December 30, 2009

Louis B. Jacques, MD
Director, Coverage and Analysis Group
Centers for Medicare & Medicaid Services
7500 Security Blvd., Mail Stop C1-09-06
Baltimore, MD 21244

Re: Joint Comment on Proposed Decision Memorandum for Positron Emission Tomography [^{18}F-NaF] to Identify Bone Metastasis of Cancer (CAG-00065R1)

Dear Dr. Jacques:

We are writing in response to the Centers for Medicare & Medicaid Services' (CMS) request for comments on the proposed decision memorandum for the use of Positron Emission Tomography (PET) (^{18}F-NaF) to identify bone metastasis of cancer. For the reasons stated in our earlier comment and reviewed below, we believe that the available evidence is sufficient to support Medicare coverage for ^{18}F-NaF PET and PET/CT (referred to herein collectively as "PET") imaging to identify bone metastasis of cancer either to inform the initial antitumor treatment strategy or to guide subsequent antitumor treatment strategy after the completion of initial treatment.

While we have been strong supporters of the Coverage with Evidence Development (CED) framework, and in particular the ^{18}F-FDG National Oncologic PET Registry (NOPR), we do not believe that ^{18}F-NaF coverage should be limited to a clinical study. We explain below why CMS would be fully justified in revising its proposed decision memorandum and providing coverage of ^{18}F-NaF PET without requiring an additional process for study enrollment and CED. We strongly believe that the evidence indicates that ^{18}F-NaF PET is equal or superior to the current covered technology in identifying bone metastasis of cancer, and encourage CMS to cover ^{18}F-NaF PET for this purpose without restriction.

This letter is submitted jointly on behalf of the Academy of Molecular Imaging (AMI) - Institute for Molecular Technologies (IMT), the American College of Nuclear Medicine (ACNM), the American College of Radiology (ACR), the American Society of Clinical Oncology (ASCO), and the Society of Nuclear Medicine (SNM). These organizations are composed of clinicians, academicians, researchers and nuclear medicine providers utilizing molecular imaging technologies, including integrated positron emission

tomography/computed tomography (PET/CT). We represent tens of thousands of physicians, providers, and patients with regard to this technology, and have worked closely with CMS over the past several years to increase beneficiary access to PET and PET/CT through the development of the National Oncologic PET Registry (NOPR).

I. Clinical Support for NaF-18 PET

^{18}F-NaF is an FDA-approved USP radiotracer that allows physicians to use PET to detect metastasis to the bone of many common cancers (including breast, lung, and prostate), thus facilitating the development of treatment programs for affected individuals. The Food and Drug Administration (FDA) conducted a formal review of PET drugs in 2000 that specifically deemed ^{18}F-NaF to be safe and effective.[1]

Our original reconsideration request provided a detailed summary of the clinical evidence supporting the use of ^{18}F-NaF PET. Most of this evidence is consolidated in the March 2009 *Review of Published Literature on the Use of Sodium Fluoride F18 (^{18}F-NaF) Positron Emission Tomography (PET) in the Evaluation of Altered Osteogenic Activity*, prepared by the Cancer Imaging Program at the National Cancer Institute.[2] The *Review* summarizes results from 41 clinical trials published since 1992, including 10 well-controlled studies of ^{18}F-NaF PET to identify bone metastases in adults. Several of these studies included subjects with multiple types of cancer; some study cohorts were specific to lung, breast and prostate cancer. These studies show that ^{18}F-NaF PET is more sensitive and specific than ^{99m}Tc-MDP bone scintigraphy for diagnosis and detection of bone metastases. In addition, at least one of these studies demonstrates that use of CT in conjunction with ^{18}F-NaF PET further improves sensitivity and specificity, and enhances the ability to distinguish benign from malignant lesions.

In addition to the studies presented in the *Review*, our original reconsideration request identified two studies of ^{18}F-NaF PET that had been published since the March 2009 *Review*, as well as an additional 2006 ^{18}F-NaF PET study that was not included in the *Review*. Our review of the literature referenced by CMS, including those studies we referenced in our original comment, supports the conclusion that sufficient evidence exists for CMS to establish unrestricted coverage for ^{18}F-NaF PET.

