Downturn in Non-PET NM Patient Visits

A report released on October 17 by IMV Medical Information Division (Des Plaines, IL), an international marketing research company, described an unexpected downturn in total numbers of non-PET nuclear medicine patient visits. In 2006, an estimated 17.7 million nuclear medicine procedures were performed during 15.2 million patient visits to 7,320 hospital and non-hospital sites. This represented a 12% decrease in patient visits, from 17.2 million in 2005. However, IMV described the drop as temporary and, based on survey results, predicted that the number of visits will rise to 16.3 million in 2007 (still below the 2005 level).

"Nuclear medicine utilization (not including PET procedures) is continuing to be dominated by cardiovascular applications, which have grown from 54% of 2002 procedures to 60% in 2006," observed Lorna Young, senior director of market research, IMV Medical Information Division. "However, the drop in total nuclear medicine patient visits from 2005 levels may be, in part, due to precertification requirements from health insurance companies, which require patients to obtain insurer approval for imaging services prior to scheduling their procedure. Insurance companies are increasingly requiring that patients obtain precertification approval for certain imaging procedures, such as nuclear medicine. Oncology is the second major application of nuclear medicine procedures, and other modalities, such as PET/CT, may be cannibalizing some oncology procedures that previously belonged solely to [non-PET] nuclear medicine."

The report describes trends in nuclear medicine patient visits by procedure type, radiopharmaceutical and pharmacologic stress agent utilization, camera and computer installed base by manufacturer and year of installation, planned purchases, networking, and site operations characteristics. The report also covers adoption trends of new technologies, including SPECT/CT. Among the findings in the report are: (1) the average number of nuclear imaging cameras installed per site is 1.8 units; (2) 60% of non-PET patient visits were for cardiovascular studies; (3) more than 75% of camera purchase activity was for replacement cameras; (4) although dual-head SPECT cameras account for more than 66% of planned cameras, SPECT/CT is making significant inroads, accounting for more than 10% of cameras installed in 2007 to date; (5) radiopharmaceutical budgets are showing continued growth, with the percentage of sites with budgets of $250,000 or more increasing from 15% to 32%; and (6) more than 66% of nuclear medicine sites surveyed have the capability to electronically transmit nuclear medicine images to other locations.

IMV's 2007 Nuclear Medicine Census Database and *Market Summary Report* are available for license and/or purchase at www.imvinfo.com.

IMV Medical Information Division

NRC Issues Transition Plan on New Regulatory Authority

On October 18, the U.S. Nuclear Regulatory Commission (NRC) published its transition plan for assuming regulatory authority over certain radioactive materials under provisions of the Energy Policy Act of 2005. The act expanded the definition of "byproduct material" subject to NRC regulatory authority to include discrete sources of ^{226}Ra, material made radioactive in a particle accelerator, and other radioactive material that the commission determines could pose a threat to public health and safety or the common defense and security. Most of these materials were previously regulated by each state.

Although NRC authority took effect immediately when the bill was enacted in August 2005, the agency issued a waiver allowing states to continue to regulate these materials while the agency drafted regulations to implement the new requirements. A final rule on the expanded definition of byproduct material was approved by the NRC on May 14 and published on October 1 in the *Federal Register.* Those regulations became effective on November 30. The governors of the 34 Agreement States that already regulate byproduct material under agreements with the NRC submitted certifications that they are prepared to continue exercising regulatory authority over the new materials. Those certifications are currently before the NRC for approval.

Approximately 400 entities currently using these materials in non-Agreement States, the District of Columbia, and U.S. territories will require new NRC licenses under this regulation. In these jurisdictions, the NRC waiver will be terminated in phases, and these applicants will have 1 year to apply for an NRC license. Current NRC licensees who also use these materials will have 6 months after waiver termination to apply for license amendments to cover the new material. The transition plan and the final rule on the expanded definition of byproduct material are available on the NRC Web site at: http://nrc-stp.ornl.gov/narmtoolbox.html.

U.S. Nuclear Regulatory Commission

New Potency Rules for Thyroid Drugs

The U.S. Food and Drug Administration (FDA) announced on October 3 that it would tighten potency specifications for levothyroxine sodium, used by more than 13 million patients, to ensure that the drug retains its potency over its entire shelf life. This action was taken in response to concerns that the potency of the drug may deteriorate prior to its expiration date. The change will help

improve the quality of the product so that consumers receive the level of medication needed to treat their thyroid disorders.

