SOCIETY SUES NRC OVER RADIOPHARMACY RULE

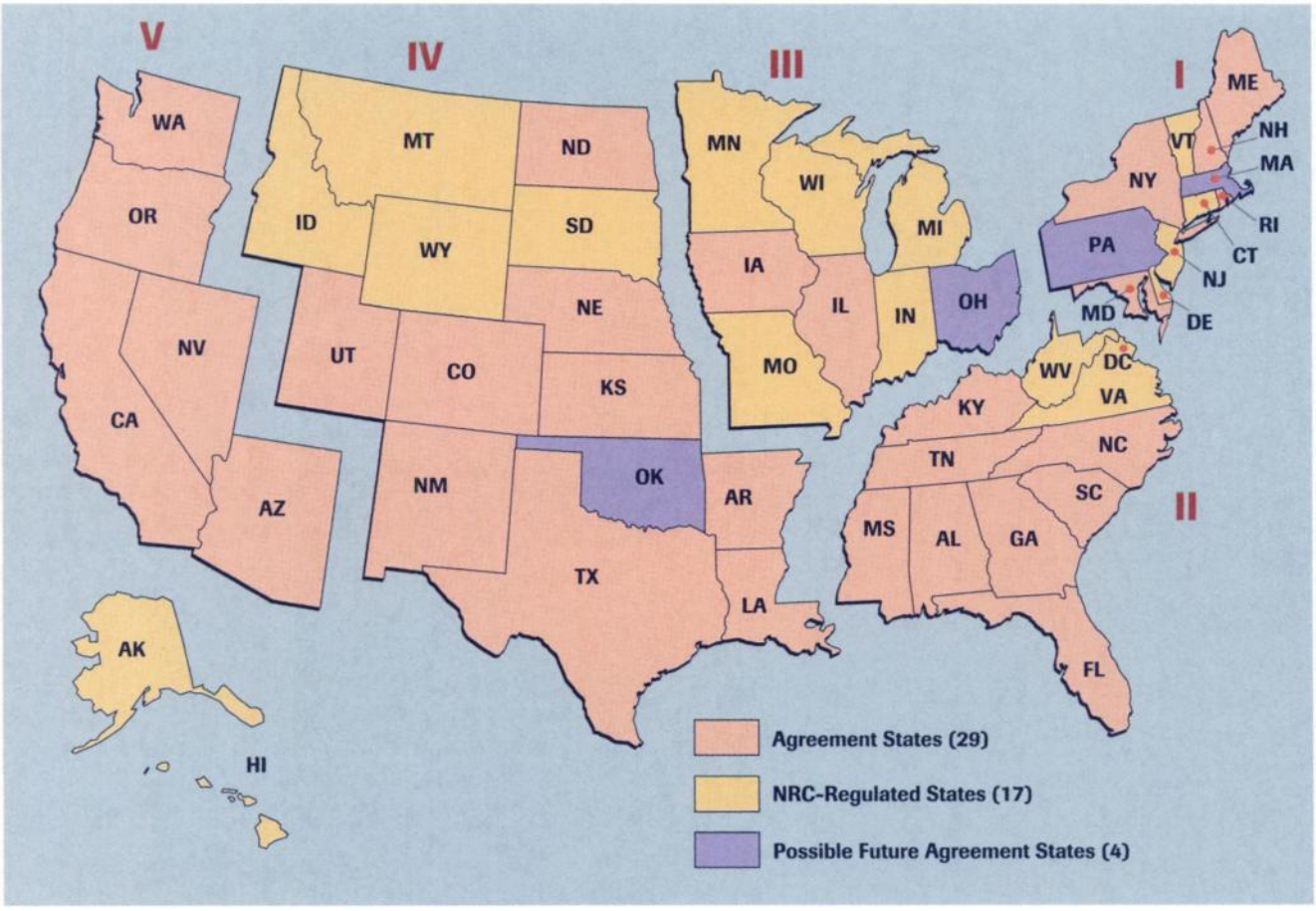
SNM and ACNP have launched a lawsuit against the NRC in an attempt to get more freedom for Agreement States. In this anti-regulatory climate, they're poised to win.

