LETTERS TO THE EDITOR

SUGGESTION FOR CAUSE OF SUBSTANDARD RADIOLABELING OF RED BLOOD CELLS USING ULTRATAG®

To the Editor: The development and introduction of the UltraTag® kit (Mallinckrodt, Inc., St. Louis, MO) offered a substantial improvement in the ability to conveniently and efficiently radiolabel red blood cells with ^{99m}Tc (*1*). This particular cell-labeling technique is especially desirable for use in studies of gastrointestinal hemorrhage (GI bleed) since even minimal levels of free pertechnetate that might occur with other techniques potentially are interferential for image interpretation (*2*). Because a variety of factors can adversely affect radiolabeling procedures, radiochemical purity testing should be routinely performed before patient administration (*3*).

A review of UltraTag's labeling procedures performed in this institution, since commercialization in 1991, revealed that 8 of 368 (2%) preparations were of substandard labeling efficiency (i.e., < 90% radiochemical purity). Preparation factors that were involved in each of these substandard products were evaluated, and are detailed on Table 1. None of these substandard products was administered to patients. In each instance a second UltraTag kit from the same lot was prepared successfully using pertechnetate from the same eluate vial (three instances) or pertechnetate from a fresh eluate (five instances).

A substandard product resulting from adding syringe components in the wrong order is not unexpected due to the nature of the sequential chemical reactions (*4*). Similarly, a substandard product due to inadequate reactant concentration (excess reaction volume) previously has been reported (*5*). However, the five instances of substandard radiolabeling associated with pertechnetate containing excessive amounts of ^{99}Tc are in contrast with previous reports. Specifically, independent studies performed at Brookhaven National Laboratory (*6*), at Mallinckrodt Medical, Inc. (*7*) and at University of Minnesota/Mayo Clinic (*8*) all demonstrated that poor labeling efficiency may result when the kit is prepared using pertechnetate containing an excessive concentration of ^{99}Tc (i.e., an initial eluate from a Monday generator with 72-hr ingrowth and/or an eluate 12 hr old) using ACD as the anticoagulant, but that high labeling efficiency is routinely acheived under the same circumstances using heparin as the anticoagulant. Since heparin was used as the anticoagulant in each of the five instances reported here, substandard radiolabeling was not anticipated.

In addition to the competitive mass effects from ^{99}Tc, other variables can influence the labeling reaction. For example, the type and quantity of anticoagulant, the volume of blood and the volume of pertechnetate can affect the labeling efficiency and the kinetics of the labeling chemistry (*5*). Except for excess pertechnetate volume involved in one instance, none of these reported variables was involved in the instances reported here.

Although substandard radiolabeling associated with pertechnetate containing excessive ^{99}Tc may be related to carrier effects, we suggest another explanation for previously unexplained poor labeling that involves the formation of oxidizing species. It has been reported that radiolytic ionization of water in generators and pertechnetate solutions produces hydrogen peroxide and hydroperoxy free radicals which readily oxidize stannous (*9, 10*). Hence, oxidation of some stannous ion by this mechanism and/or excessive levels of ^{99}Tc may be responsible for the five substandard products reported here. Additional study is required.

Regardless of the actual mechanism, pertechnetate from the first elution of a new generator and/or aged for >12 hr should not be used in the preparation of UltraTag kits. Moreover, because a variety of preparation factors, including human error, can result in a substandard product, quality control testing should be performed routinely before patient administration.

James A. Ponto, MS, RPh
University of Iowa Hospitals and Clinics
Iowa City, Iowa

References

1. Srivastava SC, Straub RF. Blood cell labeling with ^{99m}Tc: progress and perspectives. *Semin Nucl Med* 1990;20:41–51.
2. Rousseau AJ, Royal HD, Parker JA, Kolodny GM. Technical considerations of technetium-99m-labeled red blood cell scans in the detection and localization of gastrointestinal bleeding sites. *J Nucl Med Technol* 1984;12:56–58.
3. Hung JC, Ponto JA, Hammes RJ. Radiopharmaceutical-related pitfalls and artifacts. *Semin Nucl Med* 1996;26:208–255.
4. Massler J, Mento C, Shodavaram S, et al. A study of sequential factors affecting ^{99m}Tc RBC labeling efficiency using UltraTag. [Abstract] *J Nucl Med Technol* 1996;24:165–166.
5. Wolfangel RG, Srivastava SC, Bushman MJ, Straub RF. UltraTag® RBC kit—relationship between anticoagulants and reagent volume on RBC labeling efficiency and kinetics. [Abstract] *J Nucl Med* 1992;33:989.

