Compounding Radiopharmaceuticals

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Sara Rothman
Office of Compliance
CDER/FDA

Statutory Framework

- Section 503A explicitly excludes radiopharmaceuticals
  - "This section does not apply to . . . radiopharmaceuticals" (section 503A(d)(2))
- Section 503B contains no such language excluding radiopharmaceuticals.
- Accordingly, FDA has determined that section 503A does not apply to the compounding of radiopharmaceuticals, but section 503B does.
- Neither section 503A nor section 503B applies to the repackaging of radiopharmaceuticals.

Draft Guidances: Framework

- Draft guidance for entities **not** registered as outsourcing facilities:
  - Because the exemptions in section 503A do not apply, radiopharmaceuticals compounded by entities not registered as outsourcing facilities are subject to all provisions of the Federal Food, Drug, and Cosmetic Act (FD&C Act) that apply to the production of drugs by conventional manufacturers.

  - The draft guidance describes the conditions under which FDA does not intend to take action for violations of
    - new drug approval requirements,
    - labeling with adequate directions for use requirements, and
    - current good manufacturing practice (CGMP) requirements

    when a State-licensed nuclear pharmacy or Federal facility compounds or repackages radiopharmaceuticals.

Draft Guidances: Framework

- Guidance for entities registered as outsourcing facilities:
  - Describes how FDA would intend to apply section 503B of the FD&C Act to radiopharmaceuticals compounded by outsourcing facilities.
  - It also describes the conditions under which FDA would not intend to take action for violations of new drug approval requirements and labeling with adequate directions for use requirements when an outsourcing facility repackages radiopharmaceuticals.

Draft Guidances: Minor Deviations

- Applicable conditions would depend on whether the type of compounding conducted is limited to "minor deviations" or entails compounding that involves manipulations other than "minor deviations"

- The guidance defines a "minor deviation" as

  A change from the approved labeling in radioactivity, volume, and/or step-by-step procedures made when compounding the radiopharmaceutical from an FDA-approved drug product in a patient-ready dose.

Non-Outsourcing Facility Guidance: Conditions

- Examples of conditions that would be applicable to manipulations other than minor deviations:
  - Compounding by or under the direct supervision of a licensed pharmacist
  - Receipt of valid prescriptions for identified individual patients
  - Using bulk drug substances that are the subject of an applicable United States Pharmacopeia (USP) or National Formulary (NF) monograph
  - The compounded radiopharmaceutical is not essentially a copy of a marketed approved radiopharmaceutical
  - Applicable State requirements are met
  - Compliance with USP Chapter <797>
  - Product labeled with certain information

Non-Outsourcing Facility Guidance: Conditions

- Conditions that would be applicable to minor deviations are similar, with the following exceptions
  - No “essentially a copy” condition
  - No prescription condition
  - No labeling condition (except for provision to comply with NRC labeling requirements)
  - Additional condition that the radiopharmaceutical is compounded from an FDA-approved drug product
  - Additional condition that no substances are added to the radiopharmaceutical unless they are specified in the FDA-approved labeling

Outsourcing Facility Guidance

- The conditions of section 503B apply to compounded radiopharmaceuticals, with specific policies that would be applicable only to the compounding of radiopharmaceuticals by outsourcing facilities:
  - Bulk drug substances—policy consistent with the guidance, “Interim Policy for Compounding Using Bulk Drug Substances Under Section 503B”
  - Essentially a copy provision—not applicable to minor deviations

Comments on the Draft Guidances

- Commenters requested clarification on:
  - Applicability of the draft guidance to certain settings and entities
    - Nuclear medicine physicians/supervised designees
    - Hospital-based nuclear medicine departments
    - Nuclear medicine clinics
  - Beyond-use-dates applicable to compounded radiopharmaceuticals
  - “Essentially a copy” condition
  - “Minor deviations”