

GE Healthcare

December 15, 2005

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Documents Management Branch (HFA-305)
Food and Drug Administration
5600 Fishers Lane
Room 1061
Rockville, MD 20852

**Re: Docket No. 2004N-0439
Comments to Proposed Rule
Current Good Manufacturing Practice for Positron Emission Tomography Drugs**

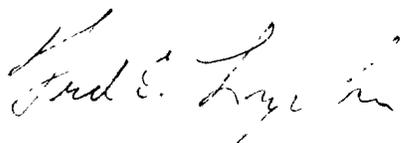
Dear Documents Management Staff:

Reference is made to the subject docket number published in the Federal Register Volume 70, Number 181, page 55038 which issued a proposed rule entitled "Current Good Manufacturing Practice for Positron Emission Tomography Drugs."

At this time, as requested by the Federal Register notice, GE Healthcare is providing its comments to the proposed rule on the following pages. Please note that in some cases our comments make cross-reference to the corresponding Draft Guidance for Current Good Manufacturing Practice for Positron Emission Tomography Drugs (Docket No. 1998D-0266 published in the Federal Register Volume 70, Number 181, page 55145).

Please call me at (609)-514-6573 if you have any questions or comments regarding this submission.

Sincerely,
GE Healthcare



Fred Longenecker
Director, Regulatory Development

2004N-0439

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Proposed Rule – September 20, 2005

Current Good Manufacturing Practice for Positron Emission Tomography Drugs

(Docket No. 2004N-0439)

GE Healthcare Comments

Section 212.1 – Definitions

The definition of *Active Pharmaceutical Ingredient* includes the phrase “is intended to furnish pharmacological activity.” By their very nature diagnostic drugs such as PET drug are specifically not intended to have pharmacological activity. This phrase should be deleted as the remainder of the definition including the phrase “direct effect in the diagnosis or monitoring of a disease or manifestation of a disease in humans” provides sufficient definition of intended use.

The definition of *PET drug* states that it “...includes any non-radioactive reagent, reagent kit, ingredient, nuclide generator, accelerator, target material, electronic synthesizer, or other apparatus or computer program to be used in the preparation of a PET drug.” This definition seems overly broad in that it includes both components and equipment used to produce the PET drug product. We believe that these other items are inappropriate to be included within the definition and ask that this definition be revised or its meaning clarified appropriately.

For the definition of *PET drug product* we suggest revising the term “finished dosage form” to read “finished dosage form suitable for administration to humans”. For a PET drug product to be administered intravenously, it should comply with the sterility requirements for parenterals.

Section 212.5(b) – The proposed rule states that the rule does not apply to production of investigational and research drugs which instead must comply with USP chapter <823> “Radiopharmaceuticals for Positron Emission Tomography—Compounding.” There is an understanding within the industry based upon experiences in Pre-Approval Inspections (which have been based upon Agency interpretation of the Guideline on Preparation of Investigational New Drug Products, March, 1991) that the Agency expects that production of investigational drugs for phase 3 clinical trials will be under CGMP conditions to link them to production of market batches. Based upon the language in the proposed rule is it correct that a similar expectation will not apply to production of PET drug products for phase 3 clinical trials? Please clarify.

Section 212.70 - Lines 1216 through 1218 of the corresponding draft guidance allow distribution of the finished drug product under controlled conditions after endotoxin testing has been initiated but before the results are available, providing the drug is not administered by the receiving facility until a satisfactory test result has been received. This allowance is not part of corresponding section (212.70) of the proposed rule. We request that this allowance be added to the proposed rule.

Section 212.71 (d) – According to this section, if appropriate, rejected batches may be reprocessed according to pre-established procedures set forth in production and process controls. Is it required that such reprocessing would be part of the approved NDA for the PET drug product or can this be accomplished via an internal process for establishment of production and process controls?

Section 212.100 (d) - According to this section, product that is returned because of a complaint may not be reprocessed and must be destroyed. The implication is that returns that are not the result of complaints may be reprocessed if appropriate. This should be clarified.