Online Dose Optimization Resource

SNMMI on March 18 launched a new online resource for imaging professionals, referring physicians, and the public on dose optimization for nuclear medicine and molecular imaging procedures. The information, available at www.snmmi.org/dose, is designed to enhance efforts to ensure that patients receive the smallest possible amount of radiopharmaceutical that will provide appropriate diagnostic information. "Advancing a better understanding of radiation dose and risk and promoting dose optimization in nuclear medicine and molecular imaging is a top priority for SNMMI," said Frederic H. Fahey, DSc, SNMMI president. "The online resource is a key component of our dose optimization initiative, because it compiles important information in an organized fashion in a central location."

The online resource includes SNMMI journal articles, abstracts, educational offerings, news articles, presentations, and links to useful Web sites, as well as other materials. The resource will be promoted to SNMMI members through various communication channels, including social media, and shared with referring physician and patient groups. In June, SNMMI kicked off the dose optimization initiative by issuing a position statement recommending that radiation dose for all nuclear medicine and molecular imaging procedures should be optimized by ensuring that patients receive the minimum radiation dose needed to provide useful diagnostic information. Dose optimization has become a part of the SNMMI communications, outreach, advocacy, and education efforts. In addition to these activities, SNMMI continues to actively participate in the Image Gently and Image Wisely campaigns.

"It is our firm belief that the right test with the right dose should be given to the right patient at the right time," said Fahey. "We hope that this online resource will provide professionals with tools they can use to implement this into clinical practice and educate the public about optimal dosing for nuclear medicine and molecular imaging procedures."

SNMMI

FDA and Early-Stage AD

An article appearing online on March 13 in the *New England Journal of Medicine* provided perspective from U.S. Food and Drug Administration (FDA) scientists on the agency's recent guidance document for Alzheimer disease (AD) therapeutic drug development. Nicholas Kozauer, MD, and Russell Katz, MD, from the FDA Center for Drug Evaluation and Research, looked specifically at the implications of the guidance for FDA assessment of drugs targeted at early-stage AD, where cognitive and functional improvements would provide ideal metrics but haven proven quite difficult to demonstrate. "We simply do not yet have drug development tools that are validated to provide measures of function in patients with AD before the onset of overt dementia," the authors wrote. "Improvement in function, moreover, could lag substantially behind cognitive improvement mediated by pharmacologic agents early in the course of the disease." They described current drug discovery efforts in AD treatment as "disappointing" and called for innovative approaches to trial design and endpoint selection.

The latest FDA guidance addresses the design and implementation of clinical trials with individuals with AD who have not yet developed dementia and in studies in individuals with no cognitive or functional impairment. The authors noted that biomarkers in such studies might include "brain amyloid load (e.g., as measured by PET) and cerebrospinal fluid levels of β-amyloid and tau proteins" and cited ongoing efforts to qualify such biomarkers in clinical trial design in early-stage AD as "important FDA priorities."

Kozauer and Katz acknowledged that traditional clinical assessment instruments for overt dementia may be ineffective in assessing early-stage AD and added "for patients whose disease is at an even earlier clinical stage, so that functional impairment would be more difficult to assess, it might be feasible to approve a drug through the FDA's accelerated approval pathway on the basis of assessment of cognitive outcome alone." This approach might speed the approval of treatments that appear to be effective in early AD, when such treatments might have the most benefit. They concluded that "further research will clearly be needed before the effect of an intervention on a single biomarker alone could be considered an adequate surrogate measure for the purposes of accelerated approval of a candidate drug for early Alzheimer's disease."

The full FDA guidance document is available at: www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM338287.pdf.

New England Journal of Medicine

MedPAC Report to Congress

The Medicare Payment Advisory Commission (MedPAC) released its 2013 *Report to the Congress: Medicare Payment Policy* on March 15. Although the 407-page report covers all Medicare payment policy issues, media focus within the diagnostic imaging community was on a reported negative growth rate (–1.0%) for medical imaging in the United States in 2011. Some professional imaging groups pointed to this as evidence that imaging should not be targeted as a central driver in rapid escalation of overall medical costs. However, the report notes that a large portion of the decrease in imaging volumes comes from 2 cardiovascular services: nuclear medicine and echocardiography. In addition, the report continues: "The more important factor,

however, is the shift in setting for these services from the nonfacility setting [ie, physician offices] to the facility setting [ie, hospitals]. If these 2 types of services are excluded from the calculations, the change in the volume of imaging services from 2010 through 2011 would be an increase of 0.5%." The full report is available at medpac.gov/documents/Mar13_EntireReport.pdf.

