CMS Reconsiders Coverage for NOPR

On April 10, the Centers for Medicare and Medicaid Services (CMS) opened reconsideration of the PET National Coverage Decision (NCD) (CAG-00181R) for public comment. The action was in response to a formal request from the National Oncologic PET Registry (NOPR) to remove current prospective data collection requirements required for ^{18}F-FDG PET in diagnosis, staging, and restaging for brain, cervical, ovarian, pancreatic, small cell lung, and testicular cancers, as well as for cancer indications not previously specified in Section 220.6 of the *National Coverage Determination Manual.* CMS received public comments from April 10 through May 10. SNM, NOPR, and other groups encouraged the imaging community to provide comments and offered templates and educational materials to assist in doing so. NOPR recently published initial results indicating that clinicians changed the intended care of more than a third of their cancer patients as the result of ^{18}F-FDG PET findings. NOPR was launched in May 2006 in response to the CMS "Coverage with Evidence Development" policy to collect data through a clinical registry to inform agency ^{18}F-FDG PET coverage determination decisions for currently noncovered cancer indications. A decision from CMS is expected later this year.

SNM

CMS Updates OCE Edits

The Centers for Medicare and Medicaid Services (CMS) on April 4 posted revised Outpatient Code Editor (OCE) edits for diagnostic radiopharmaceuticals and nuclear medicine procedures. Included in these edits is the addition of the ^{131}I therapy Healthcare Common Procedure Coding System (HCPCS) code A9517 ("Iodine I-131 sodium iodide capsule[s], therapeutic, per millicurie"). CMS also removed Common Procedural Terminology (CPT) code 78016 ("Thyroid carcinoma metastases imaging; with additional studies [eg, urinary recovery]") from the list of CPT codes in the Hospital Outpatient Prospective Payment System (HOPPS) requiring at least 1 radiopharmaceutical on the claim in order to receive full payment.

CMS made these changes in response to several inquiries from SNM members and staff, among others, after follow-up diagnostic procedure claims were returned to providers because no diagnostic radiopharmaceutical was listed. This was occurring because, according to the 2008 HOPPS Final Rule, all nuclear medicine diagnostic procedure claims must contain at least 1 diagnostic radiopharmaceutical or the claim would be sent back for correction.

In addition, through conversations with CMS officials, SNM learned that HCPCS code A9530 ("Iodine I-131 sodium iodide solution, therapeutic, per millicurie") is under consideration to be included in the OCE edits for next quarter, with a retroactive implementation date if appropriate. The complete Diagnostic Radiopharmaceutical and Nuclear Medicine HCPCS edits can be downloaded at: http://www.cms.hhs.gov/HospitalOutpatientPPS/02_device_procedure.asp#TopOfPage.

Centers for Medicare and Medicaid Services
SNM

NRC NSTS Extensions Proposed

The Nuclear Regulatory Commission (NRC) announced on April 8 details of the proposed expansion of the National Source Tracking System (NSTS) to include an additional 3,500 NRC and state licensees and nearly 17,000 additional radioactive sources to improve accountability and control of radioactive materials. The proposed rule would require the additional licensees to report information on the manufacture, transfer, receipt, disassembly, and disposal of these radioactive sources to the NSTS. Manufacturers would be required to assign a unique serial number to each nationally tracked source.

"An expanded NSTS will enable the NRC and its federal and state partners to improve the security of radioactive materials while ensuring their continued beneficial use in industry, research, and medicine," said NRC Chair Dale E. Klein.

As established in a final rule published in 2006, the NSTS covers radioactive sources in categories 1 and 2 as determined by the International Atomic Energy Agency. These sources are typically used in radiothermal generators, irradiators, radiation therapy, industrial gamma radiography, and high- and medium-dose brachytherapy cancer treatments. That rule covers approximately 1,350 licensees nationwide who possess category 1 and 2 sources. The system is to be implemented by January 31, 2009.

