Authentication Plan for PET Radiotracers Manufactured at the Yale PET Center

Radiotracers are synthesized according to validated chemistry, manufacturing, & control procedures, and quality specifications described in individual Drug Master Files (DMFs) that are approved by the FDA[1], or by the Yale University Radioactive Drug Research Committee (YURDRC). Radiotracers are manufactured according to the United States Pharmacopeia (USP) General Chapter 823 "POSITRON EMISSION TOMOGRAPHY DRUGS FOR COMPOUNDING, INVESTIGATIONAL, AND RESEARCH USES." USP Chapter <823> sets forth requirements for PET drug production, including *control of components, materials, and supplies; verification of procedures; stability testing and expiration dating; quality control; sterilization and sterility assurance*. Section 212.5(b) of the *current good manufacturing practice* (CGMP) requirements for investigational and research PET drugs (21 CFR 212) allows producers of investigational PET drugs[2] and research PET drugs[3] the option of producing PET drugs in accordance with USP Chapter <823>.

Authentication of the radiotracer is performed during the quality control stage of radiotracer manufacturing, prior to the release of the radiotracer for dispensing and administration to human research subject. Identity authentication is accomplished by performing the radiochemical identity test (USP Chapter <823>; section 212.40(c)(1)(ii) and 212.70(c)). This mandatory test is done with analytical HPLC method for EACH BATCH of radiotracer. Specifically, a sample of the labeled (either with C-11 or F-18) radiotracer is co-injected into the analytical HPLC system with a sample of the unlabeled reference standard. Co-elution of the radiotracer with the unlabeled reference standard from the analytical HPLC column authenticates the identity of the radiotracer. The molecular structure of the unlabeled reference standard is well characterized as required and supported by a Certificate of Analysis (CoA) from the supplier of this material.

[1] Under active Investigational New Drug Applications (INDs).

[2] Investigational PET drugs or drug products for human use produced under an IND in accordance with part 312.

[3] Research PET drugs or drug products produced with the approval of RDRC in accordance with 21 CFR 361.1.