LETTERS TO THE EDITORS

Re: Terminology Concerning Specific Activity of Radiopharmaceuticals

In the manufacture of artificial radionuclides, the assumption is frequently made that if no stable isotopes of the element being produced are knowingly introduced, the resultant radionuclide is "carrier-free," i.e., it contains only the nuclide of interest. However, there is increasing use of short-lived isotopes of elements widely distributed in our environment, radionuclides that have theoretical specific activities in the mCi/pmole range, and the probability of accidental dilution with stable isotope has to be considered. Modern nonradioactive analytical techniques have developed to the stage where picomole quantities of material are routinely detected (and sometimes femtomole quantities), and radioactive tracers are being applied to systems that will saturate at or below nanomole quantities of material.

Thus at present there are tracer studies that require specific activities approaching the theoretical limits, and analytical methods are available to measure the actual amounts of material present at the required levels. However, in many cases in the literature the term "carrier-free" is used when there has been no determination of actual specific activities, and the chances of significant dilution with stable isotopes approach certainties.

There is a growing awareness of this problem (*1-6*) and a recent article suggested that the term "carrier-free" be reserved for those cases in which it can be justified (*1*).

A brief survey of recent articles (*2,4,6*) suggests that there is confusion even among chemists as to the use of the term "carrier-free," and we would like to suggest that the leading journals establish a policy of limiting its use along the lines previously suggested (*1*). This then raises the question of what to term the majority of current so-called "carrier-free" procedures in which the specific activity, although undoubtedly high, has not been measured. The term "no carrier added" has the virtue of being clear and self-explanatory (*1*), although it is not easy on the tongue.

Adoption of this policy would serve to emphasize the problems of high-specific-activity synthesis for those directly involved in the chemistry and to clarify the situation for those who use the tracers.

T. J. TEWSON
University of Texas
Houston, Texas

M. J. WELCH
Washington University School of Medicine
St. Louis, Missouri

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Reply

The term "carrier" had its origins in the early work of Kasimir Fajans, Fritz Paneth, and Otto Hahn. It was applied to cocrystallization and coprecipitation phenomena observed during research with naturally occurring radionuclides. In a now classic text titled *Radioactivity Applied to Chemistry* (*1*) Bonner and Kahn had written a chapter on "Behavior of Carrier-Free Tracers" in which "Carrier-free" was communicated as follows: "However, it is [customary] to refer to all radioactive preparations to which no isotopic carrier has been intentionally added and containing no isotopic material detectable by [ordinary] chemical or spectrographic means as *carrier-free*." This definition was applied to a wide variety of coprecipitation studies and only incidentally to the question of carrier where the "isotope" and its carrier are made of nuclides of the same element or nuclides of the same element in the same chemical compound assuming accepted purity criteria. The term "carrier-free" and related terms have clearly been widely misused in the rigorous sense, and we too have been guilty of imprecise use of these terms.

Recent advances in nuclear medicine and in radiopharmaceuticals have prompted us to reassess the common usage. Advances in analytical techniques, including wholly new approaches to chemical analysis, have greatly extended the range of accurate detection of chemical species. Nuclear medicine research and application is becoming increasingly concerned with the use of organic and organometallic compounds that must be used at the true tracer level. An example is the use of labeled compounds to probe receptor sites in the brain or heart where the number of sites available and/or occupied is germane to the particular study. The increasing sophistication of physiological and biochemical models requires a knowledge of changing specific activity during the course of the study or procedure when the initial material is not truly "carrier-free."

It is for these reasons and others that the adoption of more rigorous definitions of terms was suggested at the Second International Symposium on Radiopharmaceuticals held in Seattle in 1979 by the Society of Nuclear Medicine and reiterated at the Third International Symposium on Radiopharmaceutical Chemistry held in St. Louis in 1980.