The proposed rule would expand the NSTS to include category 3 sources as well as sources in the upper range of category 4 (or at about 1/10 of the activity threshold for category 3). These sources are typically used in fixed industrial gauges, well-logging devices, medium- and low-dose–range brachytherapy, and certain radiography devices. The NRC considers category 1 and 2 sources to be the most significant from a security perspective. According to an NRC press release, "Expanding the NSTS will guard against the possibility that a small number of category 3 or 4 radioactive sources could be collected to form a category 2 amount of radioactive material."

Nuclear Regulatory Commission

Raman Spectroscopy at Sanford

In a widely covered press release and an article in the March 31 online issue of the *Proceedings of the Na-*

tional Academy of Sciences, Sanjiv Sam Gambhir, MD, PhD, and his team at the Stanford University School of Medicine (CA) described in detail the use of Raman spectroscopy to detect tumors at a resolution of nearly 1-trillionth of a meter. Gambhir, a professor of radiology and director of the Molecular Imaging Program at Stanford (and an SNM member), said, "This is an entirely new way of imaging living subjects, not based on anything previously used." He said that signals from Raman spectroscopy are stronger and longer lived than other available methods and that the type of particles used in this method can transmit information about multiple types of molecular targets simultaneously. "Usually we can measure 1 or 2 things at a time," he said. "With this, we can now likely see 10, 20, 30 things at once."

Gambhir believes this is the first time Raman spectroscopy and nanoparticles have been used to image deep within the body. When laser light is beamed from a source outside the body, these specialized particles emit signals that can be measured and converted into a visible indicator of their location. Gambhir compared the Raman spectroscopy work to the development of PET 20 or 30 y ago. "Nobody understood the impact of PET then," he said. "Ten or 15 y from now, people should appreciate the impact of this." He noted that none of the imaging methods currently in clinical or widespread research use can fulfill all the desired qualities of an imaging tool, which include being able to finely detect small biochemical details, target them 1 at a time, and still be inexpensive and easy to use.

Raman spectroscopy is based on the Raman effect, the physical phenomenon that occurs when light from a source such as a laser is shined on an object. When the light hits the object, roughly 1 in 10 million photons bouncing off the object's molecules has an increase or decrease in energy—called Raman scattering. This scattering pattern, called a spectral fingerprint, is unique to each type of molecule and can be measured. Postdoctoral students in Gambhir's group used 2 types of engineered Raman nanoparticles, gold nanoparticles and single-wall carbon nanotubes, to develop the imaging technique. They injected mice with the some of the nanoparticles and used a specially adapted microscope to view the animals under laser light. The researchers could see that the nanoparticles migrated to the liver. To be able to detect molecular events, the researchers labeled separate batches of spectrally unique Raman nanoparticles with different peptides or antibodies and injected them simultaneously in mice to follow the biodistribution. If each type of particle migrated to a different tumor site, the Raman microscope would enable separation of signals from each batch of particles.

As part of this proof-of-principle work, the team tagged the gold nanoparticles with different pieces of proteins that homed in on different tumor molecules. "We could attach pretty much anything," said Gambhir. The Raman effect also lasts indefinitely, so the particles do not lose effectiveness as indicators as long as they stay in the body. The team was able to see targets on a scale 1,000 times smaller than that now obtainable by the most precise fluorescence imaging using quantum dots. When adapted for clinical use, the technique has the potential to be useful during surgery, for example, in the precise and complete removal of cancerous tissue.

Stanford University School of Medicine

AAMC Urges Bans on Industry Gifts

The Association of American Medical Colleges (AAMC) Task Force on Industry Funding of Medical Education released in April a report examining the benefits and pitfalls associated with industry funding of medical education, with specific advice on developing principles, recommendations, and guidelines to assist colleges in refashioning industry relationships to "better conform to high standards of medical professionalism." The report will be presented to the AAMC Executive Council for consideration at its June meeting. The task force urged "all academic medical centers to accelerate their adoption of policies that better manage, and, when necessary, prohibit, academic–industry interactions that can inherently create conflicts of interest and undermine standards of professionalism." This recommendation includes not only funding from the pharmaceutical and device industries but support from providers of equipment and services as well. The report noted that necessary actions are not 1-sided: ". . .industry should voluntarily discontinue those practices that compromise professionalism as well as public trust. Both parties should work together constructively to develop new paradigms for the vital function of scientific information transfer."

