REGULATION OF PET RADIOPHARMACEUTICALS

THE REGULATION OF PET drugs is moving forward on several fronts. PET centers are working with the Food and Drug Administration (FDA) as well as state boards of pharmacy to facilitate approaches to the governance of these radiopharmaceuticals.

For its part, the FDA has maintained that it has the authority to regulate positron emission tomography (PET) radiopharmaceuticals, but it has not clearly stated how it intends to do so. The agency has indicated that each PET center will be required to submit a new drug application (NDA) and meet Current Good Manufacturing Practice (CGMP) standards for each PET radiopharmaceutical it uses.

The Society of Nuclear Medicine (SNM) and the American College of Nuclear Physicians (ACNP) outlined its position regarding the regulation of PET radiopharmaceuticals in a September 21, 1990 letter to then Acting FDA Commissioner James Benson. The letter, signed by SNM President Naomi P. Alazraki, MD, and the immediate past president of ACNP, Robert E. Henkin, MD, states, "We believe the compounding, dispensing, and administering of PET radiopharmaceuticals by physicians and pharmacists falls within the practice of medicine and the practice of pharmacy exemptions to FDA regulation. Based on current law, the on-site compounding and administering of a PET radiopharmaceutical by a physician for his or her patients or by a hospital pharmacy in the same state do not involve the introduction or delivery for introduction into interstate commerce. These activities, therefore, do not fall under FDA's jurisdiction." In addition, write Dr. Alazraki and Dr. Henkin, "It is clear that the Congress never intended the [Food, Drug, and Cosmetic Act] to limit a physician's ability to treat patients." They also point to several Court cases that have affirmed this.

Despite these objections, the FDA has remained steadfast in its position that all facilities — commercial or noncommercial—will need to file NDAs. John Palmer, MD, director of the FDA's division of medical imaging, surgical, and dental drug products, told *Newsline*, "Our working strategy is that we believe that PET products are new drugs and should be regulated as such by the FDA. So the agency's position has not changed."

To help push forward an FDA decision regarding the regulation of PET drugs, the Institute for Clincal PET (ICP) has "negotiated an arrangement whereby ICP will submit a central Drug Master File [DMF] to the FDA for PET radiopharmaceuticals," according to Michael McGehee, executive director of ICP. Each PET facility will be able to reference these DMFs for their NDAs, he notes. To complete the NDA, investigators will need to describe the particular process used to prepare each radiopharmaceutical at a facility and show that the process is safe.

ICP submitted a DMF for fluorine-18 (^{18}F) fluorodeoxyglucose (^{18}FDG) on February 15, 1991, and the FDA is now reviewing it. ICP plans to develop DMFs for other PET radiopharmaceuticals, such as nitrogen-13 ammonia and oxygen-15-labeled water and gases.

According to Mr. McGehee, "most of the clinical sites have begun preparation of NDAs for FDG," and four sites, University of California, Los Angeles (UCLA); Creighton University, in Omaha, Nebraska; Vanderbilt University School of Medicine, in Nashville, Tennessee; and the University of Tennessee Medical Center, Knoxville, planned to submit NDAs in early 1991. Mr. McGehee says he expects the FDA to approve at least one of the NDAs for FDG by August or September.

Working with state boards of pharmacy is another approach some PET centers have taken. Carol S. Marcus, PhD, MD, associate professor of radiological sciences, UCLA, director of the outpatient nuclear medicine clinic, Harbor-UCLA Medical Center, says that California started to take that approach in late 1989.

In a letter to Dr. Palmer, dated August 3, 1990, the Attorney General and Deputy Attorney General of California, acting as liaison counsel to the California Board of Pharmacy, outlined the Board's view of the regulatory requirements for PET drugs. They wrote, "Certainly, under California law and that of many other states, it has always been accepted that a pharmacy may compound medications for use within the facility of which the pharmacy is a part or pursuant to a prescription or even for a physician's office use without becoming a manufacturer . . . In light of this long history and the 1984 Nuclear Pharmacy Guidelines and the lack of a demonstrated need to treat this process as manufacturing, the Board urges the FDA to reconsider its position." The California State Board of Pharmacy determined that the compounding of PET radiopharmaceuticals was compatible with the State's Pharmacy Law and that such compounding, if carried out in accordance with that law, fell under the practice of pharmacy.

Reportedly, the Nebraska and Florida State Boards of Pharmacy have decided to regulate PET drugs in the same manner, and developers of a PET center in Arizona plan to operate a clinical PET center under the practice of pharmacy law of that state.

Ronald J. Callahan, PhD, director of the radiopharmacy at Massachusetts General Hospital, President of SNM's Radiopharmaceutical Science Council, says, "If we as a group organize in support of the practice of medicine and the practice of pharmacy, there will be a long-standing tradition behind us."

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