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

Subpart A — General Provisions
Subpart B — Personnel and Resources
Subpart C — Quality Assurance
Subpart D — Facilities and Equipment
Subpart E — Control of Components, Containers, and Closures
Subpart F — Production and Process Controls
Subpart G — Laboratory Controls
Subpart H — Finished Drug Product Controls and Acceptance
Subpart I — Packaging and Labeling
Subpart J — Distribution
Subpart K — Complaint Handling
Subpart L — Records
21 CFR Part 315
Diagnostic Radiopharmaceuticals

Contents
315.1 Scope
315.2 Definition
315.3 General factors relevant to safety and effectiveness
315.4 Indications
315.5 Evaluation of effectiveness
315.6 Evaluation of safety

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
361.1 Radioactive drugs for certain research uses

 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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• 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

• 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)

• 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

• 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