The task force recommended that medical colleges create policies that ban drug and medical device companies from offering (among other items and services) free food, gifts, travel, ghostwriting services, and quid pro quo or covert financial incentives that might influence purchases. Faculty members should be discouraged from participation in industry-sponsored speakers bureaus, and standards should be developed for faculty and staff participation in industry-sponsored programs. Among other items and services that the report advised restricting in specific and well-defined ways were distribution of pharmaceutical samples and access by pharmaceutical and device manufacturer representatives, especially to patient care areas.

The complete report is available at: www.aamc.org/research/coi/industryfunding.pdf.

Association of American Medical Colleges

Self Referring Linked to Imaging Increases

Physicians who refer patients to their own facilities or machines for scans account for much of the increase in diagnostic imaging ordered for privately

insured patients, said a Baylor College of Medicine expert in a commentary that appeared in the May issue of the journal *Medical Care* (2008;46:455–458). Referring to a study appearing in the same issue (460–466), Vivian Ho, PhD, professor of medicine at Baylor College of Medicine and associate professor of economics at Rice University, wrote: "Increases in utilization rates were substantially higher for scans performed by self-referring physicians than for images that originated from a referral to a radiologist or hospital." The increase was seen mainly in those patients covered through private insurance that provided the physician with a fee-for-service reimbursement. In the study upon which Ho was commenting, Jean M. Mitchell, PhD, professor of public policy at Georgetown University (Washington, DC), reviewed data from a large private insurer in California. This information was then compared with a report by the Medicare Payment Advisory Commission. Both reports showed an increased use of imaging tests for those with private insurance. Federal law does not allow reimbursements for many self-referral arrangements unless the imaging is done in the office. This exception is allowed because physicians who perform the procedure in office are providing a convenience to patients. However, in most cases reviewed in the Mitchell study, the doctors did not actually have the imaging devices in their offices, and physicians skirted the restriction by leasing an imaging center's facilities and employees for a fixed period per week. "This creates revenue for both parties involved," Ho said. "But it also raises a lot of questions, such as would it have mattered if another test had been done, one that didn't receive a reimbursement?" She added, "The current reimbursement system lacks incentives to provide high quality imaging in a cost effective manner." Finding an answer to this problem will take creativity, she noted: "Doing away with the reimbursements will only penalize those physicians who are actually providing imaging in-office as a convenience to their patients."

Baylor College of Medicine

Global Alliance for Pharmacogenomics

Leaders at the National Institutes of Health (NIH) and the Center for Genomic Medicine in Japan announced on April 14 the signing of a letter of intent creating a Global Alliance for Pharmacogenomics. U.S. scientists joining the alliance are members of the NIH Pharmacogenetics Research Network, a consortium of research groups. Japanese scientists in the alliance represent the newly created Center for Genomic Medicine, a component of the RIKEN Yokohama Institute that conducts high-throughput analyses of human genes involved in diseases and drug responses.

"By bringing together our resources, we will advance the understanding of how changes in DNA affect our responses to medicines. Thus we can begin to realize the promise of personalized medicine," said Yusuke Nakamura, MD, PhD, director of the Center for Genomic Medicine at RIKEN. "We expect this international agreement to speed scientific discovery and the translation of results into improved treatments for cancer, heart disease, and other serious conditions," said NIH Director Elias A. Zerhouni, MD. "Ultimately, physicians worldwide will be able to tailor the treatment of each patient—1 of the great frontiers of health care today."