---

[1] *See* Food and Drug Administration, *Positron Emission Tomography Drug Products; Safety and Effectiveness of Certain PET Drugs for Specific Indications*, 65 Fed. Reg. 12,999 (2000), *available at* http://www.fda.gov/ohrms/dockets/98fr/031000a.txt. ("FDA reviewed its records and, under Sec. 314.161, determined that sodium fluoride F 18 injection was not withdrawn from sale for reasons of safety or effectiveness. Accordingly, the agency will list sodium fluoride F 18 injection in the *Orange Book*'s 'Discontinued Drug Product List' section, which delineates, among other items, drug products that have been discontinued from marketing for reasons other than safety or effectiveness. Because sodium fluoride F 18 injection was not withdrawn from sale for reasons of safety or effectiveness, it is still a listed drug, and FDA can approve ANDAs that refer to it.")

[2] Cancer Imaging Program, Division of Cancer Treatment and Diagnosis, National Institutes of Health, *Review of Published Literature on the Use of Sodium Fluoride F 18 (^{18}F-NaF) Positron Emission Tomography (PET) in the Evaluation of Altered Osteogenic Activity* (Mar. 2009).

II. Patient Access to Bone Imaging

The clinical evidence clearly demonstrates that ^{18}F-NaF PET should be covered as medically reasonable and necessary. However, in addition, the increasing shortage of Technetium-99m (^{99m}Tc) should encourage CMS to expedite coverage for ^{18}F-NaF PET as a validated and medically appropriate technology. As CMS is aware, ^{99m}Tc is the daughter isotope of molybdenum-99 (^{99}Mo) and ^{99m}Tc is the radionuclide used in approximately 80 percent of nuclear medicine scans worldwide. No bone imaging agents other than ^{99m}Tc radiopharmaceuticals are currently covered by CMS for bone scintigraphy. The short (66-hour) half-life of ^{99}Mo and the even shorter (6-hour) half-life of ^{99m}Tc preclude efforts to maintain an inventory of either radionuclide, and any interruption in production thus immediately compromises the clinical supply.

The U.S. supply of ^{99}Mo is entirely dependent upon the production capacity of a small handful of international reactors located primarily in Canada, South Africa, and the Netherlands. Since 2007, the domestic supply of ^{99}Mo and ^{99m}Tc has fluctuated dramatically, as the aging foreign reactors have become increasingly prone to extended shutdowns for repair and maintenance. As CMS and U.S. clinicians are well aware, these shutdowns have increased in both duration and frequency in recent years, and very significantly compromise clinical care decisions that are dependent on bone scintigraphy.

For example, the unscheduled and continuing shutdown since May 2009 of the 52-year-old Chalk River facility in Ontario has forced thousands of hospitals throughout the United States to cancel or delay critical medical imaging procedures that depend upon ^{99m}Tc. The Chalk River facility failed to meet its initial estimated repair completion date of late 2009, and it was recently announced that the facility will not return to production until April of 2010 at the earliest. Similarly, the Petten High Flux Reactor in the Netherlands experienced shutdowns in the past year, and is already scheduled to go offline for over half of 2010 (from February through at least August). Even Congress has recognized the urgency of this situation, as the House of Representatives recently passed legislation (H.R. 3276) that would promote the safe and reliable domestic production of ^{99}Mo/^{99m}Tc. This legislation is currently awaiting action in the Senate. However, even the most expeditious passage of this legislation would not provide a remedy in the near term for the crisis currently facing patients.

