Positron Emission Tomography (PET): Additional Questions and Answers Based on December 9, 2009 Stakeholder Call

1. New regulations for manufacturing PET drugs are effective December 12, 2011. In the meantime, what standards will be used for inspection of PET facilities?

When the FDA Modernization Act went into effect in 1997, FDA identified the United States Pharmacopeia (USP), Chapter <823>, as the standard for PET drug production facilities to follow until FDA put new CGMP requirements into effect. During the two-year transition period, FDA will continue to use this standard, although PET drug producers who intend to produce PET drugs for commercial use may choose to transition to the CGMP final rule (21 CFR Part 212) requirements published in the Federal Register of December 10, 2009 (74 FR 65409). After December 12, 2011, producers of PET drugs intended for commercial use will be required to follow the manufacturing requirements specified in Part 212 of Title 21 of the Code of Federal Regulations.

2. What is ”commercial use”? Commercial use means the use of a PET product for diagnosis not under an investigational new drug application (IND) or under the review of a Radioactive Drug Research Committee (RDRC).

3. After the new regulations for manufacturing PET drugs go into effect on December 12, 2011, will PET drug used for investigational and research purposes be subject to the same CGMP requirements as PET drugs intended for commercial and clinical use? Under §212.5(b), PET drugs intended for clinical investigations only, or for research only, may be produced in accordance with either the USP General Chapter <823> titled ”Radiopharmaceuticals for Positron Emission Tomography–Compounding (USP 31/ NF27) 2009 or the CGMP regulations, when effective, at 21 CFR Part 212.

4. USP is a ”living document,” meaning chapters and monographs are often revised. What happens if USP revises Chapter <823> to a different edition? FDA is required under the rules associated with developing regulations to reference a specific edition of the USP. FDA recognizes that the USP is a living document and that it does change from time to time. FDA will propose changes to the rule if the Agency believes that significant acceptable changes are made to the USP such that a different edition should be incorporated into the regulation.

5. After the new PET drug manufacturing rules go into effect on December 12, 2011, will there be circumstances under which PET drugs can be manufactured without an NDA or ANDA? Yes, if the PET drug is being used for clinical research purposes, it does not need an NDA or ANDA. For instance, if a PET drug is produced for the purposes of conducting an investigational study, then an NDA or ANDA is not required. In those cases, the IND or RDRC requirements cover the production of the drug. However, after December 12, 2011, if the PET drug is produced for commercial distribution and use in humans for clinical practice to diagnose a patient, maker of the PET drug must have submitted a new drug or abbreviated new drug application for that drug. The PET drug can continue to be marketed after the application is submitted. PET drug producers who intend to produce PET drugs intended for commercial and clinical use will be required to follow the manufacturing requirements specified in Part 212 of Title 21 of the Code of Federal Regulations.

submission of an appropriate application for one of the PET drugs described in the March 2000 notice.

7. After December 12, 2011, is FDA going to require inspections before PET drug producers can begin making PET radiopharmaceuticals?

FDA generally conducts pre-approval inspections for facilities making PET products, and will continue performing pre-approval inspections of PET drug producing facilities in connection with the approval of NDAs and ANDAs. FDA will also continue to perform routine surveillance inspections of a number of PET facilities each year. FDA does not routinely inspect facilities producing drugs only for clinical investigational work under an IND for compliance with the USP Chapter <823> or CGMP regulations. However, "for cause" inspections of clinical investigational work under an IND or for work under protocols approved by a RDRC will be conducted if FDA needs to evaluate one or more specific issues, such as indications of possibly deficient practices or product quality problems that might affect the safety of research participants.

FDA does require that PET drug facilities producing drugs for commercial use be registered with the FDA and a list of all drugs produced be submitted in accordance with section 510(g) of the Act and 21 CFR Part 207. Any PET facility producing drugs for commercial use that has not yet registered and listed should do so as soon as possible. PET drug facilities that only produce PET drugs for research purposes under an IND or RDRC are not required to register or list.

8. How do the new PET drug manufacturing regulations impact the traditional practices of medicine and pharmacy, where licensed practitioners compound and administer a variety of agents for the treatment of specific conditions?

FDA does not believe that the new PET CGMP’s affect the traditional practices of medicine or pharmacy. The Modernization Act specifically requires NDAs and ANDAs for the production of PET drugs for commercial use in human beings and that manufacturers of PET drugs follow current good manufacturing requirements. Although the CGMP regulations govern the production of PET drugs, they do not apply to the prescribing and dispensing of PET drugs to patients which are done under the traditional practices of medicine and pharmacy.

Related Information

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