NRC Issues Interim Rule on Medical Use of Radionuclides

The Nuclear Regulatory Commission (NRC) has amended, on an interim basis, its regulations governing the medical use of nuclear material, giving nuclear physicians and pharmacists more discretion to determine how they prepare, use, and administer radiopharmaceuticals for diagnosis and therapy.

The rule is "a step in the right direction," says ACNP President Robert E. Henkin, MD, professor of radiology, director of nuclear medicine at Loyola University of Chicago in Illinois. "It gives physicians a latitude that they didn't have before." But The Society of Nuclear Medicine (SNM) and the American College of Nuclear Physicians (ACNP) have reservations about the vagueness of the rule's wording and its reporting requirements for commercial radiopharmacies.

SNM President Naomi P. Alazraki, MD, co-director of the division of nuclear medicine at Emory University Hospital and chief of nuclear medicine at the VA Medical Center in Atlanta, Georgia, says, "The way in which the rule came out, the wording of it is not entirely consistent with what we expected." Similarly, Dr. Henkin notes, "The biggest problem is that we don't know what they mean. . . .What they tell you verbally is not clear in the [written] language." The interim rule, which addresses segments of 10 CFR Parts 30 and 35, will be in effect through August 23, 1993. The rule is a partial response to a petition for rulemaking change that was filed by SNM and ACNP in June 1989 (see *Newsline,* August 1989, p. 1296). The rule permits authorized nuclear physicians or their designees to depart from manufacturers' instructions in the preparation of radiopharmaceuticals and to depart from package inserts for therapy indications and methods of administration. The rule requires licensees to record the nature of and reason for such departure. The NRC will review these records over the next three years to determine whether to extend the interim period for the rule, make the rule permanent, or revise the rule. The rule only applies to radiopharmaceuticals for which the Food and Drug Administration (FDA) has approved a New Drug Application (NDA). The rule does not allow departure from the manufacturers' instructions for eluting generators or preparing therapy kits, departure from investigational new drug (IND) generator elution instructions, or departure from IND protocol directions for reagent kit preparations.

In the *Federal Register* notice announcing the rule, the NRC wrote, "The NRC believes that continued application of [the current] restrictions governing the preparation of radiopharmaceuticals and the indications and the method of administration for therapeutic use of radiopharmaceuticals would not permit proper patient care to be provided to some patients" *(1)*.

The rule's phraseology concerns some members of the nuclear medicine community, however, because, they argue that it can be interpreted to limit the practice of medicine and pharmacy. The rule's background material states, "For some uncommon disease states or patient conditions, in order to provide proper patient care, it may be necessary to depart from the FDA-approved instructions to obtain diagnostic or therapeutic medical results not otherwise attainable or to reduce medical risks to particular patients because of their medical condition" *(1)*. "But this is too limiting a set of circumstances," says Captain William H. Briner, (USPHS, ret.), associate professor of radiology, director, radiopharmacy and nuclear medicine laboratory, Duke University Medical Center, Durham, North Carolina. "The NRC needs to rethink its position." Capt. Briner and others point to situations in which the results might be attainable through other means or the departure might not reduce the patient's risk and yet a physician still might deem it appropriate to depart from the package insert. Dr. Alazraki notes, "[SNM's] interpretation, colored somewhat by [its] discussions with the NRC, is that a physician's prescription would suffice in justifying a package insert deviation. The justifications should be recorded in the department's procedure manual." She acknowledges, however, that the rule's wording could be construed in a more rigorous manner, "so it is important that the NRC promptly clarify the rule."

In search of such clarification, SNM and ACNP have sent a letter to John H. Glenn, Jr., chief of the NRC's medical, academic, and commercial use safety branch. The organizations are requesting clarification of the rule and information about how it might be enforced. The letter, signed by Dr. Alazraki and Dr. Henkin, asks, "If. . . the physician involved believes for reasons that he cannot define well, that his deviation from the package insert is in his patient's best interest, what would NRC's response be to this?. . . Physicians are often forced to make judgments based on their best estimations and are unable to predict the outcome. If an outcome is not more beneficial than the standard method, it should still be acceptable."

