DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
Bethesda, Maryland 20892

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Ms. Cindy Bladey, Chief
Rules, Announcements and Directives Branch
Office of Administration
TWB-5 B1M
U.S. Nuclear Regulatory Commission,
Washington, DC 20555-0001

6/29/2010
75FR37483 (5)

RE: Public Comments on the Draft Policy Statement on the Protection of Cesium-137 Chloride Sources
Docket ID NRC-2010-0209

Dear Ms. Bladey,

In response to the Request for Comments by the Nuclear Regulatory Commission on the issue referenced above, the National Institutes of Health (NIH) wishes to state the following on behalf of the approximately 650 individuals who use Cs-137 self-shielded irradiators at the NIH:

Irradiation of cells, blood, animals, pathogens or other materials is an essential component of many research projects performed at the NIH and at grantee institutions. This is particularly true for immunologists and basic science researchers. The Cs-137 irradiators are considered to be the "gold standard" in providing an effective, reliable, dependable and experimentally reproducible means of irradiation. With the implementation of increased controls and further security upgrades already accomplished to enhance the security of these irradiators, therefore, the NIH agrees with the NRC's draft policy statement that adequate protection of public health and safety is maintained.

A short-sighted urgency to remove or replace Cs-137 irradiators would unequivocally be detrimental to basic science. The NIH has invested in multiple Cs-137 irradiators in multiple locations, all of which have been upgraded for security at great expense. In some cases, site locations were modified to support the irradiator (i.e., floor support) and space constraints were considered for the irradiator location based on its footprint. Some irradiators are located in very small spaces indeed, and there is no practical way to substitute a new type of equipment in the same space. Regarding NRC's draft policy statement that "the development and use of alternative forms of cesium-137, while not required for adequate protection, is prudent", the NIH notes that, for biomedical research, the only alternative to practically consider is a cabinet x-ray device. Alternate chemical forms of Cs-137 are not currently deemed suitable for full-scale replacement in sealed source irradiators. Alternate radionuclide sources (i.e., Co-60) require greater shielding, a larger footprint, a greater structural support requirement for the floor, and a more frequent source replacement schedule. Alternative technologies (i.e., linear accelerator) are vastly more expensive and require additional room shielding, a larger footprint, and a more complex maintenance and operation program. Thus, the cabinet x-ray device remains as the alternative technology of choice for biomedical research applications.

However, not all irradiation needs will be met by x-ray technology. It is a useful technology for some applications, and in fact NIH already possesses and uses five x-ray devices for the irradiation of small animals and cells. The limitations, as researchers and manufacturers alike will testify, are three-fold: 1) depth dose; 2) chamber size; and 3) irradiation time. These three factors are all inter-related.

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Regarding depth dose, it is likely that this is the biggest factor affecting the decision to use a sealed source irradiator instead of x-ray. As has been previously explained elsewhere, an x-ray beam is collimated and filtered, and emits of spectrum of energy that will range from zero to the maximum kVp value. With a tungsten target, it will penetrate relatively uniformly up to 3 cm in a sample of tissue-equivalent density. At greater depths there is a significant decrease in dose deposition, due to the attenuation of the x-ray beam through the tissue. Increasing the x-ray beam energy (kVp) is not a viable alternative, since this will cause a higher surface dose which may harm the sample. In fact, this is seen in animal studies, where ulceration, necrosis and increased mortality rates are observed post-irradiation at higher beam peak energies. It is true that filtration of the low energy x-ray beam will avoid the higher surface doses, but results in a much reduced dose rate such that irradiation time is prohibitive.

Thus, small animals up to the size of a mouse may be irradiated via x-ray devices, but larger animal models will require the depth dose of a gamma photopeak (e.g., Cs-137 at 662 keV) which has no broad energy spectrum with which to cause surface damage. X-ray devices may be used for partial-body irradiation of larger species, but not for whole body irradiation. With regard to in-vitro studies, cells may be irradiated via x-ray devices when the sample volume is small (i.e., 15 mL tube) but not when the sample volume is great (i.e.,200 mL tube).

Secondly, the chamber size of an x-ray device allows for variable sample sizes to be irradiated, depending on the shelf position (distance from the x-ray beam). Due to the need for uniform irradiation, it is important to maintain a sample configuration with minimal depth. Small samples may easily fit near the top shelf setting, which allows for a more intense x-ray beam and thus a lower irradiation time. Larger samples, however, will require a lower shelf position and will result in a longer irradiation time needed; also in the case of small animal irradiation, they will further require a holder to maintain a "monolayer geometry". Some believe this requirement increases the level of distress experienced by the animals and will avoid x-ray irradiation on this principle alone. Others must avoid x-ray irradiation because their experimental protocol dictates irradiation of 15-20 mice at a time, requiring a larger sample configuration with the result that mice are freely able to climb atop one another – thus forfeiting the monolayer.