This shortage has led to a significant reduction in the availability of bone scintigraphy. As a result, many Medicare beneficiaries with cancer who need bone imaging now face the prospect of lengthy delays or alternative diagnostic procedures that may involve greater radiation dosage, less accuracy, or higher cost. Fortunately, the radiotracer ^{18}F-NaF is unaffected by this severe shortage, as ^{18}F-NaF is also widely available across the United States through a network of cyclotrons. Indeed, our best estimate is that ^{18}F-NaF is currently available to 99 percent of all hospitals nationwide. Thus, the availability of ^{18}F-NaF PET bone imaging as a CMS-approved alternative to conventional bone scintigraphy performed with ^{99m}Tc agents (e.g., ^{99m}Tc-MDP) will ensure that beneficiaries suffering from cancer will have access to these essential imaging procedures.

III. Request for Coverage Without Restriction

On the basis of the evidence presented above and in our original comment letter, we strongly encourage CMS to amend NCD CAG-00065R and adopt a policy providing coverage for ^{18}F-NaF PET in identifying bone metastasis of cancer that is not restricted to study enrollment. This will afford Medicare cancer beneficiaries clinically necessary access to accurate bone imaging, even if they are distant from a trial center.

Should CMS nevertheless determine that ongoing evidence collection is necessary on the clinical value of oncologic ^{18}F-NaF, we would work with CMS to support a ^{18}F-NaF PET clinical data registry developed and operated by the professional societies and imaging community stakeholders. While the literature supports coverage of NaF bone imaging outside of CED, we believe that coverage of ^{18}F-NaF PET via CED could be conducted efficiently, so as to offer Medicare beneficiaries broad access to a much-needed imaging technology while simultaneously allowing CMS to collect even more information than already exists on the clinical value of oncologic ^{18}F-NaF PET.

Based on our considerable experience with the National Oncologic PET Registry (NOPR) we would be willing to meet with CMS and the Agency for Healthcare Research and Quality (AHRQ) to discuss appropriate study design for a ^{18}F-NaF PET registry. We estimate that the number of oncologic ^{18}F-NaF PET bone scans that would be performed under CED would be relatively limited, perhaps totaling half the number of oncology scans that were registered through the original NOPR process.

IV. Conclusion

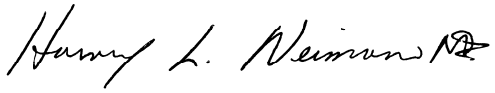
Regardless of the precise parameters of CMS's final coverage decision, the PET imaging community notes that while many providers have significant experience with FDG-PET imaging techniques, fewer providers have routinely offered bone imaging with ^{18}F-NaF PET. We have assured CMS that we recognize the importance of ensuring that PET imaging centers and physicians quickly gain the imaging, interpreting and reporting skills necessary to maximize the benefit for these cancer patients. To this end, we have already begun to develop training materials to educate providers on the relevant technical and clinical challenges, and will diligently disseminate such information widely through webcasts, self-guided training programs, FAQs, sample protocols, and other means. (For example, AMI will broadcast the first of several educational webcasts on January 19, 2010, at no charge to the imaging community.) These resources will be both publicly accessible on imaging organizations' websites and made available via other means of communication.

Finally, in light of the aforementioned severity and expected long-term duration of the ^{99m}Tc shortage, we urge CMS to act quickly and expeditiously to reach a determination on ^{18}F-NaF PET to mitigate further disruption in the availability of bone imaging to beneficiaries.

We appreciate the opportunity to provide comments regarding ^{18}F-NaF PET, and look forward to working with CMS to provide any additional information that you would find valuable in your decision making process.

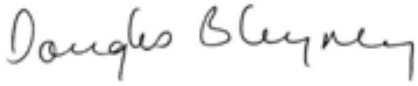
Sincerely,

Timothy J. McCarthy, PhD
President, AMI



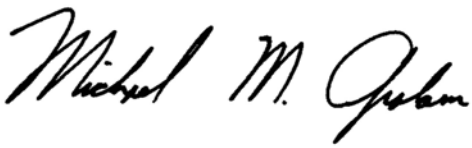
Harvey L. Neiman, MD, FACR
Executive Director, ACR

Jay A. Harolds, MD, FACNP
President, ACNM



Douglas Blayney, MD
President, ASCO

Thom Tulip, PhD
Chairman, IMT Steering Committee



Michael M. Graham, PhD, MD
President, SNM