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DATE: October 19, 2005

TO: FDA
Division of Dockets Management (HFA-305)
Docket No. 2004N-0439
5630 Fishers Lane, Room 1061,
Rockville, MD 20852

FROM: Thomas Chaly Ph.D., FAIC
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I have the following comments about the Draft Guidance on Current Good Manufacturing Practice for Positron Emission Tomography Drug Products.

The PET community was trying hard to convince the FDA to consider our request in the acceptance of the starting materials such as O 18 Water and Mannose triflate for the manufacture of Fludeoxyglucose F 18 Injection without additional testing. In the case of mannose trflate, established venders like ABX Advanced Biochemical Compounds, are providing a certificate of analysis and the NMR spectra along with the purchase of mannose triflate. During our NDA process I was trying to convince this to the FDA Chemistry Team and I am very happy that FDA has considered this request in the proposed Draft Guidance.

There was no mention about the validation of Chlorodeoxyglucose and fluoro deoxymannose in the new proposal. In the NDA, we have agreed to do the validation of these two impurities on a yearly basis as requested by the FDA Chemistry Team.

Based on our validation studies, we have found only trace amount of mannose in the final product (far below the limit set by USP). This was very consistent during all the validation studies. This is the case with the chlorodeoxyglucose also. In all

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our validation studies, the amount of chlorodeoxyglucose found in the final drug product was far below the limit established by USP. We have an established track record based on our thousands of FDG preparations.

Since the components are purchased from an established company that has standardized these components for the manufacture of Fludeoxyglucose F 18 Injection, there is very little or no chance for an increased amount of fluorodeoxymannose and chlorodeoxyglucose in the final drug product.

Yearly validation of these components (chlorodeoxyglucose and fluorodeoxymannose) require special HPLC detectors and are very expensive. At present we are sending the samples to a University center for the validation. There are no established vendors to test these impurities. The university center was doing us a favor and is not willing to help us with the analysis any more. From my experience (20 years of synthesis), one time validation of these impurities for a particular method will be sufficient to establish the percentage impurities of this possible byproducts. Therefore, I request the FDA to consider my proposal to have the validation of Chlorodeoxyglucose and Fluorodeoxymannose as a one time validation process during the establishment of the synthetic procedure for the manufacture of Fludeoxyglucose F 18 Injection. This is also based on our long time experience with patient studies using this Radiopharmaceutical. I hope FDA will consider this request (one time validation) in establishing the GMP standard for the manufacture of Fludeoxyglucose F 18 Injection.

I like to express my sincere thanks to the FDA for accepting reasonable suggestions from the PET community to establish GMP standard for PET Radiopharmaceuticals.