THE NUCLEAR REGULATORY COMmission (NRC) recently relaxed some of its regulations regarding the medical use of nuclear material, but many nuclear medicine leaders feel the agency has double crossed them. On December 2, 1994, the NRC published "Preparation, Transfer for Commercial Distribution, and Use of Byproduct Material for Medical Use," (10 CFR Parts 30, 32 and 35; 59 FR 61767). The final rule is based on a petition for rulemaking filed in 1989 by the Society of Nuclear Medicine (SNM) and American College of Nuclear Physicians (ACNP), which asked the NRC to allow greater flexibility for the practice of nuclear pharmacy in NRC-regulated states.

Although the rule contains many of the petition's requests, it also leaves the NRC with a tighter hold on Agreement States. It specifies new regulations for the medical use of radioactive drugs containing byproduct material and definitions concerning who is qualified to prepare or administer these drugs. Believing that these new restrictions are unjustified, the SNM and ACNP decided to embark on a joint lawsuit by filing a petition with the U.S. Court of Appeals which asks for the NRC rule to be reviewed. The ultimate outcome could be the abolishment of NRC regulation over Agreement States, or it could be a futile effort that costs both the Society and College thousands of dollars.

The issue at hand is whether the NRC has overstepped their bounds in trying to tighten their control over the Agreement States by regulating the practice of medicine and pharmacy. Under the Atomic Energy Act of 1954, states can choose

"We have yet to gain the full trust and confidence of the Agreement States," said NRC Chairman Ivan Selin.



The above map shows the Agreement States, NRC-regulated states and those states considering joining the Agreement State Program. It is divided into the NRC's five regions.

to set their own standards for licensing the production and administration of radionuclides by joining the Agreement State Program. As the new Republican Congress tries to shrink big government and put more power in states' hands, the SNM and ACNP couldn't have chosen a better time to wage a battle for the Agreement States' independence. "The NRC is facing extinction from the nuclear medicine materials program as more and more states become agreement states," said SNM Vice-President Carol Marcus, PhD, MD, director of nuclear medicine and the outpatient clinic at Harbor-UCLA Medical Center in Torrance, CA. "Now the bureaucracy is trying to take back power from Agreement States by requiring them to follow NRC rules."

At Marcus' urging, the SNM and ACNP hired a lawyer and filed a petition for review. "The petition basically buys us time to see if negotiations with NRC will be successful and leaves us the opportunity to challenge the rule in court," said David Nichols, regulatory affairs coordinator at the Washington Office. The organizations are challenging the NRC's determination regarding Agreement State compliance with specific sections in the rule called compatibility requirements. They recently sent letters to the 29 Agreement States asking them to join the lawsuit as co-petitioners.

Should the NRC Be Taken to Court?

Although united in ideology that the NRC should bow out of regulating the nuclear medicine industry, the SNM leadership is divided over how far to take action. Some, like Marcus, believe the NRC should be taken to court over violations of the Agreement State program in the Atomic Energy Act of 1954. "I think we have the firm legal footing to win this thing," said Marcus. Others agree with Marcus in principle but feel that the legal grounds for the lawsuit are shaky given that the NRC has the authority to regulate radionuclides produced in nuclear reactors in the interest of public safety. (The SNM and ACNP lost a lawsuit three years ago that they waged against the NRC in opposition to the quality management rule. See "Meddling with the Doctor's Orders" on page 21N.)

The NRC flexed its regulatory muscle in the Federal Register by recalling the Atomic Energy Act, which the agency said gives it the "broad statutory responsibility to regulate all uses of byproduct material, including medical use." In its response to critical comments, the NRC frequently quoted the section of the Act which puts it under the obligation "to protect the health and safety of the public." In a briefing with the Organization of Agreement States this February, NRC Chairman Ivan Selin said, "It is clear we have yet to gain the full trust and confidence of the Agreement States." But he stressed that the NRC must still implement key regulations in order to harmonize the Agreement States' programs with the NRC's.

In fairness, the NRC did grant the bulk of the changes that SNM and ACNP asked for in their 1989 petition, which was authored by Marcus. They made permanent the interim rule allowing authorized user physicians to deviate from FDA-approved package inserts. They granted the medical use of radiolabeled biologics. And they deleted many of the regulations regarding the use of radionuclides for research in humans.