Another concern shared by nuclear pharmacists is over the rule's reporting requirements. The rule requires information about the nature of a departure,

a description of the departure, and a brief statement delineating the reasons for the departure. In an emergency, physicians would not have to submit a written directive prior to preparation of the radiopharmaceutical if the "physician determines that the delay . . .would jeopardize the patient's health" *(1)*. The physician would be required to prepare the written directive as well as a statement of emergency within three days. The licensee is required to retain each written directive and a record of the number of patient administrations under each departure for five years.

Dr. Henkin says, "The record-keeping is a pain in the neck but probably not burdensome for most people. . . .It's only one sentence." Dr. Alazraki agrees that for nuclear medicine departments the record-keeping is not a problem. "As far as record-keeping goes, each individual nuclear medicine department can include in their procedure manual their accepted deviations from package insert directions. . .and a sentence explaining why they need to deviate." She adds, however, that "the record-keeping is onerous for commercial radiopharmacies."

Syncor International of Chatsworth, California has filed a petition requesting that the NRC reconsider and stay the interim final rule. In the document, Syncor argues that "the interim final rule was promulgated in violation of the Atomic Energy Act, the Administrative Procedures Act, and the NRC's implementing regulations" and that "the record-keeping requirements of the interim final rule will have a direct and negative impact on nuclear pharmacies." If the NRC does not respond to Syncor's petition by October 22, the company will file the document as a suit against the agency.

Mr. Glenn acknowledges that "the justification [for departure] does have to be recorded," but he adds that this need only be "a one sentence kind of justification." He also notes that "one justification of a departure could apply to future use of that radiopharmaceutical" and the physican would "keep track of how many times the prescription was filled." Noting that the NRC set up the reporting requirements to generate data on which to base further decisions about the regulations, he further predicts, "My guess is that the recording would only be for the interim period."

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Dr. Henkin says SNM and ACNP "want the NRC to write a statement of clarification, amend the rule, or accept our letter." He notes that if the rule is not clarified, problems and misinterpretations could arise during inspections or in the future among NRC staff members who were not part of the verbal discussions. He says that he expects the Agency to eventually clarify the language. "The NRC tried to do the right thing but got bollixed up in the language."

In the interim, however, there exists a range of interpretations of the rule. Based on her discussions with the NRC, Dr. Alazraki is broadly interpreting the rule. Dr. Henkin, however, cautions nuclear physicians to "take the rule literally" until there is written clarification. Carol S. Marcus, PhD, MD, director of the nuclear medicine outpatient clinic at Harbor-University of California, Los Angeles Medical Center, a member of the NRC's Advisory Committee on the Medical Uses of Isotopes, told [ital]Newsline[italx], "There's a real difference of opinion. Some are skeptical. . . .Almost everything does not fall into the exempt category."

Mr. Glenn told *Newsline,* "The point of the interim rule isn't to put the NRC in the position of second-guessing physicians." While he would not be more specific about how the rule should be interpreted and how it would be enforced, he said that he was "hoping in a few weeks" to be able to respond to the SNM and ACNP letter. Mr. Glenn said that the NRC will continue to review unauthorized departures at the Office of Nuclear Materials Safety and Safeguards rather than at regional offices, a policy which was established in December 1988 through what is referred to as the "Cunningham Memo of Understanding."

The NRC reserves the right to modify the interim rule or take other regulatory action it deems necessary to protect public health over the three years the rule is in effect.

Send comments on the interim rule to: Secretary of the Commission, US Nuclear Regulatory Commission, Washington, DC 20555, Attn: Docketing and Service Branch.

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References

1. Authorization to prepare radiopharmaceutical reagent kits and elute radiopharmaceutical generators; use of radiopharmaceuticals for therapy. *Federal Register* 1990; 55 (164):34513-34518.