

Whither Nuclear Pharmacy?

The Commissioner of the Food and Drug Administration published a notice in the Federal Register of July 25, 1975, terminating the exemption for radioactive new drugs from the investigational new drug requirements of the Federal Food, Drug, and Cosmetic Act (40 FR 31298). All radioactive drugs, except those for certain research uses, introduced into interstate commerce are now subject to a "Notice of Claimed Investigational Exemption for a New Drug" (IND), an approved new drug application (NDA), or a biologic product license. This means that all radiopharmaceuticals, including cold kits and radioactive biologics, are now under FDA regulation.

Our concern is the companion notice concerning the FDA's posture toward the regulation of nuclear pharmacies, also published July 25, 1975, entitled "Notice to Nuclear Pharmacies Regarding the Development of Proposed Regulations and Interim Enforcement Policy" (40 FR 31314). The intent of the FDA to consider new regulations for nuclear pharmacy, or at least central radiopharmacies (CRPs), is spelled out in that notice. This notice was published with the lifting of the exemption to assure the nuclear medicine community that the FDA plans no specific regulation of CRPs for the present, i.e., until the dust settles after the termination of the exemption itself. This means that there is time to consider the question posed by the FDA: Is there a need for additional regulations specifically for nuclear pharmacies?

The possibility of specific regulation of CRPs was extensively discussed in an open meeting of the FDA Radiopharmaceuticals Advisory Committee in Washington on April 24, 1975. There appeared to be a consensus in only two areas: (A) there is no significant public health hazard due to the operation of nuclear pharmacies (including CRPs) at the present time, and (B) representatives in attendance from federal and state government, industry, medicine, academe, pharmacy, radiopharmacy, and radiochemistry had widely varying points of view on the need for and degree of regulation that should or should not be applied.

The FDA initially attempted to define manufacturing as it might relate to the operation of nuclear pharmacies and to differentiate between what is compounding and what is manufacturing in the nuclear pharmacy. More recently, the FDA has attempted to determine what constitutes the practice of nuclear pharmacy and when should (or should not) the IND/NDA provisions of the act be applied to a particular radiopharmacy.

Radiopharmaceuticals are unique drugs in many ways, and it has been said that special regulations may be required because they are different. We will enumerate several of these differences here, because consideration of the very uniqueness of diagnostic radiopharmaceuticals should assist in deciding whether you believe that existing regulations (FDA, NRC, agreement state, state pharmacy acts, and others) can be applied to CRPs, or whether in fact new regulations may be required.

1. The radioactive label is the important part of the radiopharmaceutical. The primary considerations are diagnostic efficacy and radiation dosimetry rather than pharmacology.
2. Most diagnostic radiopharmaceuticals in current use are compounded locally, immediately prior to their use.
3. Most of the radiopharmaceuticals in current use were developed in university medical centers, and industry admits that this trend will continue for the foreseeable future.
4. Radiopharmaceuticals have an enviable safety record. The number of adverse reactions reported to the Adverse Reaction Registry of the SNM is extremely small (24 in 1974, eight in 1975).
5. The principles of quality control inherent in drug production are designed to detect bad preparations prior to patient administration. However, should faulty control procedures be applied to radiopharmaceuticals, a single bad preparation or lot would be immediately evident (e.g., stomach or liver uptake during bone imaging).

Consideration of the above leads us to the following conclusions: The individual compounding of radiopharmaceuticals on prescription to individual patients or physicians in a single institution or family of affiliated institutions is the practice of pharmacy. In this situation, the radiopharmaceuticals pre-

pared, whether in unit dose or multidose vials, are still under the control of the preparing pharmacy. The central radiopharmacy preparing large quantities of radiopharmaceuticals in bulk from raw materials is a manufacturer and should be subject to applicable FDA rules and regulations. Somewhere in between these two examples falls a group of CRPs that have caused concern, especially in several of the agreement states. Some of these CRPs probably are manufacturers. Others, although "commercial", are clearly engaged in the classical practice of pharmacy, compounding radiopharmaceuticals from approved ingredients on individual prescription.

We believe that the gap in regulatory authority sensed by the FDA and some agreement states can be bridged by the application of existing state and federal regulations, by the generation of USP monographs for diagnostic radiopharmaceuticals to legitimize the in-house compounding of radioactive drugs, and by the development of guidelines which may be applied by the states to assist in the determination of whether or not a particular CRP is a manufacturer. If new guidelines or regulations are required at all at the federal level, they may be necessary to further define when existing IND/NDA provisions of the Food, Drug, and Cosmetic Act should be applied to nuclear pharmacy. As these questions are resolved, it behooves all of us to work closely with our respective state boards of pharmacy and with the FDA to ensure that any regulatory actions which are taken will be designed to improve the quality of patient care, to increase the efficiency of the regulatory process so that better agents will be promptly available, to encourage development of new radiopharmaceuticals, and to promote the responsible development of nuclear pharmacy as a profession.

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