

MPFS and OPFS Final Rules Expand Nononcologic PET Coverage

On November 9 SNMMI issued comments on the newly finalized Centers for Medicare and Medicaid Services (CMS) Medicare Physician Fee Schedule (MPFS) and Hospital Outpatient Prospective System (OPPS) rules. SNMMI summarized and provided commentary on the highlights of the final rules:

- CMS removed the “exclusionary language” from NCD 220.6 Positron Emission Tomography (PET) Scans. This will leave nononcologic PET indications (unless noted by NCD 220.6.1–220.6.20) to the discretion of local Medicare Administrative Contractors (MACs). The SNMMI applauded the coverage decision, noting that it resulted from years of work by SNMMI and industry partners, saying in a press release: “We resoundingly agree that ‘local contractor discretion provides an immediate avenue to potential coverage in appropriate candidates for nononcologic indications.’ Various new PET agents for nononcologic indications are currently in FDA trials. Retiring the national noncoverage policy for nononcologic indications upon the agents’ FDA approval will eliminate the regulatory bottleneck leading to Medicare beneficiary access issues.”
- CMS did not retire national noncoverage decisions for amyloid PET (220.6.20) and NaF (220.6.19). SNMMI noted that the society is working with CMS to rectify coverage decisions for both: “We hope CMS will change its position on amyloid PET when they release their national coverage analysis decision on Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer’s Disease on January 12, 2022.”
- The PFS final rule cuts the conversion factor to \$33.59 in CY 2022 from \$34.89 in CY 2021. This follows the expiration of the 3.75% payment increase, a 0.00% conversion factor update, and a budget neutrality adjustment. SNMMI reported that the society is working with the medical community to prevent cuts to physician reimbursement.
- CMS delayed implementation of the payment penalty phase of the Appropriate Use Criteria program to the later of January 1, 2023, or the January 1 that

follows the end of the current public health emergency.

- CMS will be phasing in the clinical staff wage increase over 4 years. As a result, the impact to nuclear medicine procedure codes will not be as acute as in the proposed rule (3%–4% decrease versus a 10%–15% decrease).
- The final CY 2022 OPPS Rule included no changes to what the SNMMI termed the “inequitable” reimbursement policy of precision diagnostic radiopharmaceuticals. These drugs continue to be packaged after the expiration of a 3-year pass-through period. SNMMI urged members and interested members of the community to send a letter to Congress in support of the Facilitating Innovative Nuclear Diagnostics (FIND) Act, legislation aiming to expand patient access through appropriate payment. More information is available at: <https://snmmi.quorum.us/campaign/34856/>.

SNMMI

U.S., Canada, UK Collaborate on Good Machine Learning Practice

On October 27, the U.S. Food and Drug Administration (FDA), Health Canada, and the United Kingdom Medicines and Healthcare Products Regulatory Agency jointly issued the “Good Machine Learning Practice for Medical Device Development: Guiding Principles” to identify 10 principles that are important in development of Good Machine Learning Practice (GMLP). GMLP is intended to advance high-quality artificial intelligence/machine learning-enabled medical device development. The 10 principles identify areas in which alignment in efforts related to research, building resources and tools, regulatory policies, regulatory guidelines, international harmonization, and consensus standards could be developed by the International Medical Device Regulators Forum, international standards organizations, and other collaborative bodies to advance the maturation of GMLP.

In a press release, FDA said that these guiding principles could be used to either specifically tailor practices

applicable to health care, create new practices, or adopt from practices that have been proven in other domains. “With artificial intelligence and machine learning progressing so rapidly, our 3 regulatory agencies, together, see a global opportunity to help foster good machine learning practice by providing guiding principles that we believe will support the development and maturation of good machine learning practice,” said Bakul Patel, director of the FDA Digital Health Center of Excellence in the Center for Devices and Radiological Health. The GMLP guiding principles are available at: <https://www.fda.gov/medical-devices/software-medical-device-samd/good-machine-learning-practice-medical-device-development-guiding-principles>.

U.S. Food and Drug Administration

DOE Tri-Lab Project and ²²⁵Ac

In a news feature released on November 17, the Department of Energy (DOE) Oak Ridge National Laboratory (ORNL; TN) described a national laboratory collaborative effort to provide accelerator-produced ²²⁵Ac for therapeutic use. Since 2014, the DOE Isotope Program has sponsored the Tri-Lab research project with a goal of production of large batches of ²²⁵Ac more quickly and more frequently in anticipation of regulatory approval of routine use in clinical treatment. A number of private and global public/private partnerships are also addressing the challenge to safely and reliably produce ²²⁵Ac.

