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John Hoyle, Secretary
US Nuclear Regulatory Commission
11555 Rockville Pike
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RE: RIN 3150-AF70; Fed. Reg.:62(115)32552-32558, 16 June 97: Exempt Distribution of a Radioactive Drug Containing One Microcurie of Carbon-14 Urea

DOCKET NUMBER
PROPOSED RULE PR 30 + 32
(62FR32552)

Dear Secretary Hoyle:

I wish to offer some comments on the above Proposed Rule.

First, I agree with the Commission that ".....the potential long-term impact from widespread releases of the long-lived C-14 (5730-year radiological half-life) from breath tests are insignificant." That being the case, why is NRC forbidding research use of this drug to the same physicians who may use it clinically? A gastroenterologist still has to put his research protocol through his institutional review board (IRB). The IRB will probably ask him to put it through the Radiation Safety Committee (RSC) even if it is an exempt radioactive drug. That is an ample review process and there is no reason why this activity should be forbidden. Why is NRC suddenly inserting itself into a regulatory process in which it has no business? Medical research is in the hands of FDA and OPRR, and NRC has absolutely no legitimate role here. NRC's lack of scientifically and medically valid thinking is conspicuous by its absence. Please remove this part of the Proposed Rule. I strongly recommend, therefore, that clinical and research activities take place with exempt C-14-urea capsules.

Second, I cannot fathom the naiveté of NRC in the area of radiopharmaceutical manufacturing, an area of regulatory responsibility that belongs to FDA, with drug standards being determined by the USP. If a manufacturer sets out to make 1 μCi capsules, he will make capsules of 1 μCi ± some percent, let us say a standard deviation of 10%. That means that about 95% of his capsules will be ± 20%, and about 99% will be ± 30%. With your proposed regulation limiting every single capsule to 1 μCi (32.2 (a)), fully half of each batch will represent a regulatory violation! Whether this was purposeful viciousness or plain incompetence on the part of NRC I can only surmise, but I recommend that this requirement be eliminated completely. The USP will set the standard, the FDA will oversee manufacturing practices, and NRC's job is to get out of the way and do

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virtually nothing. Stop trying to usurp the statutory authority of the FDA and the USP. NRC has absolutely nothing to contribute here but harm.

Third, it has taken four months short of three years to publish a poor quality proposed rule regarding this insignificant radiation risk. It should not have taken more than 30 days, and the decision should not have taken more than 30 minutes. I recommend that NRC review its personnel, management, and procedures to find out why such a trivial petition became maximally bureaucratized with nasty portions sneaked in.

Fourth, I see that NRC has again permitted only 30 days for public comment. As NRC has been told many times before, it is impossible to obtain broad-based public comment in such a short time frame. Has FDA already approved an impending hostile takeover of part of its regulatory authority by NRC? Has OPRR? It appears that this 30-day comment limit is merely a trick to whisk through dangerous precedents. There isn't that big a hurry; it took the staff almost three years to produce this decision, and the manufacturer of C-14-urea is already in trouble. Another manufacturer got C-13-urea capsules through FDA recently, and NRC can't touch that product, so the NRC lurch to closure is of doubtful importance. Patients will get their urea breath tests. It is most unfortunate that NRC is doing everything in its power to destroy the C-14 alternative, however.

Fifth, I wish to compare the ionizing radiation burden from the expected use of C-14-urea to that of Tc-99m and I-131, the principal byproduct radionuclides of nuclear medicine. If, as stated in NRC's Federal Register article, 10% of Americans can be expected to undergo testing for ulcers at some time in their lives, we have 26,500,000 people over, say, 50 years, or 530,000 workups/year. If half of these use C-14-urea breath tests, that is 265,000 tests/year.

The total energy released from the complete decay of 1 μCi is as follows:

C-14: 4.7×10^{14} Mev
Tc-99m: 1.63×10^{8} Mev
Tc-99m incl. Tc-99: 2.8×10^{8} Mev
I-131: 2.1×10^{10} Mev

$$\frac{4.7 \times 10^{14}}{1.63 \times 10^{8}} = 2.9 \times 10^{6}$$

$$\frac{4.7 \times 10^{14}}{2.8 \times 10^{8}} = 1.7 \times 10^{6}$$

$$\frac{4.7 \times 10^{14}}{2.1 \times 10^{10}} = 2.2 \times 10^{4}$$

Therefore, in terms of total ionizing radiation released, 1 μCi C-14 = 2.9 Ci Tc-99m, 1.7 Ci Tc-99m + Tc-99, or 22 mCi I-131.

Assuming 265,000 C-14-urea breath tests per year, this is equivalent to 450,500 Ci Tc-99m + Tc-99, or 5830 Ci I-131. In nuclear medicine in the United States each year we perform about 8,000,000 procedures a year using Tc-99m. If the average administered activity is, say, 15 mCi, that is 120 million mCi/year. Figuring an equal activity lost to decay, we have 240 million mCi/year or 240,000 Ci in nuclear medicine departments, approximately half of the C-14-urea equivalent.

Our I-131 patient administrations total about 1250 Ci/year; with decay losses, say 1500 Ci/year. This is 26% of the C-14-urea equivalent.

This means that the total ionizing radiation debt incurred with a year's worth of Tc-99m and I-131 in nuclear medicine is about 80% of that which would be incurred with a year's worth of C-14-urea breath tests. Even if we include the rest of byproduct nuclear medicine and all of accelerator nuclear medicine, we see that the C-14-urea breath test ionizing radiation energy release is about equal to that of all of nuclear medicine combined.

If the radiation risks from C-14-urea breath tests are "insignificant", well, so are those of diagnostic and therapeutic nuclear medicine. As the Commission purports to now base regulation on risk, it would appear that a large paradigm shift is necessary in nuclear medicine regulation, because the risks of nuclear medicine have now been finally recognized by NRC as being insignificant.

While fewer people have the potential to be exposed to higher levels of radiation in nuclear medicine than in C-14-urea breath tests, the simple requirement that all authorized user physicians and pharmacists be well qualified in basic nuclear and radiation sciences, and that all technologists be sufficiently trained to work effectively under the supervision of qualified authorized users, should be all that is required for safety.

Thank you for your attention and consideration.

Sincerely,

Carol S. Marcus, Ph.D., M.D.
Director, Nuclear Med. Outpt. Clinic
and
Professor of Radiological Sciences,
UCLA

cc: Chairman Shirley Ann Jackson
Commissioner Greta J. Dicus
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