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TERRANCE ALEXANDER, EXECUTIVE DIRECTOR

August 1, 2017

Kevin Null
Senior Health Physicist
Division of Nuclear Materials Safety
U.S. Nuclear Regulatory Commission, Region III
2443 Warrenville Road., Suite 210
Lisle, IL 60532-4352

SUBJECT: **Request to Amend University of Michigan Materials License No. 21-00215-07**

Dear Mr. Null:

The University of Michigan is submitting a request to amend NRC Materials License No. 21-00215-07 to add gallium-68 as a listed radionuclide. The University is engaging in research and developmental work in collaboration with General Electric to develop a practical targetry system for the production of gallium-68 using a GE PETtrace cyclotron. Eventually, the system will be used by the University to routinely produce gallium-68 and then transfer it to the University's Broad Scope - Materials License No. 21-00215-04 for medical and research use under that license.

A complete description of the proposed amendment is attached. Please do not hesitate to contact Senior Health Physicist Dennis Palmieri or me at Radiation Safety Service / EHS [(734) 764-6200] should you have any questions or comments regarding this amendment request.

Thank you for your time, effort, and assistance with respect to this request.

Sincerely,

Mark L. Driscoll

Mark L. Driscoll
Director / Radiation Safety Officer
Environment, Health & Safety / Radiation Safety Service

DAP/MLD
NRC License Amendment Cyclotron Ga-68 08-01-17]

cc: Files

Request for Amendment to NRC Byproduct Material License No. **21-00215-07**

The University is asking to amend Items 6, 7 and 8 of Byproduct Material License No. 21-00215-07 to add gallium-68 as an approved radionuclide. Specifically:

- Item 6 - Byproduct Material: Gallium-68
- Item 7 – Chemical / Physical Form: Any
- Item 8 – Maximum Amount Licensee May Possess: 250 millicuries

Purpose and Summary of Amendment Request

The University of Michigan Department of Radiology is collaborating with General Electric on the development of a liquid target system for the production of gallium-68 along with attendant operations related to transferring the material out of the vault into hot cells. Gallium-68 is a positron emitting radionuclide with a half-life of about 1.1 hours and has found beneficial medical use for diagnostic imaging especially as it currently involves use of Ga-68 labeled DOTATATE. Currently, PET imaging facilities use commercially available Ge-68 / Ga-68 generators to obtain Ga-68 and radiolabel compounds using commercial kits. But there are practical limitations and complications with the use of commercially available generators that make accelerator production of gallium-68 attractive to PET imaging facilities like that at the University of Michigan.

Significant research in production design has already been done by others. See: M. Pandey, J. Byrne, H. Jiang, A. Packard, T. DeGrado (2014). Cyclotron Production of ^{68}Ga via the ^{68}Zn(p,n)^{68}Ga Reaction in Aqueous Solution, *Am J Nucl Med Mol Imaging v4(4),* 303-310. General Electric is interested in expanding upon that work and is collaborating with the University to develop a viable and practical target assembly and delivery system for application with its GE PETtrace cyclotron system. If successful, the University intends to routinely produce gallium-68 for ongoing research, development and medical use under its separate broad scope Byproduct Materials License No. 21-00215-04.

> *Note: NRC License No.* ***21-00215-07*** *authorizes the University to produce byproduct material using its cyclotron for the purposes of: i) research and development, and ii) for transfer to another licensee; that licensee being the University under its broad scope NRC Byproduct Materials License* ***No. 21-00215-04****. The proposed amendment to 21-00215-07 is to obtain approval to produce gallium-68 and to do so for the same purposes as already approved—namely research and development and transfer to the broad scope license for further research, development or for medical use. License No. 21-00215-04 is sufficiently adequate to accommodate the proposed research and medical uses of gallium-68 without amendment.*

Description of Proposed Targetry System

General Electric will provide target assemblies designed specifically for use with enriched zinc-68 salts in solution with a dilute acid. The proposed target design is similar to that described in the literature. Research and development will involve developing and refining the target assembly, the target solution and the cyclotron beam operating parameters.

