LETTER TO THE EDITOR

PARTICLE REDUCTION OF A MACROAGGREGATED ALBUMIN KIT

To the Editor: In a recent article, Levine et al. (*1*) described a method of reducing the number of macroaggregated albumin (MAA) particles in a commercially available kit. The method involved reconstituting the MAA kit with sodium chloride injection (USP) and removing a portion of the total volume containing a lesser number of particles before introducing sodium pertechnetate for labeling of the MAA. This modification allows the preparer to maintain the prescribed number of particles and dose activity needed for each patient and at the same time, have a workable volume of MAA to draw up and inject. Apparently, the authors' main objective in the use of this methodology for particle reduction was to utilize it on perfusion lung scans for neonates, young children, and patients with right-to-left cardiac shunts, which require much smaller number of MAA particles than normal. This method may also have several useful advantages that were not mentioned in the article. Minimizing the number of particles used in a study is also a concern when performing lung scans on patients with pulmonary hypertension (*2,3*). The method also allows the preparer to use smaller activities of pertechnetate. This is advantageous for two reasons: First, during those times when large amounts of pertechnetate may not be available (i.e., in departments that use commercial radiopharmacies or small activity generators) to prepare the MAA kit using accepted reconstituting guidelines. Second, the use of smaller activities will potentially decrease the exposure to technologists and radiopharmacists, which is consistent with the Nuclear Regulatory Commission's (NRC) ALARA (as low as reasonably achievable) principle.

The problem we perceive with the use of this method to prepare a commercially available MAA kit in the majority of hospitals in the United States is that it deviates from the package insert instructions on reconstitution supplied by the manufacturer. The NRC clearly states in 10 CFR 35.200 (b) that "a licensee shall elute generators and prepare reagent kits in accordance with the manufacturer's instructions." Utilizing this method would constitute a direct violation of NRC regulations. This problem has been addressed by the NRC. There were proposed rule changes (*4*) with respect to manufacturer recommendations that were submitted in June 1989 by the American College of Nuclear Physicians and The Society of Nuclear Medicine for consideration by the NRC. Among the proposed rule changes, the above described modification of a kit preparation will be allowed by the NRC. Currently, it is already allowed under Food and Drug Administration guidelines. Action on these changes is pending NRC review of submitted comments for approval.

We favor the proposed rule changes and would use the method of particle reduction in preparing MAA kits if and when it is allowed by the NRC. Before using the method, further evaluation of the preparation should be performed to supplement Levine's article review of percent binding of the pertechnetate to the MAA. This should also include evaluation of particle size and number after preparation, product stability over time, and the effect on binding efficiency with varying time delays between reconstitution of the MAA with sodium chloride and the addition of pertechnetate.

NOTE ADDED IN PROOF: Since the above letter to the editor was accepted for publication, the Nuclear Regulatory Commission (NRC) has issued an interim final rule (*5*) in part concerning 10 CFR 35.200(b). This interim rule allows persons licensed by the NRC to depart from the manufacturer's instructions when eluting generators and preparing reagent kits if they have written directive from an authorized user physician for a particular patient(s) or radiopharmaceutical. This directive must include the specific nature of the departure, a detailed description of the departure, and a brief statement as to the reasons why the departure from the manufacturer's instructions would obtain medical results not otherwise attainable or would reduce medical risk to particular patients because of their medical condition. In the case of emergencies where time is of the essence, the NRC allows the authorized user/physician to proceed without a written directive if obtaining one would jeopardize the health of the patient. A written directive must be completed within three days of the emergency that includes a statement describing this situation. This interim rule applies only to radiopharmaceuticals that are approved by the Food and Drug Administration (FDA) and is effective from August 23, 1990 to August 23, 1993. The NRC is requesting comments on the interim rule during this time period.

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REFERENCES

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3. Kowalsky RJ, et al. Safety and effectiveness considerations with particulate lung scanning agents. *J Nucl Med Technol* 1982;10:223-227.

4. Proposed rules. *Federal Register* 1989;54:38239-38241.

5. Rules and Regulations. *Federal Register* 1990;55:34513-34518.