FDA is mandating that levothyroxine sodium drug products tighten their potency specifications to meet a 95%–105% potency specification until their expiration date. The lower potency (95%) specification will ensure the drugs do not degrade by more than 5% of the labeled claim before their expiration date, and the 105% upper specification is appropriate to address occasional analytical testing variability. Currently, these products are allowed a potency range of 90%–110%.

The action is consistent with the recommendations of a joint FDA advisory committee and follows concerns expressed about levothyroxine sodium products by health care professionals and patients. Manufacturers and marketers have 2 years to comply with the revised specification.

The action was based on results gathered when the FDA requested and received stability data from manufacturers of all approved, marketed levothyroxine sodium drug products manufactured between July 2003 and June 2005. These data revealed a trend toward loss of potency, with some preparations approaching 90% of labeled potency by the expiration date. The stability data showed that some products rapidly degrade over their labeled shelf life. Some strengths or package types, such as blister packs, degrade more rapidly than others, resulting in varying expiration dates within product lines. In addition, variability in expiration dating periods was noted in products from different manufacturers. Some levothyroxine sodium tablets remain quite stable, losing less than 5% of labeled potency within 24 months, whereas others lose approximately 10% of labeled potency in 9 months. By tightening the potency specification and limiting the amount that products can degrade throughout their shelf lives, the FDA hopes to reduce extremes in variability that could have clinical consequences in achieving target thyroid levels, especially for those with thyroid cancer.

More information is available at: www.fda.gov/cder/drug/infopage/levothyroxine/default.htm.

U.S. Food and Drug Administration

GE Discontinues Some Radioisotope Production

GE Healthcare (Waukesha, WI) announced on October 19 that it will discontinue production of all products with the short-lived radioisotopes ^{32}P, ^{33}P, ^{35}S, and ^{125}I. This includes nucleotides, nucleosides, amino acids, receptor ligands, and custom products labeled with these isotopes. A listing of more than 1,000 discontinued products with these radioisotopes is available at www1.gelifesciences.com/APTRIX/upp01077.nsf/Content/portfolio_simplification/$file/GEHC_Short-lived_Products.10.19.07.pdf. The final date that orders may be placed will vary by country, and the GE Healthcare Web site advised users to check with local support teams for additional information.

The company will continue to manufacture the ^{14}C and ^{3}H products in its general catalogue and high-throughput screening ranges. A press release noted that the company "remains committed to offering our custom ^{14}C and ^{3}H radiolabeling services" and will continue to expand its portfolio of luminescent G-protein coupled receptor and kinase screening products. Accord to the press release, GE Healthcare is discontinuing many older, more generic, and less well used research products to focus its general research products to "more accurately meet the demands of bioresearchers today."

The last ship date for these products will be December 31. Customers were advised to check the company's Web site (www1.gelifesciences.com/APTRIX/upp01077.nsf/Content/portfolio_simplification), which will feature regular updates.

GE Healthcare

DOE Office of Science Looks Ahead

On October 11, the U.S. Department of Energy (DOE) Office of Science released a comprehensive update of its 2003 publication, *Facilities for the Future of Science: A Twenty-Year Outlook*, reporting that the agency has made "significant progress" in deploying these scientific facilities and instruments "that the United States needs to capture world scientific leadership, extend the frontiers of science, and support the Department's missions." The 2003 facilities outlook was the first long-range facilities plan prioritized across disciplines to be issued by a government science funding agency anywhere in the world and has served as a model for other countries and regions that are developing roadmaps for research infrastructures.

"The world-leading scientific facilities we create, maintain, and operate are key to continued U.S. leadership in physical and biological research," wrote Under Secretary for Science Raymond L. Orbach, PhD, in the introduction to *Four Years Later: An Interim Report on 'Facilities for the Future of Science: A Twenty-Year Outlook.'* "This leadership, and the transformational scientific discoveries that flow from it, are critical to meeting the challenges our nation faces in the twenty-first century in the areas of both global economic competitiveness and energy security."

The 2003 plan listed 28 new scientific facilities and upgrades of current facilities that will define scientific opportunities over the next 20 years in all fields of science supported by the Office of Science, including fusion energy, advanced scientific computation, materials science, biological and environmental science, high energy physics, and nuclear physics. The new interim report provides a summary update on the status of the original 28 facilities, detailed status updates, and rationales for changes in planning. "Contemporary science and technology are undergoing change, as always, and the Office [of Science] has been careful not to adhere with inappropriate rigidity to the 2003 snapshot, but to respond to technological progress in reordering and restructuring its priorities," said Orbach. "Some planned facilities have been accelerated; a number have been reoriented, some in a substantial way. One was terminated in light of facilities abroad."

