

December 15, 2005

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, rm. 1061
Rockville, MD 20852

**Re: Food and Drug Administration
Docket No. 2004N-0439
Proposed Rule on Current Good Manufacturing Practice for Positron Emission
Tomography Drugs**

Dear Madams/Sirs:

I would like to provide the Food and Drug Administration (FDA) with the following comments and suggestions regarding the Proposed Rule concerning the current good manufacturing practices (CGMP) for positron emission tomography (PET) drugs, which was published in the September 20, 2005 issue of the *Federal Register*.

Please note that my comments as follows do not necessarily represent the viewpoints of the Mayo Clinic, the Society of Nuclear Medicine (Chair, Committee on Pharmacopeia and Member of the PET CGMP Working Group), as well as the United States Pharmacopeia (Vice-Chair, Expert Committee on Radiopharmaceuticals and Medical Imaging Agents).

For your information, the text of my suggested revisions as stated below appears in red.

Definition of "PET Drug"

Since a PET drug (e.g., I 124 sodium iodide) may also be used for tumor therapy, I would like to suggest that the definition for "PET drug" be revised as follows:

A radioactive drug that exhibits spontaneous disintegration of unstable nuclei by the emission of positrons and is used for providing dual photon positron emission tomographic diagnostic images **or therapeutic procedures**. The definition of PET drug includes any nonradioactive 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.

Definition of “Active Pharmaceutical Ingredient”

In keeping with the above rationale, the definition for the term “active pharmaceutical ingredient” should be revised as follows:

Active pharmaceutical ingredient means a substance that is intended for incorporation into a finished PET drug product and is intended to furnish pharmacological activity or other direct effect in the diagnosis, **treatment**, or monitoring of a disease or a manifestation of a disease in humans, but does not include intermediates used in the synthesis of such substance.

Definition of “Sub-Batch”

As the term “sub-batch” was repeatedly mentioned in the Proposed Rule, section § 212.1 titled “What are the meanings of the technical terms used in these regulations?” should include a definition for the term “sub-batch”. I would like to suggest the use of the definition as per General Chapter <823>, “Radiopharmaceuticals for Positron Emission Tomography—Compounding,” in the 28th edition of the United States Pharmacopeia (USP 2005; USP 28).

Sub-batch means a quantity of PET drug product having uniform character and quality, within specified limits, that is produced during one succession of multiple irradiations, using a given synthesis and/or purification operation.

“PET Production Facility”

As per the proposed definition, the term “PET production facility” means a facility that is engaged in the production of a PET drug product. However, the term “PET production facility” does not accurately depict the actual function of the facility. The term “PET production facility” may mistakenly be interpreted to be a facility for the production of PET scanners or a facility for the acquisition of PET images. As such, I would like to recommend that the term “PET production facility” be revised to “PET **drug** production facility” to more precisely reflect the aforementioned proposed definition.

Conditional Final Release of PET Drug Products

The Proposed Rule recommends that the conditional final release of PET drug products in the event of equipment breakdown should be allowed provided certain conditions are met. One of the stipulated conditions (i.e., § 212.70(f)(v)) is listed as below:

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- Complete the omitted test using the reserve sample after the analytical equipment is repaired and document that reasonable efforts have been made to ensure that the problem does not recur,

Pending on when the analytical equipment is repaired, one may not be able to obtain meaningful data for testing (e.g., radionuclidic identity, radionuclidic purity) as the radioactivity of the radionuclide of interest may be decayed to background level. As such, I would like to propose that the above-mentioned condition (i.e., § 212.70(f)(v)) be revised as follows:

- Complete the omitted test, **if possible**, using the reserve sample after the analytical equipment is repaired and document that reasonable efforts have been made to ensure that the problem does not recur;

Many thanks for the opportunity that the Agency has provided to the PET community in allowing us to express our concerns and comments with regard to the Proposed Rule on CGMP for PET drugs. If you have any questions or need additional information regarding my comments and suggestions, please do not hesitate to contact me by phone: (507) 284-4399, fax: (507) 266-4461, or e-mail: jhung@mayo.edu. Thank you very much for your kind attention and consideration.

Sincerely yours,



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