....

Typical Post-Approval CMC Changes

• Drug Product - Changes to:
  – New manufacturing site
  – Manufacturing process and/or equipment
  – Formulation
  – Container closure system
  – Specifications
  – Shelf-life (extension or reduction)
  – Introduction of new strengths
Regulatory Basis for Post-Approval Changes

• 21 CFR 314.70
  § 314.70 Supplements and other changes to an approved application.
  – The applicant must notify FDA about each change in each condition established in an approved application

Regulatory Basis- FDA Guidances

• Changes to an approved NDA or ANDA
• Scale-up and post-approval changes (SUPAC)
• SUPAC: Manufacturing equipment addendum
• CMC post-approval manufacturing changes to be documented in annual report
• Comparability protocol – Chemistry, Manufacturing, and Controls information
• PAC-ATLS: post-approval changes – analytical testing laboratories sites
Classification of CMC Changes

- Major changes (Prior Approval Supplements)
  - High impact to the product quality
  - Cannot be implemented until approved
  - Four months review clock

- Moderate changes (Changes Being Effected in 30 Days or Changes Being Effected in 0 Days Supplements)
  - Moderate impact to the product quality
  - Can be implemented 30 days after submission at the applicants own risk
  - Six months review clock

- Minor changes (Annual Reportable)
  - Minimal risk to product quality
  - Can be implemented immediately after submission
  - Six months review clock for supplements

Response to Some Questions?

Question:
- For CMC, if the equipment changes, but the testing and specifications do not change, can this be submitted as part of the product’s Annual Report?

Response:
It depends upon the exact change- PAS or CBE-30 certainly not AR!
Response to Some Questions?

Question:
• What is FDA’s current response/approval timelines for PAS submissions?

Response:
Prior Approval Supplements have a PDUFA clock of Four months from the date of receipt.

Thank you!