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September 26, 1989

Secretary of the Commission
US Nuclear Regulatory Commission
ATTN: Docketing and Service Branch
One White Flint North Building
11555 Rockville Pike
Rockville, Maryland 20852

SUBJECT: Docket No. PRM-35-9

I am writing in general support of the PRM filed by the ACNP and SNM under the subject docket. I am a board-certified nuclear medicine physicist with more than 16 years experience as a medical radiological physicist and as a medical health physicist. All of my clinical nuclear medicine experience has been in clinics operating under a broad-scope medical license and staffed by either a nuclear pharmacist (R.Ph.; baccalaureate or advanced degree) or a radiochemist (Ph.D. in chemistry). Our clinics have always been enrolled with one or more physician- or vendor-sponsored IND's (e.g., PIPIDA, NP-59, MIBG). Additionally, I served as Radiation Safety Officer for one of these broad-scope-licensed medical centers.

My experience has been that the requests contained in the PRM are reasonable and provide an acceptable degree of radiopharmaceutical quality and of patient safety, <u>if</u> a number of conditions are satisfied:

1. the pharmacist/chemist must be properly trained and experienced in drug manufacturing techniques, including preservation of sterility and prevention of pyrogenicity, and in the USP-prescribed methods for testing sterility and apyrogenicity;

2. inhouse radiopharmaceuticals must be tested in an appropriate animal prior to first use in humans in each nuclear medicine clinic to assure proper in vivo behavior;

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3. the local Radiation Safety Committee should review each individual compounding "recipe" and should not issue a blanket approval for all agents;

4. NRC should publish a Regulatory Guide describing good manufacturing practices, sterility and apyrogenicity testing, animal biodistribution testing, recordkeeping, establishment of expiration date, and other safety-related factors in order to assure at least modest uniformity among licensees;

5. local compounding should be permitted under non-broad scope licenses, but only if a suitably trained nuclear pharmacist/chemist is on the staff;

6. physicians do not inherently possess the expertise and competence to compound radiopharmaceuticals simply because of their M.D. degree or their ABR or ABNM certification, and they should not be permitted to do so unless they can demonstrate specific training and experience and if they themselves perform the labwork;

7. a junior nuclear pharmacist/chemist should be permitted to compound radiopharmaceuticals for inhouse use if the nuclear medicine clinic has been doing so under the pharmacist/chemist's predecessors and if the nuclear medicine physician has suitable experience supervising such work, as determined by the RSC under guidelines in the USNRC Regulatory Guide; and

8. there must be a strict prohibition against giving or selling a locally-compounded radiopharmaceutical to another licensee unless specifically permitted by license conditions in each license (local RSC should not have this authority). Any such application for a license amendment should be signed by the CEO of each licensee institution to assure that institution management has considered product liability issues.

Item 8 of the PRM addresses free-standing radiopharmacies. The term "free-standing" is not defined, but the remainder of my comments will be based on the assumption that such pharmacies are commercial, for-profit ventures not controlled by a medical licensee who is organized primarily as a patient care provider. My experience with local commercial radiopharmacies is that they are hectic places staffed by pharmacists with no advanced education past the B.S. in Pharmacy, little specialized radiopharmacy training, and a primary concern of cranking out the hundreds of dosages per day necessary to pay their salaries and augment their incentive bonus plans. In such operations, a careless or

sloppy error has the potential for affecting thousands of patients in a very short time. I am opposed to allowing commercial free-standing radiopharmacies to compound agents for general distribution and sale. There are no dispassionate RSC's and IRB's to keep an eye on them. They usually do not have the facilities for in vitro and in vivo quality control testing and for imaging of animals. A qualified nuclear medicine physician usually in not on staff in a relationship free of conflict of interest.

A final issue that needs to be addressed in greater detail is how non-NDA agents are to be licensed. Radiopharmaceuticals in an NDA status should be approved by the RSC and should not require informed consent and IRB review. RDRC rules are well-established and are satisfactory for agents covered by RDRC. The trickier questions involve agents for which an IND exists and agents developed locally that are intended for routine clinical use (non-RDRC). My recommendation is that these agents be permitted only if:

1. the nuclear pharmacist/chemist and nuclear medicine physician are very experienced in human radiopharmaceutical research and in radiopharmaceutical compounding;

2. the IRB and RSC approve each agent individually, based on review of toxicity, animal biodistribution studies, preliminary human data, and estimated radiation dosimetry;

3. patients sign an informed consent document that clearly states that the agent has not received FDA approval.

If the process of local compounding is made too easy, some physicians and pharmacists/chemists will eventually abuse the system. While these diagnostic agents are not likely to kill or seriously injure anyone, either from the radiation or the chemical moiety, the bad press the NRC and the medical community will receive justifies having local RSC approval as a bare minimum requirement.

The opinions expressed in this letter are my own and do not necessarily represent the position of my employer or of any professional or scientific organization of which I am an officer or member.

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