Panel Discussion: Industry Perspective on PET Drug Manufacturing

Standards for ImagingEndpoints & Manufacturing of PET Radiopharmaceutical Products in Clinical Trials
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Panel Presentations

1. Introduction, **Sally Schwarz**, MS, BCNP, Washington University, St. Louis, MO
2. Issues in PET Drug Manufacturing, **Steve Zigler**, PhD, PETNET (ANDA, Contract Manufacturing & User Fees)
4. Experience with FDA Inspections of PET Manufacturing Sites, **Jack Coffey**, Cardinal Health
5. How to Establish a Model Compliance Program for PET Manufacturing, **Anwer Rizvi**, PhD, IBA Molecular
6. Comparison US and EU Guidance on PET GMP, **Richard Frank**, MD, PhD, GE Healthcare
Introduction: Why is PET Unique?

- Short half-life, usually minutes to hours
- Batch produced provides a limited supply—usually hours—and can be produced for a single dose
- Mass contained in the final product is usually nanogram-microgram
- Quality control issues due to short half-life
- Most quality control testing performed for each batch
Why is PET Unique?

- Similar PET drugs produced at multiple sites; impossible to supply all US locations from same site.
- Multiple modules for production of FDG at a single site. Same? Different?
- Small-scale production facilities have a limited number of personnel and resources dedicated to preparation and testing activities.
- Non-proprietary nature of current PET drugs—process for NDA submission?
- PET drug products involve distributed manufacturing.
US Food & Drug Administration Modernization Act (FDAMA) 1997

- 1997: US Food & Drug Modernization Act (FDAMA) required establishment of PET Radiopharmaceutical (RP) Good Manufacturing Practice (GMP)

- FDAMA required a new approval path and separate Current Good Manufacturing Practices (CGMP) for PET from those CGMP for drugs

- Prior to adoption of final PET CGMP rule, FDAMA required PET Radiopharmaceutical (RP) production to follow:
  - United States Pharmacopeia (USP) PET RP monographs, if available and
  - USP General Chapter <823> for Production of PET RP
FDA Published Final Rule
21 CFR Part 212; Current Good Manufacturing (CGMP) for Positron Emission Tomography (PET) Drugs

December 10, 2009

- Regulation is effective December 12, 2011
- Regulation applies solely to PET drugs.
- Submission of a New Drug Application (NDA) or an Abbreviated New Drug Application (ANDA) is required for all PET drugs no later than 2 years after the enactment date of the Final Rule
  - F-18 FDG, F-18 Fluoride, N-13 Ammonia
21 CFR Part 212 is a rule/regulation that contains binding requirements.

The rule §212.5(b) provides that investigational and research PET drugs, CGMP may be met by producing PET drugs:

- in accordance with Part 212, or
- in accordance with USP General Chapter <823> “Radiopharmaceuticals for Positron Emission Tomography – Compounding,” May 1, 2009, 32nd Edition, and USP Monographs if available

1. PET Drugs produced under Investigational New Drug (IND) Application in accordance with Part 312 of this chapter or
2. PET Drugs approved through a Radioactive Drug Research Committee (RDRC) in accordance with Part 361 of this chapter
FDA Guidance
PET Drugs—Current Good Manufacturing Practice (CGMP), December 2009

- Describes FDA’s current thinking on individual issues addressed by the CGMP rule
- Not binding on FDA or the public
- Recommends approaches to complying with statutory rules and regulatory requirements
- You can use alternative approaches if they satisfy the requirements
Issues for Consideration for the PET Community & FDA

🎁 Need to file NDA or ANDA for current PET drugs by 12-12-11—which one?

🎁 What is involved in an ANDA submission?
  ➢ should be equivalent (?) to the label of the NDA drug
  ➢ How can we best reach the PET community to assist them?

🎁 Can a “template” be developed to assist the community?
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- Fee structure ??? for ANDAs and NDAs

- Overall there are significant impacts for stakeholders and the FDA