Finally, the total irradiation time is an important factor for many researchers, especially those doing cell studies. Cells are cultured in vitro, in highly controlled environments, and therefore the length of time they remain out of culture is critical to their survival and function. When irradiated over a longer period, the cells require intermittent re-suspension which further adds to the time commitment. Already with *cesium* irradiation, typical feeder cells require 2-8 minutes exposure time, while tumor cell irradiations can require more than 30 minutes and some pathogen irradiations can require over an hour. X-ray beam irradiation can provide a comparable dose rate to cesium irradiation and may even be higher, but is only useful if the volumetric cross-section of cells permits a sufficient depth dose penetration. Again, increasing the x-ray beam energy (kVp) is not the answer since this will require greater beam filtration, which dramatically decreases the measured dose rate for the samples.

It is crucial to note that basic science research needs are currently being met using Cs-137 irradiators and to eliminate such a valuable tool to the NIH research mission would be devastating. Indeed, some research protocols would be forced to terminate; for example, a current cancer treatment with great promise ("A Phase II Study Using Short-Term Cultured Anti-Tumor Autologous Lymphocytes Following a Lymphocyte Depleting Regimen in Metastatic Melanoma" by Dr. Steven Rosenberg, the National Cancer Institute) relies upon Cs-137 irradiation to generate feeder cells which support the cultured lymphocytes that are isolated from a patient's tumor. The lymphocytes proliferate in vitro and are then infused back into the patient, where in certain cases they are able to mediate tumor regression. Replacement of Cs-

137 irradiation with x-ray irradiation is not possible in this protocol, since the volume of required feeder cells (8.4 billion in 200 mL media) does not allow a sufficient depth dose of radiation in a feasible irradiation time period.

Transitioning to x-ray irradiators will cause a great number of research scientists time and effort to repeat previously-established experiments, and this cannot be understated. Quality science is a rigorous discipline, and changing technologies will require extensive testing in order to verify that the change will not alter an experimental outcome. There is known to be a radiobiological difference in effective dose between x-ray and monoenergetic (e.g., Cs-137) photon radiation. Furthermore, for the success of their numerous research protocols, scientists need an accessible irradiation option that will not have prohibitive constraints imposed by factors such as a distant physical location, need for advance scheduling, or dedicated operator support. They may have adapted to the increased access control requirements of Cs-137 irradiators; however, those for whom precise radiation dose is necessary will have less capacity to absorb the extensive quality control, maintenance, and dosimetry issues that x-ray technology brings.

Such a transition will also cause a major negative budgetary impact on the NIH and its grantees. The replacement expense is a cost that will need to be borne by the Institutes at a time when budgets are flat; already there have been major cuts to the NIH supplies, services and equipment operating budgets. NIH cannot afford to replace the Cs-137 irradiators on a more than end-of-useful-life basis, which is a significantly long time given the 30-year half-life of Cs-137. There is currently no disposal outlet for cesium irradiators, and this causes an increased safety and security threat by placing these sources into a storage (as opposed to active use) mode. Faced with long-term storage of these irradiators, the NIH will not be able to reduce from the same level of enhanced access control already in place.

The NRC's draft policy statement on the protection of Cesium-137 Chloride sources gives credit to the biomedical research need for these irradiators. However, more text in the policy statement regarding the absolute need for Cs-137 irradiators would better underscore their useful and necessary contribution to the advancement of science at the NIH and elsewhere, since it is important to go on record with all of the reasons why alternative technologies cannot meet all of the needs of the biomedical research community.

At an institution such as the NIH, whose mission is to pursue novel and promising basic, translational, and clinical research in order to improve the public health, the loss of Cs-137 irradiators would be a grave disservice. The NIH intends to follow the topic of cesium chloride protection very closely, and I appreciate the opportunity to provide these comments to you.

Sincerely,

Michael Gottesman, M.D.

Dr. Michael Gottesman,
Deputy Director for Intramural Research, NIH

cc: Dr. Ira Levin, Chair, Radiation Safety Committee, NIH
Mr. Robert Zoon, Radiation Safety Officer, NIH