The leadership of both nuclear medicine organizations, however, were dismayed when the final rules came out citing new definitions and requirements that will apply for Agreement States as well as NRC-regulated states. "The NRC, took our petition and used it as an excuse to throw in a bunch of new rules," said Marcus. "The definitions read like mandates."

For instance, the NRC added definitions—which must be adopted verbatim by Agreement States by January 1998—concerning who is an authorized user or practitioner of nuclear medicine. The definition includes any physician who holds an NRC license and is certified by the American College of Radiology. "There are plenty of diagnostic radiologists who have virtually no experience with nuclear medicine therapies, yet the NRC is now saying that we must consider them qualified nuclear physicians," said Marcus. In California and many other Agreement States, physicians need to demonstrate that they have training and experience in radionuclide therapy before they can be licensed by the state's board of medicine. "We actually have to make our

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The Good News for NRC Regulated States

The final NRC radiopharmacy rule contained many changes that are advantageous to the 21 states that fall under its authority. Here's a summary of the changes:

1. NRC regulations now include the concept of "authorized nuclear pharmacists." Those pharmacists who meet specified training and experience requirements will be authorized to prepare radioactive drugs from scratch. Before this rule was enacted, all pharmacists were restricted to preparing radioactive drugs from kits and generators.

2. NRC licensees have been given the authority to use radioactive materials in research involving humans as long as they obtain informed consent and approval of the research project by an institutional review board. In the past, physicians needed special permission from the NRC to use radioactive materials in human research studies.

3. Radiolabeled biologics (such as antibodies to which radioactive material has been affixed) may now be used for clinical purposes to detect and treat tumors. Previously, physicians were only allowed to use these drugs for research that was approved by the NRC.

4. The NRC interim rule of 1990 that allowed nuclear physicians to deviate from the instructions on FDA-approved package inserts is now permanent. Pharmacists are also allowed to deviate from manufacturers' instructions for preparing radioactive drugs from kits and generators.

those who reside permanently at high altitudes, according to Javier Villanueva-Meyer, PhD, an expert on high-altitude studies in South America at the University of Texas in Galveston.

Beginning the first nuclear medicine studies at the Institute in the 1950's, Cesar Reynafarje, MD, conducted research on ferokinetics, plasma volume, red blood cell mass quantitation and red blood cell survival. He and his colleagues performed in vitro nuclear medicine studies with ^{59}Fe, ^{131}I human serum albumin, and ^{14}C. They found that high altitude dwellers had a 30 percent higher blood volume than those who lived at normal altitudes, according to Villanueva-Meyer. They reasoned that the body adapts to high altitudes by increasing the oxygen concentration in its blood supply and by generating a greater number of blood vessels—especially around the heart.

Other researchers have since found that coronary artery disease and strokes are very rare in individuals who live at high altitudes, said Villanueva-Meyer. Unfortunately, no nuclear medicine studies have been done to assess whether there's a link between chronic hypoxia and a lower risk of these illnesses. "Given the current interest in heart disease prevention," he said, "it would make sense to study these populations in more detail."

Conducting nuclear research in other areas, physiologists at the Instituto Boliviano de Biologia de Altura (Bolivian Institute of Altitude Biology) recently studied the effect of testosterone on the ability of men to adapt to high altitudes. They performed a series of radioimmunoassays to measure testosterone concentrations in native Aymara men who lived at high altitudes and compared these measurements with the testosterone levels of urban men who live at sea level. The scientists concluded that very high testosterone levels could compromise adaptation to high altitudes, particularly in older men.

Although the scientific importance of this research goes unquestioned, the work was conducted in a lab that stands about 3000 feet closer to sea level than Monte Rosa. The Peruvian research labs, alas, also fall short by a mere 300 to 650 feet.

The True World Record, Perhaps?

A nuclear medicine practitioner at the Mallinckrodt Institute of Radiology at Washington University in St. Louis responded vigorously to Cradduck's e-mail. "As a member of the team that does hold the world record, I believe this mistaken claim should be refuted!" wrote Marcus E. Raichle, MD.