The DOE Office of Science leads the world in the conception, design, construction and operation of large-scale facilities. These facilities include particle accelerators, synchrotron light sources, neutron scattering facilities, supercomputers, high-speed networks, and genome sequencing facilities. Each year, they are used by more than 21,500 researchers and students from universities, private industry, and other federal science agencies. These facilities are located at national laboratories and universities, are open to researchers on a peer-reviewed basis, are shared with the science community worldwide, and feature technologies and capabilities available nowhere else. Both the original *Facilities Outlook* and the new interim report are available on the Facilities for the Future of Science Web site at www.sc.doe.gov/about/Future/Facilities for the Future of Science.htm.

U.S. Department of Energy
Office of Science

Petition to Alter NRC Training Regs Denied

The U.S. Nuclear Regulatory Commission (NRC) announced in the *Federal Register* on October 24 that it had denied a petition for rulemaking (PRM-35-19) originally submitted by William Stein, III, MD (Metairie, LA), on June 14, 2006. Stein had requested that the NRC amend Title 10 *Code of Federal Regulations* (*CFR*) 35 regulations governing training for parenteral administration of ^{153}Sm-lexidronam (Quadramet), ^{131}I-tositumomab (Bexxar), and ^{90}Y-ibritumomab tiuxetan (Zevalin).

During the 2002 revision to 10 *CFR* part 35, the NRC increased the required amount of training and experience from 80 to 700 hours for most medical uses of unsealed byproduct material requiring a written directive. In 2005, the NRC noted that to properly cover the topics important for safety for these uses, the minimum amount of classroom and laboratory training was 200 hours for the alternate pathway to authorized status. To achieve authorization via the board certification pathway, the individual must successfully complete multiple-year residency training in a radiation therapy or nuclear medicine training program or a program in a related medical specialty, each of which also includes a total of 700 hours of training and experience. Stein asserted in his petition that these regulations were burdensome and requested that they be amended to stipulate that 80 hours of laboratory and classroom training, supervised work experience, and written attestation should be sufficient for physicians seeking authorized user status for therapeutic administrations of these unsealed byproduct materials. Stein provided 3 options for addressing this issue, but, after review and a period for public comment, the NRC rejected both the petition and the proposed remedies.

In summarizing the 25 comments received, the NRC noted that 18 supported the petition. In general, "these commenters stated that not granting the petition would intrude into the practice of medicine, discourage physicians from treating patients, and establish barriers to the use of potentially effective therapies, thus adversely affecting patient access to these therapies and increasing health care costs." Commenters also noted that the activity administrations of Quadramet, Bexxar, and Zevalin are from a radiation safety perspective less hazardous than oral administration of ^{131}I, for which the NRC requires only 80 hours of classroom and laboratory training.

Among the 7 letters opposing the petition were statements from the American Association of Physicists in Medicine, the American College of Radiation Oncology, the American College of Radiology, and the American Society for Therapeutic Radiology and Oncology. Many of these commenters raised concerns about radiation safety issues and exposure of patients to additional risk if medical oncology/hematology training does not include the extensive background necessary for administering these radiopharmaceuticals.

In denying the petition, the NRC noted that current 10 *CFR* 35.390 and 35.396 regulations establish "the appropriate amount of training and experience for a physician to become an authorized user for the parenteral administration of unsealed byproduct material requiring a written directive, including Quadramet, Bexxar, and Zevalin." In reviewing the various reasons for this decision, the complexity of product-specific variations in training was noted: "The current approach to training and experience for the medical use of unsealed byproduct material accommodates the introduction of new radiopharmaceuticals without requiring additional rulemaking, with its associated costs to the Agreement States. Attempting to tailor the training and experience requirements to specific uses of unsealed byproduct material and to the amount of flexibility that a user may wish to have would significantly increase the complexity of the regulatory oversight. The NRC does not believe that such added complexity would be of benefit to patients, the Agreement States, licensees, current and prospective authorized users, or the medical specialty boards."

The full NRC ruling is available at http://a257.g.akamaitech.net/7/257/2422/01jan20071800/edocket.access.gpo.gov/2007/E7-20918.htm.