Initial projects will focus on: (1) understanding genetic factors that influence the effectiveness of breast cancer treatments (aromatase inhibitors); (2) determining the optimal length of treatment for 2 drugs used to treat early-stage breast cancer (cyclophosphamide and either doxorubicin or paclitaxel); (3) discovering new genetic factors linked to serious side effects from certain pancreatic cancer drugs (gemcitabine and bevacizumab); (4) exploring how genes contribute to drug-induced long-QT syndrome, an irregular heart rhythm that can cause sudden cardiac arrest; and (5) working with the International Warfarin Consortium to tailor initial doses of the anticlotting drug based on the genetic profiles of patients.

A steering committee will manage the alliance and will meet twice yearly to discuss progress, future directions, intellectual property issues, the approval of additional members, and communication with the public. Alliance members will share data and research results with the scientific community.

National Institutes of Health

New Protein Structures Web Portal

The Protein Structure Initiative (PSI), an effort supported by the National Institutes of Health (NIH), has launched an online resource that will enable scientists from across biomedical disciplines to easily access a wealth of information about proteins and to speed discoveries about these molecules, according to an April 3 NIH press release. The new portal, the PSI Structural Genomics Knowledgebase (PSI SGKB), is an entry point to all of the protein structure and production resources created by the PSI, a program started in 2000 to determine the 3-dimensional structures of thousands of proteins. PSI research centers have generated 2,800 protein structures, and, in the process, developed techniques that significantly improve the steps of structure determination.

"Many of these products have always been available, just not all in 1 place," said Jeremy M. Berg, PhD, director of the NIH National Institute of General Medical Sciences, which supports the PSI. "The ability to search the resources developed through the PSI should help a wide range of scientists make use of them to advance their own studies."

From the home page, researchers can enter the sequence of a protein into a search box to quickly find the corresponding structure and others like it, plus details about function and reports on how the structures were generated. A glossary of terms and acronyms helps to translate the information.

The site is a gateway to other useful information, including descriptions of new technologies and methods, a list of publications detailing key findings, supplemental funding opportunities for

functional studies, and links to resources outside of the PSI. Users also can easily access the PSI Materials Repository, a resource under development for ordering PSI-generated clones that can speed studies of protein structure and function. Researchers can visit the PSI SGKB site to learn how to make a protein of interest or find out about tools they could use in their labs. They can also identify potential collaborators and read about the latest developments in specific areas of structural biology.

The PSI SGKB can be accessed at http://kb.psi-structuralgenomics.org/KB, and background information is available at www.nigms.nih.gov/Initiatives/PSI/.

National Institutes of Health

AAN Potamkin Prize Goes to Alzheimer's Researchers

At its annual meeting in Chicago, April 12–19, the American Academy of Neurology awarded the 2008 Potamkin Prize to 3 researchers for their work in brain imaging in Alzheimer's disease (AD). The award went to Clifford R. Jack, Jr., MD, of the Mayo Clinic (Rochester, MN), and William E. Klunk, MD, PhD, and SNM member Chester A. Mathis, PhD, both with the University of Pittsburgh School of Medicine (PA). The Potamkin Prize honors researchers for their work in helping to advance the understanding of AD and related disorders. The $100,000 prize is to be used toward continuing AD research and will be shared evenly among the 3 researchers.

Klunk and Mathis were recognized for their collaboration on the development of Pittsburgh Compound-B (PiB), a novel PET amyloid-imaging tracer. "This research could help identify AD subjects earlier in the course of the disease and aid in the testing and development of new drugs capable of reversing the root cause of AD," said Mathis. "It could facilitate the development of newer, more effective drugs for AD and allow earlier, more accurate diagnosis, so therapy could be started earlier when the chances of success are greatest," said Klunk.

Jack was recognized for his work with a variety of MR imaging techniques to study the neurodegenerative features of AD. He was among the pioneers in the use of MR imaging to understand differences that distinguish normal aging from mild cognitive impairment and AD over time. "We believe that we have helped improve the understanding of the natural history of AD," said Jack. "We have shown that MR measurements are meaningful markers of AD pathology and hence provide useful information about the stage of the disease, the likelihood that subjects will progress to dementia, and provide information that is helpful in assessing progression of the disease."

American Academy of Neurology