In 1987, Raichle worked with a group of British and Danish scientists who studied cerebral blood flow in acute mountain sickness. The team trekked to the Karakoram mountains at the Pakistani-China border, whose grand height is recorded at 17,800 feet above sea level. They measured changes in brain emissions using ^{133}Xe and an array of six collimated sodium iodide crystal detectors. The researchers found that headaches and central nervous system disorders caused by acute mountain sickness don't result from increased cerebral blood flow since the climbers who had symptoms had the same increase in cerebral blood flow as those who had none. They also confirmed that administering carbon dioxide (CO_2) at high altitudes can rapidly relieve symptoms of acute mountain sickness. Brain studies with $^{133}Xe_2$ showed increased cerebral blood flow in some climbers who inhaled the CO_2, which indicates that they had an improved oxygen delivery to their brains. In terms of the nuclear medicine world record, Raichle and his colleagues had indeed surpassed Noelpp's self-proclaimed record by 2854 feet!

No one has yet reported a nuclear medicine study that tops the Karakoram expedition, but one astute Internet correspondent pointed out that it should perhaps be qualified as the "earthbound" record. Sylvain Houle, MD, of the Clarke Institute's PET Centre in Toronto, noted that scientists from the National Aeronautics and Space Administration (NASA) performed radiotracer studies aboard spacecraft to study the effects of weightlessness in space.

During a mission launched on October 18, 1993, astronauts were injected with three radionuclides: ^{125}I, to determine plasma volume; ^{35}S, to measure extracellular fluid space; and ^{59}Fe, to study erythrokinetics and red-blood-cell volume. However, "no radiation detection devices were used, other than the crew's personal occupational dosimeters," said a NASA spokesperson. With plans to build an international East-West space station over the next seven years, researchers may soon have the means to land gamma cameras at high altitudes via spaceships rather than helicopters.

Lawsuit Over NRC Rule

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laws less strict to comply with this rule—which is crazy considering that Agreement States have one-third the misadministration rate as NRC states," she says.

The final rule also defines who is qualified to practice nuclear pharmacy and includes labeling requirements for radionuclides which are independent of the FDA's requirements. "The NRC doesn't have the jurisdiction to make these regulations," said Marcus. "The agency says it's going to supersede the board of medicine, supersede the board of pharmacy and override state law."

Although Marcus raises persuasive arguments, some nuclear medicine experts feel she is being unrealistic and is waging a quixotic battle against windmills. "I think the lawsuit is much ado about nothing," said Barry Siegel, MD, director of the division of nuclear medicine at Mallinckrodt Institute of Radiology and chairman of the Advisory Committee on the Medical Uses of Isotopes. "Carol [Marcus] thinks getting anything less than what she asked for is a resounding defeat. But I think it's a good rule considering where the NRC was when we started."

Society leaders are hoping that filing the petition for review will spur fruitful negotiations with the NRC allowing the issues to be settled out of court. Cost is definitely a factor on their minds. According to Nichols, the petition for review has already cost about $1000 in legal fees. Formal negotiations with the NRC, the next step, could run up to $7500. Presenting an oral argument and filing a brief in court could cost up to $50,000.

The Concern Over Licensing Fees

The factor that will play a major role in determining the direction of the lawsuit: the yet-to-be-published regulatory guides. These guides, which accompany every final rule, outline the details

Meddling with the Doctor's Orders

The SNM and ACNP have waged other lawsuits against NRC rules. In fact, three years ago they brought an action protesting the quality management rule that was argued in front of the U.S. Court of Appeals. The panel of judges ruled in favor of the NRC saying that the agency acted within the bounds of its broad mandate to regulate the medical use of radionuclides. "They suggested that we lobby Congress to change the regulatory authority of the NRC," said David Nichols, regulatory affairs coordinator at the Washington Office.