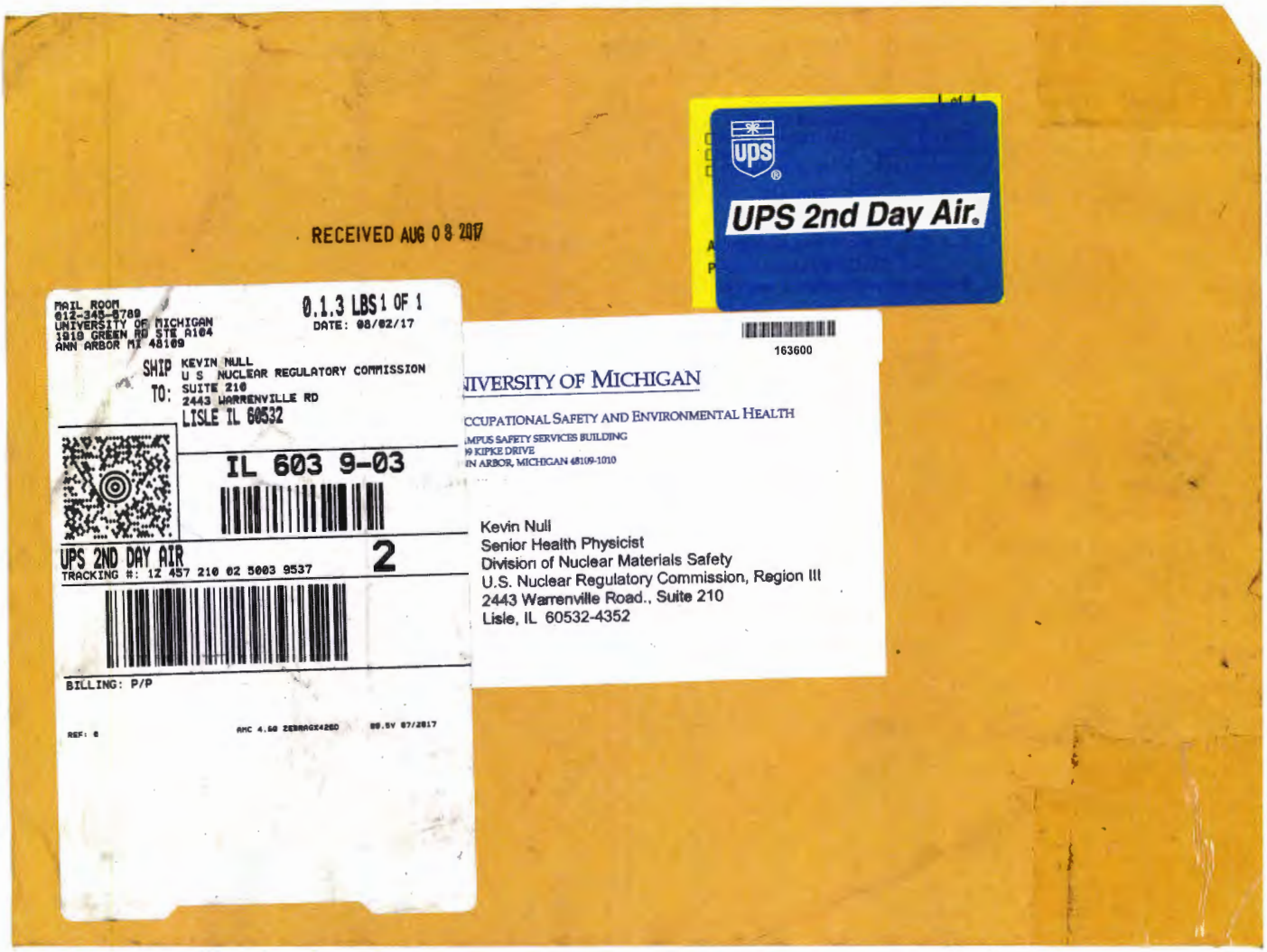
Target solution evaluation consists of refining the concentration of zinc salt along with the acid normality of a useful solution. The proposed target solution will consist of a zinc salt enriched in zinc-68 dissolved into a solution of dilute acid (e.g 1M Zn-68 dissolved in 0.2-0.4 N nitric acid). The exact concentration of zinc and acid is to be determined as part of the collaborative research work.

Additional research will involve determining optimum beam parameters including beam time and optimum proton energy. The target assembly will include a proton energy degrader to reduce proton beam energy from the standard 16.5 MeV developed in the GE PETtrace cyclotron to an energy of 15 MeV or less. The lower proton energy will discriminate against the inadvertent production of gallium-67 which is an undesirable contaminant having a half-life of about 3.3 days. The degrader consists of an aluminum window of variable thickness; it is interposed—along with a helium cooling system--between the beam port entrance and the target assembly's primary window which is followed by the zinc solution chamber that is water-cooled. The primary window is expected to consist of Havar which is a durable window resistant to rupture and is commonly used with GE PETtrace systems.

The variable thickness of the aluminum degrader window facilitates determining the optimum proton beam energy to reduce Ga-67 impurities without negatively impacting Ga-68 production. Pandey, et al estimated Ga-67 impurity at about 0.1% of activity after a 60-minute irradiation at 20 uA. According to General Electric, it anticipates a yield of about 9 mCi of Ga-68 per microAmp-hour of beam current using a 1M Zn-68 enriched salt solution. Using 14 MeV protons, General Electric estimates end-of-bombardment (EOB) production yields to be about 124 mCi using a 30 uA beam of 14 MeV protons and an irradiation time of 1 hour. These numbers are estimates and may be refined during the course of the collaboration work.

Finally, research will also evaluate the adequacy of current product delivery systems for transferring the product from the cyclotron vault into hot cells in the adjacent Radiochemistry Laboratory. At this time, General Electric anticipates that delivery systems similar to that currently used for fluorine-18 should be sufficient. However, there may be additional research and testing to evaluate optimal transfer line distances, tubing and valve materials, and transfer conditions.

The University of Michigan will transfer and use accelerator-produced gallium-68 under its Broad Scope Byproduct Materials License No. 21-00215-04. Gallium-68 will be used for research and medical use under that license.



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