TABLE 1
Preparation Errors Associated with Substandard Radiolabeling of UltraTag® Kits

Number of instances	Preparation errors
1	Syringe components added in wrong order.
1	Excess reaction volume (4 ml pertechnetate added).
1	Used pertechnetate from the first elution of a new Monday generator.
1	Used pertechnetate from a routine eluate, but which was >12 hr old.
3	Used pertechnetate that was both from the first elution of a new generator and was >12 hr old.
1	Unexplained.

6. Srivastava SC, Straub RF. Evaluation of heparin and anticoagulant citrate dextrose in the preparation of technetium-99m-red blood cells with UltraTag® RBC kit. [Letter] *J Nucl Med* 1992;33:307–308.
7. Wolfangel RG. Evaluation of heparin and anticoagulant citrate dextrose in the preparation of technetium-99m-red blood cells with UltraTag® RBC kit. [Letter] *J Nucl Med* 1992;33:308.
8. Wilson ME, Hung JC. Evaluation of heparin and anticoagulant citrate dextrose in the preparation of technetium-99m-red blood cells with UltraTag® RBC kit. [Letter] *J Nucl Med* 1992;33:306–307.
9. Colombetti LG, Barnes WE. Effect of chemical and radiochemical impurities from eluants on ^{99m}Tc-labeling efficiency. *Nuklearmedizin* 1977;16:271–274.
10. Molinski VJ. A review of ^{99m}Tc generator technology. *Int J Appl Radiat Isot* 1982;33:811–819.

AN ACCURATE AND INEXPENSIVE GAMMA CAMERA-BASED SYSTEM FOR WIPE TESTING

To the Editor: I read the article, "An Accurate and Inexpensive Gamma Camera-Based System for Wipe Testing," by Curtis B. Caldwell (*J Nucl Med Technol* 1997;25:201–204) with a great deal of interest. I like the concept of using a damaged collimator that is stashed away in an out-of-the-way corner to count wipe tests and save the technologist time when time is at a premium. However, there may be an error in the methodology.

I could not discern from the article if wipe efficiency (i.e., the ratio of radioactive atoms on a contaminated surface that are physically transferred to the wipe) was taken into account. If wipe efficiency was not taken into account and one assumes the conventional ratio of 0.1, then the reported MDAs are underestimated by a factor of 10 and the cited regulations are not met. If the error is real (and I am not certain that it is), I also wonder if this is a widespread error in methodology within the nuclear medicine community. Apparently the error was not caught during the review process. I would not like anyone to be cited for a violation of the regulations when the concept of using a damaged collimator for wipe testing is really quite excellent.

Dave Horn, CNMT
Powhatan, Virginia

Reply: Dave Horn raises an important point regarding the need to incorporate a wipe efficiency or collection factor into the calculation of removable activity. This factor was not taken into account in my paper (*1*). I did not make it clear that I was calculating minimum detectable activity (MDA) *on the wipe*, to which one must apply the collection factor to derive an estimate of removable activity. Note that one must be aware of the vagaries of local regulations in this matter. For example, when reporting leak tests of sealed sources in Canada, one need not take into account a collection factor. In my experience in Canada, the federal regulatory body has not enforced the use of a collection factor for contamination monitoring in nuclear medicine (despite the fact that Canadian regulations require the use of a collection factor). If the collection factor has not been determined experimentally, it should be assumed to be 0.1, as noted by Mr. Horn. Note that there have been few publications regarding collection factors for nuclear medicine radiopharmaceuticals (*2*).

If the collection factor must be assumed to be 0.1, then it would be necessary to modify the acquisition time used to ensure that less than 50 Bq per 100 cm^2 of removable contamination was present (i.e., 5 Bq on the wipe). In order to obtain an MDA less than 5 Bq (on the wipe) in a reasonable counting time, it would be necessary to perform the testing when the background count is low (i.e., after normal working hours). For our set-up, a 10-min acquisition time in "after hours" background conditions is sufficient to reduce the MDA to below 5 Bq (on the wipe) for all radioisotopes tested. In our department a much longer acquisition time would be required during normal working hours due to the higher background count rate.

I certainly agree with Mr. Horn that I would not wish anyone to be cited for a violation of regulations due to unclear writing on my part.

Curtis B. Caldwell, PhD, MCCPM
Department of Medical Imaging
Sunnybrook Health Science Center
Toronto, Ontario, Canada

References

1. Caldwell CB. An accurate and inexpensive gamma camera-based system for wipe testing. *J Nucl Med Technol* 1997;25:201–204.
2. Scott LE, Gibson CJ. Wipe tests to assess ^{99m}Tc surface contamination: effects of surface type, swab type and chemical form. *Nucl Med Comm* 1991;12:127–133.