As of January 25, 1995, all Agreement States were required to comply with the quality management rule (10 CFR Parts 2 and 35) which dictates that physicians need to be more extensively involved in the therapy of their patients and which ultimately means more paperwork. (At press time, one-third of the Agreement States still had not come into compliance with this rule according to Richard Ratliff, PE, chairperson of the Organization of Agreement States.) One particular aspect of the rule that enrages many SNM leaders is the new requirement pertaining to written directives. The rule specifies that nuclear physicians can no longer prescribe ranges on written directives but must specify an exact dose. The NRC requires a written directive for all radionuclide therapy procedures and for imaging procedures using ^{131}I in doses over 30 μCi. Any dose administered that is off by 10 percent must be reported to the NRC; any that is off by 20 percent is considered a misadministration subjectable to a fine.

Practically all SNM leaders agree that eliminating ranges doesn't make any sense. "With the ranges that we prescribe, it makes no difference whether a patient receives the higher or lower end of a dose both in terms of medical safety to the patient and the effectiveness of the diagnostic image," said Richard C. Reba, MD, section chief of nuclear medicine at the University of Chicago Hospital and chairman of the SNM/ACNP government relations committee. Not only will the rule be an inconvenience to nuclear physicians—who often don't know the exact dose the radiopharmacy will deliver when they order—but it may be a danger to pharmacists. "Technicians who fill the prescriptions may be exposing themselves to more radiation if they have to calibrate and draw up the radiopharmaceutical several times in order to get the exact dosage," Reba said.

Officials at the NRC assert that this section of the rule has been misinterpreted. "We're not saying that a physician can't order a dose range from a radiopharmacy," said Larry Camper, MS, section leader for the medical and academic section of the NRC. "What we are saying is that somewhere in the loop the physician needs to know the exact dose being given to the patient. It's not appropriate for a technologist to be making the final analysis on what dose to give."

From a legal standpoint, the prescribing of drugs falls under the authority of the state boards of medicine and licensing and, some SNM leaders contend, not the NRC. "They're getting into areas assuming more authority where they have no competence," said Reba. Marcus concurs and said that California, the state where she practices, has decided not to implement the quality management rule citing the reason that the NRC has no jurisdiction over these issues.

In lieu of the outcome of the quality management suit, should SNM and ACNP think twice before bringing an action against the NRC again? "I don't think so," said Nichols. He said the lawsuit over the radiopharmacy rule is over the jurisdiction that NRC has over Agreement States, not states that fall under its regulation.

for how the NRC will interpret and enforce its new regulations. "The rule itself is written in very vague language," says Marcus, "but I'm positive the regulatory guides are going to be venomous." She claims the NRC waited to publish the guides as a ploy to prevent the SNM and ACNP from filing a petition in court. Under federal law, there is a 60 day deadline for filing such a petition. "They wanted to wait until after the deadline to publish the guides to keep us from suing," Marcus said.

Marcus fears the guides will give the NRC regulatory control over nuclear pharmacy. Worst case scenario: "The agency could oversee how every pharmacist makes drugs, control what is put into the mix and review each and every label," she says. This could lead to vast inspections of pharmacy sites costing pharmacists $133 per hour. The NRC may increase licensing fees to pay for the extra staff they would need to implement these new policies.

NRC officials deny that fees will be increased as a result of the guides. "We foresee that the main changes will be in the wording of the licenses to reflect the broader privileges of the licensee," said Larry Camper, MS, the section leader for the medical and academic section of the NRC in Bethesda, MD. As of press time, the NRC had completed a draft of the regulatory guides and Camper predicted they would be published within the next few weeks—although a date had not yet been set. "We are going to arrange a meeting with members of the radiopharmaceutical community sometime this Spring to discuss the guides," he said.

Until then, the lawsuit against the NRC will remain in the preliminary stages. Richard C. Reba, MD, section chief of nuclear medicine at the University of Chicago Hospital and chairman of the SNM/ACNP government relations committee sums up the general feeling among SNM leaders: "I think a full fledged lawsuit may be a bit extreme. However, this rule does seem to be worse than the others." Like Reba, most nuclear medicine experts seem to be reserving judgement until they can read the regulatory guides or "fine print" of the radiopharmacy rule. Copies of the rule are available from the Joint Government Relations Office, 1200 19th Street, NW, Ste. 300, Washington, DC 20036, Attn: David Nichols; tel. (202) 429-5120.

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