U.S. Nuclear Regulatory Commission

NIBIB Invests in Quantum Research

The National Institute of Biomedical Imaging and Bioengineering (NIBIB), part of the National Institutes of Health (NIH), announced on October 4 the award of more than $12 million in grants to 4 investigators developing groundbreaking technologies, including disposable microchips for the diagnosis of metastatic lung cancer, a bioartificial kidney to eliminate dialysis procedures, insulin-producing cells to treat diabetes, and nanoparticles that selectively leave the blood and bind to cancer cells to assist in removal of brain tumors. The 3-year grants, each of which was for approximately $3 million, were part of the NIBIB Quantum Grants program, designed to create significant ("quantum level") advances in health care.

"This innovative program from the NIBIB promises to harness the power of technological discovery and team science to translate new knowledge into practical healthcare benefits for our nation," said Elias A. Zerhouni, MD, NIH director.

Among the recipients were Anthony Atala, MD, from Wake Forest University Health Sciences (Winston-Salem, NC), for "Insulin Producing Cells from Amniotic Stem Cells for Diabetes Therapy"; Raoul Kopelman, PhD, from the University of Michigan at Ann Arbor, for "Nanoparticle Enabled Intraoperative Imaging and Therapy"; Shuvo Roy, PhD, from Cleveland Clinic Lerner College of Medicine (OH), for "Miniaturized Implantable Renal Assist Device for Total Renal Replacement Therapy"; and Mehmet Toner, PhD, from the Massachusetts General Hospital (Boston), for "Point-of-Care Microfluidics in Lung Cancer."

More information about the NIBIB Quantum Grants program is available at www.nibib.nih.gov/Research/QuantumGrants.

National Institute of Biomedical Imaging and Bioengineering

NRC Creates Panel on Licensing Vulnerabilities

The U.S. Nuclear Regulatory Commission (NRC) announced on October 5 the establishment of a special advisory panel, the Independent External Review Panel to Identify Vulnerabilities in the U.S. NRC's Material Licensing Program, in response to criticism of the agency's licensing process in 3 recent reports. The NRC Office of the Inspector General earlier this year recommended that the agency "convene an independent panel of experts external to the agency to identify agency vulnerabilities concerning NRC's material licensing and tracking programs and validate the agency's ongoing by-product material security efforts." In July, the U.S. Senate's Homeland Security and Government Affairs Permanent Subcommittee on Investigations issued a staff report on "Dirty Bomb Vulnerabilities," which identified an "apparent good-faith presumption that pervades the NRC licensing process," and recommended that NRC staff physically inspect the premises of most materials license applicants before issuing a license. Also in July, the U.S. Government Accountability Office published a study in which investigators were able to apply for and obtain an NRC materials license for a dummy corporation.

The NRC took immediate steps to address this issue and formed a task force to develop an action plan for further improvements in the materials licensing process. That task force recommended chartering the external review panel to identify weaknesses in the agency's materials licensing process. The panel will assess existing and potential security vulnerabilities related to NRC's import, export, and specific and general license programs. It is expected to develop an agenda and plan for the review, including an assessment of prelicensing guidance, licensing procedures, the licensing process, possession limits on licenses, and license reviewer training and oversight. The panel will document each significant issue and propose recommended improvements. Some of its meetings will be public, and others will be closed for discussion of security matters.

The panel will report directly to NRC Executive Director for Operations Luis A. Reyes and will periodically update the commission on its work. It is expected to submit its report in early 2008. The panel, established under the Federal Advisory Committee Act, will include Benjamin Nerud, of the Defense Threat Reduction Agency; Thomas Hill, former director of the Georgia Radiation Control Program; and Michael Ryan, currently chair of the NRC Advisory Committee on Nuclear Waste and Materials.

U.S. Nuclear Regulatory Commission

U.S. Dementia Numbers Growing

A new analysis suggests that about 3.4 million Americans ages 71 and older (1 in 7 in that age group) have dementia and that 2.4 million of these individuals (more than 2/3) have Alzheimer's disease (AD). The study, supported by the National Institutes of Health (NIH), is the latest in a series of analyses attempting to assess the prevalence of dementia and AD. Published online on October 30 in *Neuroepidemiology*, the study is the first to estimate rates of dementia and AD using a nationally representative sample of older adults across the United States.

Brenda L. Plassman, PhD, of Duke University Medical Center (Durham, NC)—with Kenneth M. Langa, MD, PhD, and David R. Weir, PhD, of the University of Michigan (Ann Arbor); Robert B. Wallace, PhD, of the University of Iowa (Iowa City); and others—conducted the analysis as part of the Aging, Demographics, and Memory Study (ADAMS). ADAMS is a substudy of the larger Health and Retirement Study (HRS), a leading resource for data on the combined health and economic circumstances of Americans older than 50. ADAMS and the HRS are sponsored by the National Institute on Aging, a component of NIH, under a cooperative agreement with the University of Michigan.

