Panel Discussion: Industry Perspective on PET Drug Manufacturing

Standards for Imaging Endpoints & Manufacturing of PET Radiopharmaceutical Products in Clinical Trials
RSNA/SNM/FDA Natcher Center
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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)
3. Introduction of a New Proprietary PET Drug in a Changing Manufacturing Environment **John Lister James**, PhD, Avid Radiopharmaceuticals
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

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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

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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

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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; Final Rule CGMP for PET Drugs

December 10, 2009

- 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

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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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Issues for Consideration for the PET Community & FDA

- Fee structure ??? for ANDAs and NDAs
- Overall there are significant impacts for stakeholders and the FDA