Overview of FDA Regulations and Guidance Documents related to PET Drug Chemistry

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I will not discuss investigational agents, nor will I discuss indications or uses of any approved products

What this portion of my talk isn't:

A comprehensive review of regulations with instructions on how to comply

What this portion of my talk is:

An overview designed to stimulate discussion of chemistry best practices

FDA Laws and Regulations

- Congress enacts laws
  - Food, Drug, and Cosmetic Act (FD&C Act)
  - FDA Modernization Act (FDAMA)
  - Prescription Drug User Fee Act (PDUFA)
  - Drug Quality and Security Act (DQSA)
  - Etc.
- Government agencies prepare regulations
  - Code of Federal Regulations
  - 21 CFR contains regulations administered by FDA for foods and drugs
- Agencies may also prepare guidance documents that describe current thinking on a particular regulation
  - Non-enforceable and non-binding

Some Pertinent Regulations…

21 CFR Part 212

Current Good Manufacturing Practice for PET Drugs

Contents

21 CFR Part 315

Diagnostic Radiopharmaceuticals

Contents

Defines radiopharmaceuticals and FDA expectations for safety, efficacy, and indications

21 CFR Part 361

Prescription Drugs For Human Use Generally Recognized As Safe And Effective And Not Misbranded: Drugs Used In Research

Contents

Defines conditions and requirements for Radioactive Drug Research Committees (RDRCs)

Some Pertinent Guidance Documents…

Not an exhaustive list

- Developing Medical Imaging Drug and Biological Products
  - Part 1: Conducting Safety Assessments
  - Part 2: Clinical Indications
  - Part 3: Design, Analysis, and Interpretation of Clinical Studies
- Investigational New Drug Applications for Positron Emission Tomography (PET) Drugs (describes Expanded Access)
- The Radioactive Drug Research Committee: Human Research Without An Investigational New Drug Application
- PET Drugs — Current Good Manufacturing Practice (CGMP) (Small Entity Compliance Guide)
- PET Drugs — Current Good Manufacturing Practice (CGMP)
- Media Fills for Validation of Aseptic Preparations for Positron Emission Tomography (PET) Drugs
- Validation of analytical procedures (see also ICH harmonization documents)

CMC Section is not specifically discussed in many of these Guidance Documents…

…except one

Not an exhaustive list

- Developing Medical Imaging Drug and Biological Products
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Guidance: Investigational New Drug Applications for PET Drugs (2012)

- Describes FDA expectations for Chemistry, Manufacturing, and Controls Section
- Radioactive Drug Substance, Reference Standards, and Precursors
  - Recognizes that drug substance may not be isolated separately from the drug product
  - Names, structures, relevant physical, chemical, and biological properties

Guidance: Investigational New Drug Applications for PET Drugs (2012)

- Radioactive Drug Substance, Reference Standards, and Precursors (cont.)
  - Manufacturers
  - Description of synthesis and production processes for the radionuclide, precursor, and the radioactive drug substance
  - Materials controls
  - Control of critical steps (e.g., intermediate isolation)

Guidance: Investigational New Drug Applications for PET Drugs (2012)

- Radioactive Drug Substance, Reference Standards, and Precursors (cont.)
  - Characterization of non-radioactive version of the radioactive drug substance and chromatographic comparisons
  - Characterization of precursor
  - Reference standards and/or materials

Guidance: Investigational New Drug Applications for PET Drugs (2012)

- Radioactive Drug Product
  - Container closure
  - Excipients or other additives
  - List of all testing performed

I hope this has served to stimulate discussion of chemistry best practices amongst speakers and attendees