Centers for Medicare & Medicaid Services

McEwan Named to CNSC

Joe Oliver, Canada's Minister of Natural Resources, announced on March 14 the appointment of Alexander (Sandy) McEwan, MD, as a member of the Canadian Nuclear Safety Commission (CNSC) for a 5-y term. "Dr. McEwan is a leading expert in nuclear medicine and medical isotopes," said Oliver. "His insight and leadership will be great assets to the CNSC as it continues to ensure safety, security, health, and environmental stewardship in the nuclear industry."

McEwan, a past president of SNMMI, has more than 25 y of experience in nuclear medicine and served as a special advisor to the Canadian Health Minister during the medical isotope shortage in 2009. He is the chair of the Department of Oncology at the University of Alberta (Edmonton) and medical director of the Cross Cancer Institute (Edmonton).

Canadian Nuclear Safety Commission

^{99m}Tc-Tilmanocept Approval

The U.S. Food and Drug Administration (FDA) announced on March 13 the approval of Lymphoseek (^{99m}Tc-tilmanocept) Injection (Navidea Pharmaceuticals, Inc.; Dublin, OH) for sentinel lymph node localization in patients with breast cancer or melanoma. Lymphoseek is the first new drug for lymph node mapping to be approved in more than 30 y. Other FDA-approved drugs used for lymph node mapping include sulfur colloid (1974) and isosulfan blue (1981). The agency emphasized in its announcement that "Lymphoseek is an imaging drug that helps locate lymph nodes; it is not a cancer imaging drug."

"Removal and pathological examination of lymph nodes draining a primary tumor is an important diagnostic evaluation for some patients with breast cancer or melanoma," said Shaw Chen, MD, deputy director of the Office of Drug Evaluation IV in the FDA Center for Drug Evaluation and Research.

Lymphoseek's safety and effectiveness were established in 2 clinical trials of 332 patients with melanoma or breast cancer. All patients were injected with Lymphoseek and blue dye. Surgeons subsequently removed suspected lymph nodes for pathologic examination. Confirmed lymph nodes were examined for their content of blue dye and/or Lymphoseek. Results showed Lymphoseek and blue dye had localized most lymph nodes, although a notable number of nodes were localized only by Lymphoseek. The most common side effects identified in clinical trials were pain and irritation at the injection site. The clinical studies on which the approval was based included only comparisons of Lymphoseek and blue dye; ^{99m}Tc-sulfur colloid was not included in the studies.

In a press release issued on March 14, SNMMI commended the FDA for its approval of the agent.

U.S. Food and Drug Administration

Merck and Luminex AD Partnership

Merck (Whitehouse Station, NJ) and Luminex Corporation (Austin, TX) announced on March 13 a collaboration and license agreement to develop a companion diagnostic device that will be evaluated to help screen patients for recruitment into Merck's clinical development program for MK-8931, a novel oral β-amyloid precursor protein site cleaving enzyme (BACE) inhibitor and Merck's lead investigational candidate for Alzheimer disease (AD). "Evaluation of biomarkers that may provide an indicator of disease onset and enable earlier diagnosis is an important goal toward facilitating early intervention and potentially improving the treatment of AD," said Darryle D. Schoepp, PhD, senior vice president and head of neuroscience and ophthalmology at Merck Research Laboratories. "We look forward to working with Luminex to advance our ongoing clinical development program for MK-8931."

Luminex will be responsible for development, regulatory submission, and commercialization of the candidate companion diagnostic device, which will employ the Luminex xMAP technology to measure concentrations of 2 candidate biomarkers (Aβ42 and total τ) in cerebrospinal fluid (CSF) samples from patients with mild cognitive impairment (MCI). The candidate device will be evaluated as a means to identify subjects with MCI who have a higher risk of developing AD to support patient selection for Merck's therapeutic BACE inhibitor clinical program.

"This collaboration has the potential to deliver a novel companion diagnostic to identify patients at increased risk of developing AD," said Patrick J. Balthrop, president and CEO of Luminex. "We are pleased to leverage our technologies and development capabilities and look forward to expanding our activity into the companion diagnostic segment of personalized medicine."

