SOCIETY OF NUCLEAR MEDICINE & MOLECULAR IMAGING

June 6, 2022

Ms. Lauren K. Roth
Associate Commissioner for Policy
Food and Drug Administration
Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852
Submitted electronically via https://www.regulations.gov/

Re: **Docket No. FDA-2013-N-0242;** Agency Information Collection Activities; Proposed Collection; Comment Request; Current Good Manufacturing Practices for Positron Emission Tomography Drugs

Dear Ms. Roth:

On behalf of the Society of Nuclear Medicine and Molecular Imaging (SNMMI),[1] I appreciate the opportunity to comment and inform the U.S. Food and Drug Administration (FDA) on the impact of the collection of information related to current Good Manufacturing Practices (GMP) for Positron Emission Tomography (PET) drugs, particularly on academic sites. We ask that the agency consider the following as it reviews the implications the proposed collection of information for nuclear medicine and molecular imaging products.

SNMMI estimates that about 150 manufacturing facilities are required to provide nationwide coverage of currently approved PET drugs. This is due to the short radioactive half-lives of PET products, ranging from 10 - 110 minutes. Each PET drug facility is a very small operation staffed by two to eight employees. Many PET drug manufacturing facilities are part of academic medical centers or national laboratories that produce PET drugs solely for internal use. In addition, some PET drug manufacturers are not-for-profit organizations associated with government agencies such as the National Institute of Health and state university hospitals.

Proposed collection of information is necessary for FDA's functions

SNMMI supports the collection of this information as it believes it is necessary for the proper performance of FDA's functions. We believe that accurate assessments of the recordkeeping requirements are important for the FDA to fully understand the full impact recordkeeping has on PET drug manufacturers, including academic sites. Due to the small size of a PET drug manufacturer this impact is proportionately much greater than that experienced by a general pharmaceutical manufacturer. Furthermore, SNMMI supports

[1] SNMMI's more than 15,000 members set the standard for molecular imaging and nuclear medicine practice by creating guidelines, sharing information through journals and meetings, and leading advocacy on key issues that affect molecular imaging and therapy, research, and practice.

the standardization of record contents amongst PET drug manufacturers. This standardization will provide benefits not just to the PET drug manufacturers but also FDA.

Accuracy of FDA's estimate of the burden of the proposed collection of info, including the methodology and assumption validity

The Federal Register Notice states, "A total of 63 combined sites represent academia and small commercial firms, including some IND and RDRC sites manufacturing ANDA-approved and NDA-approved PET drugs, and high-risk component manufacturers. . . The 63 entities will expend approximately 8 hours each to create MBRs and manufacturing and quality procedures." The 8 hours for a MBR seems very low. An additional challenge is this approach does not take into consideration the diversity of the PET sites. Further, outside the MBR, there are other items to consider.

One-time burden. The creation of procedures does not take into account time for the approval process, which requires multiple disciplines to review and approve the record. Also, it appears that the following are significantly underestimated or not included:

- Analytical Method Validation (No mention)
- Change Control Management (No mention)
- Product Complaint (Underestimate)
- Perform quality assurance (QA) and release of manufactured PET drugs (Underestimate)
- Create equipment and facility related procedures (Underestimate – includes no mention of the equipment and facility assessment and qualification activities that support the creation of said procedures).
- Creation of component specification sheet (underestimate – many firms produce multiple products requiring additional component specifications) is underestimate by 50%.
- Out of specification events average is underestimated.
- Third-party disclosure burden is underestimated with respect to the number of Field Alert Reports submitted.
- For all paperwork (SOPs, etc.) cited in this document there is no consideration for the significant amount of training that has to take place for all of this documentation (creation, deployment and capturing training records).

Annual burden. There is insufficient time for investigations taken into account (e.g., retesting may be required). The total number of batches release for corporate entities is significantly underestimated. Regulations are silent on the burden for Annual Product Review (APR). Due to the Covid-19 Pandemic the utilization of 704/706 Records Requests was heavily utilized by FDA. There is no accounting for the annual burden associated with these records requests.

Annual Recordkeeping Burden for Academia and Small Firms. We would like to emphasize that it is imperative that the FDA not craft regulations that place one type of PET drug manufacturer at a disadvantage. Even between the two general categories of commercial vs. academic PET drug manufacturers there exists a large diversity within each of these two categories. This diversity will

complicate the FDA's attempt to use "averages" to accurately address the impact for all PET drug manufacturers. The small sites only have 2-3 full time employees and will not have a dedicated quality assurance department. Thus, the burden on academic sites is more than 100% underestimated due to fewer personnel as is common for non-profit corporations. Further, academic sites and national labs are bringing up novel tracers that require more time to develop the MBR and testing methods.

Third-Party Disclosure Burden for Sterility Test Failure Notices. SNMMI has noted in the past that we believe that, through FDA inspectional practices, letters to physicians are actually required for all sterility test out-of-specification results, even if the out-of-specification result is not due to a true sterility test failure (note that an out-of-specification result could be caused by a laboratory error and not a product failure). We believe the average number of hours per disclosure is likely to be underestimated. For example, a single batch of a PET drug may be dispensed under prescription orders from numerous physicians and a notification is required for each prescribing physician. In addition to e-mail and fax, the notification may require telephone calls to explain the details of the notification and answer questions

Ways to enhance the quality, utility and clarity of the info to be collected

SNMMI believes that the quality of the information can be significantly enhanced by improving the accuracy of the estimated recordkeeping burden for each section of 21 CFR 212. This could be achieved by directly involving individual PET drug manufacturers, including small and academic sites in the establishment of these estimates.

We also would like to note that annual product review (APR) is not specified in this docket but is being requested by field investigators. Time for APR collection/review is not discussed and is inconsistent with expectations of investigators, as well as the review and approval of any investigation. Therefore, we request that FDA clarify as to whether APR is or is not required for PET. If it is, APR needs to be included in these metrics.

Thank you again for the opportunity to provide public comment and help improve the accuracy of recordkeeping burden for current PET GMP. Please contact Julia Bellinger, Director of Health Policy at jbellinger@snmmi.org or (703) 326-1182 with any further questions on this important issue.

Respectfully Submitted,

Richard L. Wahl, MD
President, SNMMI