ORNL currently produces the majority of the world’s ²²⁵Ac by harvesting it from a supply of ²²⁹Th, produced by ²³²Th targets irradiated in proton accelerators at Los Alamos and Brookhaven National Laboratories. However, the amount of the radioisotope currently “milked” from the ²²⁹Th “cow” (about 1 Ci/year) is not enough even for large-scale clinical trials, and options for scaling up production are limited. In June, ORNL processed the largest batch of ²²⁵Ac ever put into its inventory,

processed from targets irradiated at Brookhaven, which produces ²²⁵Ac using a high-energy proton beam. “We demonstrated that the accelerator route can generate about 60% of the current annual supply of ²²⁵Ac in just 12 days,” said Dmitri Medvedev, a scientist in the Brookhaven Collider Accelerator Department.

In 2020, FDA acknowledged receipt of a drug master file for the Tri-Lab accelerator-produced ²²⁵Ac, outlining details about the facilities and processes used in manufacturing, processing, packaging, and storing the radioisotope to ensure that the product meets specifications. “The drug master file is one step forward toward this ultimately being used in an FDA-approved product,” said Roy Copping, who leads the Tri-Lab production program from the ORNL side. Researchers at ORNL are currently looking at 2 ways to further increase output: processing batches more frequently and processing larger targets. As part of the Tri-Lab effort, a research and development team developed in-cell technology to manage gas created in the production process. The team began developing the technology in November 2020, spent several months testing it outside the hot cell, then implemented it in the hot cell in April 2021. The technology benefits production at ORNL and is extensible to future target processing at Brookhaven and Los Alamos. For more information about the Tri-Lab effort, see: <https://www.isotopes.gov/sites/default/files/2021-01/Actinium>

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Oak Ridge National Laboratory

Gene Therapies for Rare Diseases

On October 27 the National Institutes of Health (NIH), U.S. Food and Drug Administration (FDA), 10 pharmaceutical companies, and 5 nonprofit organizations announced a partnership to accelerate development of gene therapies for individuals who suffer from rare diseases. Although ~7,000 rare diseases have been identified, only 2 heritable diseases currently have FDA-approved gene therapies. The new Bespoke Gene Therapy Consortium (BGTC), part of the NIH Accelerating Medicines Partnership program and project-managed by the Foundation for the National Institutes of Health, is intended to optimize and streamline the gene therapy development process.

“Most rare diseases are caused by a defect in a single gene that could potentially be targeted with a customized or ‘bespoke’ therapy that corrects or replaces the defective gene,” said NIH Director Francis S. Collins, MD, PhD. “There are now significant opportunities to improve the complex development process for gene therapies that would accelerate scientific progress and, most importantly, provide benefit to patients by increasing the number of effective gene therapies.”

Gene therapy development for rare diseases is time consuming and expensive. NIH cited numerous challenges,

including limited access to tools and technologies, lack of standards across the field, and a “1-disease-at-a-time” approach to therapeutic development. A standardized therapeutic development model that includes a common gene delivery technology (a vector) could allow for a more efficient approach to specific gene therapies, saving time and cost.

A clinical component of BGTC-funded research will support between 4 and 6 clinical trials, each focused on a different rare disease, expected to be rare, single-gene diseases with no gene therapies or commercial programs in development but with substantial groundwork already in place to rapidly initiate preclinical and clinical studies. For these trials, the BGTC will aim to shorten the path from studies in animal models of disease to human clinical trials. The BGTC also will explore methods to streamline regulatory requirements and processes for FDA approval of safe and effective gene therapies, including developing standardized approaches to preclinical testing.

NIH and private partners will contribute ~\$76 million over 5 years to support BGTC-funded projects. This includes about \$39.5 million from the participating NIH institutes and centers, pending availability of funds. Additional information and a complete list of participating NIH entities, industry partners, and nonprofit groups is available at: <https://www.nih.gov/research-training/accelerating-medicines-partnership-amp/bespoke-gene-therapy-consortium>.

National Institutes of Health

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(5) Following the Fukushima-Daiichi accident, more than 100,000 individuals were evacuated and forced to abandon their family farms, homes, and jobs. The physical and psychological harm caused by these LNT/ALARA-driven evacuations vastly outweigh the imagined hazard of low levels of ionizing radiation.

I offer the following rallying cry to those seeking to use reason and scientific evidence to overthrow the LNT/ALARA dogma (with apologies to Winston Churchill): We shall challenge the proponents of LNT/ALARA in scientific journals, at conferences, in the media, on the internet, in public forums, and in classrooms. We shall defend valid science, whatever the cost may be.

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