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Dockets Management Branch
Food and Drug Administration, HFA-305
5630 Fishers Lane, Room 1061
Rockville, MD 20852

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

Docket No. 1998D-0266 – Draft Guidance on Current Good Manufacturing Practice for Positron Emission Tomography Drug Products

Dear Sir or Madam:

Bristol-Myers Squibb Medical Imaging is pleased to have the opportunity to offer comments on the Proposed Rule and Draft Guidance for Positron Emission Tomography Products. Our company's mission is to help extend and enhance human life by providing innovative approaches to image the heart and vasculature. As leaders in medical imaging, we are interested in commenting on the Proposed Rule and Draft Guidance for Positron Emission Tomography (PET) Products. Our comments are set forth below.

Summary of Bristol-Myers Squibb Medical Imaging Comments on Proposal

We commend the FDA for recognizing that compounds in development should be handled as outlined in USP PET compounding <823> Radiopharmaceuticals for Positron Emission Tomography-Compounding. This approach assures quality during the development process while being scientifically practical. There are, however, several aspects of the proposed rule and draft guidance that we propose modification to or clarification of as cited below:

COMMENTS ON THE PROPOSED RULE

1. **Definitions.**

The proposed definition of "PET drug" is: 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. The definition 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.

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We believe the definition as stated is not useful or practical because generators, accelerators, electronic synthesizers, and computer programs are not “PET drug products” but rather ancillary items. We therefore suggest deleting these items from the definition.

Active pharmaceutical ingredient:

An “active pharmaceutical ingredient” is currently defined as “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 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.”

Because PET drug products are not intended to furnish pharmacological activity, the phrase “pharmacological activity” should be deleted from the definition.

COMMENTS ON THE DRAFT GUIDANCE

1. Quality Assurance. The draft guidance on line 286 addressing the QA functions states that all errors must be investigated and corrective action taken. This appears to contradict the proposed language of § 212.20(d), which provides that, with respect to errors in production records, the manufacturer “must determine the need for an investigation, conduct investigations when necessary, and take appropriate corrective actions.”

FDA should address this inconsistency by revising the language of the guidance to conform to that of the rule since this would be an industry standard Quality Assurance approach.

2. Control of Components, Containers, and Closures. The draft guidance recommends that facilities accept reagents, solvents, gases, purification columns and other auxiliary materials provided they meet applicable specifications from approved reliable media sources.

PET drug producers rely on commercially prepared growth media for purposes of sterility testing, we recommend the addition of “commercially prepared growth media” to the list of components in Line 694-95 of the draft guidance.

Bristol-Myers Squibb and Bristol-Myers Squibb Medical Imaging appreciate the opportunity to provide comment and respectfully requests that FDA give consideration to our recommendations. We would be pleased to provide additional pertinent information as may be requested.

Sincerely,



William J. Regan
Director, Global Regulatory Affairs