The study included 856 HRS participants ages 71 and older from 42 states surveyed from 2001 to 2003. ADAMS interviewers conducted at-home evaluations to gather information about each participant's cognitive and functional status and symptoms, neuropsychiatric symptoms, current medications, medical history, and family history of memory problems. Prior neuroimaging and laboratory results were also obtained. A team of clinicians reviewed the evaluation information and made a preliminary assessment of each person's cognitive status. A consensus panel of other medical experts then used validated diagnostic criteria to determine if the participant had normal cognitive function, cognitive impairment without dementia, or dementia. Such criteria were used to discern the type of dementia, including AD or vascular dementia.

Based on the experts' classifications, the authors estimated the national prevalence and total numbers of people ages 71 and older, by age group, with

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cm^3; SUV $\leq$ 13.8) and only 29% of high-risk ROIs (SUV $>$ 13.8). Limiting the target volume to predominantly PET-positive disease resulted in a low rate of isolated out-of-field recurrences, for which SUV and volume were predictors. SUV $>$13.8 was noted as the best identifier of ROIs at the greatest risk of recurrence.

International Journal of Radiation Oncology, Biology, Physics

Image-Guided Adenovirus-Mediated RT of MTC

In an article published in the October issue of *Human Gene Therapy* (2007;18:916–924), Spitzweg et al. from the Ludwig-Maximilians University (Munich, Germany) reported on a study of the feasibility of image-guided radioiodide therapy of medullary thyroid cancer (MTC) after human sodium iodide symporter (hNIS) gene transfer, using a tumor-specific carcinoembryonic antigen (CEA) promoter for transcriptional targeting. NIS gene transfer was performed in human MTC cell (TT) xenografts, using adenoviral vectors carrying the NIS gene linked either to a cytomegalovirus promoter or a CEA promoter fragment. Functional NIS expression was confirmed by immunostaining and in vivo ^{123}I gamma camera imaging, followed by application of a therapeutic ^{131}I dose. TT cell xenografts in nude mice injected intratumorally with 2 dosages of Ad5-CEA-NIS accumulated 7.5 $\pm$ 1.2% ID/g and 12 $\pm$ 2.95% ID/g, compared with accumulation of 8.4 $\pm$ 0.9% ID/g after application of Ad5-CMV-NIS. Administration of a therapeutic dose of 111 MBq (3 mCi) of ^{131}I resulted in a significant reduction of tumor growth, associated with significantly lower calcitonin serum levels, as well as improved survival. The authors concluded that "a therapeutic effect of ^{131}I was demonstrated in vivo in MTC cell xenografts after adenovirus-mediated induction of tumor-specific iodide accumulation by CEA promoter-directed hNIS expression."

Human Gene Therapy

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and maintenance costs are associated with the MOC program. Our primary sources of income—examination fees and your generous contributions—are not sufficient to meet these expenses. In 2006 the ABNM began charging an annual MOC fee of $150. Diplomates who delay their participation in MOC must pay all delinquent MOC fees so that the cost of MOC is shared equally by all diplomates. The annual MOC fee charged by the ABNM does not include the costs of products developed by the SNM or other organizations to meet MOC requirements.

Henry D. Royal, MD
Executive Director, ABNM

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any dementia and with AD or vascular dementia in 2002. According to their calculations, 13.9% of Americans ages 71 and older have some type of dementia, 9.7% of Americans in that age group have AD, and 2.4% have vascular dementia. AD accounted for about 70% of all dementia cases among people 71 and older. As in other studies, the ADAMS analysis showed that the prevalence of dementia increases significantly with age. Five percent of people ages 71 to 79, 24.2% of people 80 to 89, and 37.4% of those 90 years or older were estimated to have some type of dementia. The estimated rate of AD also rose significantly with age, from 2.3% of people ages 71 to 79 to 18.1% of people 80 to 89 to 29.7% of those age 90 and older. The ADAMS investigators found fewer years of education and the presence of at least 1 APOE e4 allele, a genetic risk factor for AD, to be strong predictors of AD and other dementias.

The ADAMS and HRS data are made publicly available to researchers seeking to conduct studies about the older U.S. population. For further information about the HRS and ADAMS, visit hrsonline.isr.umich.edu or www.nia.nih.gov/ResearchInformation/HRS.htm.

National Institutes of Health