BACE is believed to be a key enzyme in the production of β-amyloid peptide, which contributes to the formation of plaques in the brain. Evidence suggests that inhibiting BACE decreases the production of β-amyloid and may therefore reduce amyloid plaque formation and modify disease progression. Results of phase I clinical studies indicated that Merck's MK-8931 can reduce levels of β-amyloid in CSF by >90% in healthy volunteers and people with AD, without dose-limiting side effects. Based on these results, Merck is conducting a global, multicenter phase II/III clinical trial to evaluate the safety and efficacy of MK-8931 in patients with mild-to-moderate AD and has plans to initiate a trial in prodromal subjects. In December 2012, Merck and GE Healthcare (Princeton, NJ) announced a clinical study collaboration, license, and supply agreement for use of ^{18}F-flutemetamol, an investigational PET agent, to support development of MK-8931.

Merck
Luminex Corporation

Funding for Canadian ^{99m}Tc Development

Natural Resources Canada, a government agency, announced on February 28 the signing of 4-y contribution agreements with 3 Canadian organizations for development and commercialization of new sources of ^{99m}Tc. The projects, funded through the Isotope Technology Acceleration Program (ITAP), will be at the University of Alberta (Edmonton), TRIUMF (Vancouver, British Columbia), and Prairie Isotope Production Enterprise (Winnipeg, Manitoba). This funding will support the development and application of cyclotron and linear accelerator production technologies to improve the security of medical isotope supplies, reduce radioactive waste, and meet nuclear nonproliferation goals. ITAP was designed to bring innovative isotope production to market; support collaboration among academic, private, and public sector partners; and help ensure that isotope production is reliable and on a sound commercial footing.

The University of Alberta funding will total $7 million (CA) and will go to Alexander McEwan, MD, and his research team. The funding for their cyclotron research project now provides the necessary resources to continue their research and position the product as a model for similar cyclotron centers to be built elsewhere. "This funding provides a real opportunity for the University of Alberta to demonstrate and validate a new, cost-effective, and safe means of medical isotope supply that does not require the construction of a new nuclear reactor," said McEwan. "It is a true made-in-Canada solution."

At TRIUMF, the CycloTech99 consortium will receive $7 million (CA). In February 2012 the group demonstrated the capability to produce ^{99m}Tc with medical cyclotrons already installed in Ontario and British Columbia. Like the other funding recipients, the group's plan includes regulatory approval and commercial rollout as part of a national isotope strategy designed to be in place when the National Research Universal reactor at Chalk River (Ontario) stops production in 2016. The CycloTech99 consortium includes the British Columbia Cancer Agency, the Centre for Probe Development and Commercialization, Lawson Health Research Institute, and TRIUMF. Several industrial partners are also involved and are developing commercialization pathways consistent with program objectives.

The agreement allocates $7.46 million (CA) to the Prairie Isotope Production Enterprise for completion of a 45-mo development project titled "Commercializing Accelerator Isotope Production for a Secure and Sustainable Supply of ^{99m}Tc." The total budget for this linear accelerator program is $11.71 M. The research team will develop a regional supply market for ^{99m}Tc, including commercial scale production of ^{99}Mo for some customers, processing of ^{99m}Tc at a centralized facility, recovery and reuse of ^{100}Mo for new targets, and completion of preclinical and clinical evaluations of ^{99m}Tc-based radiopharmaceuticals.

Natural Resources Canada

"Omni-Tomography" Targets MR/CT Hybrid

In an article published in the April issue of the *IEEE Spectrum*, science writer Neil Savage profiled hybrid modality imaging research at the laboratory of Ge Wang, PhD, director of the Rensselaer Polytechnic Institute Biomedical Imaging Center (Troy, NY). The lab group has developed a technology called "interior tomography," which takes a novel approach to data gathering and algorithm construction in imaging. Over the last 8 y the group has published numerous reports of the technology, which provides accurate image reconstruction from only locally truncated projections, resulting in lower radiation exposures (see, for example, *J Comput Assist Tomogr.* 2011;35:762–764). Most recently the group has expanded the technology from its initial focus on CT to a general tomographic principle, designated as "omni-tomography," described as "a grand fusion of multiple tomographic modalities for simultaneous data acquisition in a region of interest" (*PLoS One.* 2012;7:e39700). The group noted that this approach will be especially useful in studying physiologic processes that are "multidimensional, multiscale, multitemporal, and multiparametric." Wang, along with collaborators in Australia, China, and the United States, has used the technology in a new design for a hybrid CT/MR scanner and will present the design and plans at the International Meeting on Fully 3D Image Reconstruction in Radiology and Nuclear Medicine at Lake Tahoe, CA, in June.

IEEE Spectrum