Advisory Committee on the Medical Use of Isotopes (ACMUI)

Germanium-68 (Ge-68) Decommissioning Funding Plan (DFP) Subcommittee

Draft Report

Subcommittee Members: F. Costello; S. Langhorst; S. Mattmuller (Chair); C. Palestro; and P. Zanzonico

Challenge: The restrictive aspects of a decommissioning funding plan (DFP) for Ge-68 that arise from the current Part 30 regulations are preventing and/or deterring the use of promising Gallium-68 (Ga-68) diagnostic imaging agents for patients.

Charge:

1) **Estimate the number of potential Ge/Ga-68 generator licenses affected, and**
2) **Recommend to the Committee on which route of action it believes NRC should pursue to address the decommissioning funding plan issue.**

Background: Neuroendocrine tumor imaging (NET), why Ge-68 is so important to NET patients.

Neuroendocrine tumors (NET) present a difficult diagnostic challenge. For NET patients, it currently takes on average seven years for a proper diagnosis to be made and appropriate therapy prescribed. Fortunately, diagnostic imaging of patients with NET is on the verge of making dramatic advancements in this area.

There is a new class of radiopharmaceuticals using a positron emitter radionuclide, Ga-68, that are nearing FDA approval. The Ga-68 is attached to one of several somatostatin receptor (SSR) binding peptides via the DOTA chelator, that is, DOTA-TATE, DOTA-TOC, and DOTA-NOC, (DOTAs). The advantages of these new radiopharmaceticals can be best demonstrated by a comparison of their images in the same patient (Figure 1).

In the left two panels are images produced with In-111 DTPA-Octreotide (In-111 Octreotide), the current SSR radiopharmaceutical in routine clinical use today. In the right panel is a positron emission tomography (PET) image produced with the Ga-68 DOTA-TOC.

The advantages of the Ga-68 imaging are readily apparent. This PET image leads to greater sensitivity and specificity resulting in superior accuracy for this diagnostic imaging procedure. There is also greater patient convenience as the Ga-68 DOTA image only takes one day versus two days needed for the In-111 Octreotide image. For a patient who has to travel several hours for this procedure, this shorter time can save them from a potential overnight stay. Finally, the radiation dosimetry burden to the patient is less for the Ga-68 DOTAs image versus the In-111 Octreotide image, with a nearly a five-fold reduction in the effective dose to the patient (2.3 and 10.8 mSv, respectively, for Ga-68 and In-111).

Importantly, the source of Ga-68 is a generator, rather than a cyclotron. As a result, the availability and clinical utility is potentially far greater than those of current-generation PET isotopes. Ga-68 is continuously produced in this generator by the decay of its parent radionuclide Ge-68. Additional information regarding the Ga-68 generator is presented below in the section on the design and operation of a Ge-68 generator.

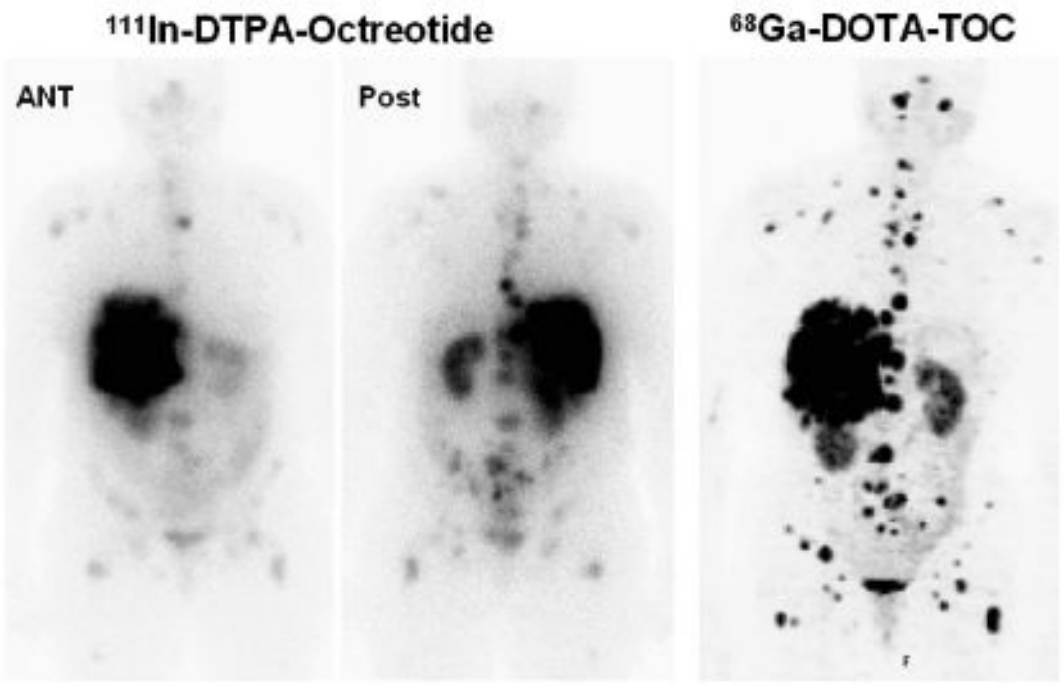

Figure 1

Background: Regulatory DFP trigger for a Ga-68 generator

The regulations requiring licensees to submit decommissioning funding plans (10 CFR 30.35) became effective on July 27, 1988. The trigger level (i.e., a quantity of a given radionuclide) for a DFP comes from a calculation using a labeling quantity for a radionuclide listed in the appendix entitled, "Quantities of Licensed Material Requiring Labeling." The calculation involves multiplying the labeling quantity by 10^5 to derive the trigger level. At this time, however, Ge-68 is not listed on the table, so a very small default quantity of only 10 mCi (0.1 uCi x 10^5) is derived as the trigger level. Initially, this was not problematic as Ge-68 was not regulated by the NRC.

Prior to 2007, a site with a Ga-68 generator did not need a DFP since the NRC did not yet have the authority to regulate it. The NRC's regulatory authority for Ge-68 came into effect in 2007, with the adoption of an expanded definition of by-product material to include accelerator-produced radionuclides

Despite now having authority over these additional radionuclides, the NRC did not amend Appendix B to Part 30 at that time. Appendix B continues to have no listing for Ge-68 and the same calculated 10 mCi trigger level exists as first established in 1988. This 27-year-old 10-mCi trigger level persists and a DFP is thus required for the use of a new Ga-68 generator.

Impact of DFPs on medical licensees

For a medical licensee, the foregoing regulatory considerations creates a cascade effect leading to an extensive and expensive DFP, as a DFP must cover not only the one area where a Ga-68 generator is used but also all areas where radioactive materials are used under the same license.

Consider the example of a mid-size medical center and the various areas of use its license may include:

- Nuclear Medicine facility, including SPECT imaging rooms and a radiopharmacy for the preparation of radiopharmaceuticals;
- PET imaging rooms;
- Multiple satellite cardiac imaging suites throughout the surrounding area;
- Radiation Oncology, including gamma knife and brachytherapy;
- Affiliated hospital with its own Nuclear Medicine facility, including SPECT imaging rooms and a radiopharmacy

Without a Ga-68 generator, a DFP is very likely not needed for such a medical center. However, if such a center were to add a Ga-68 generator, it would have to develop a DFP and not just for the one room that would house the generator, but for all of the foregoing areas. A DFP thus becomes very extensive and very expensive, perhaps prohibitively so for a licensee with numerous areas of use.

This scenario did, in fact occur last year at a large university-based medical center on the East Coast. This center attempted to acquire a Ga-68 generator for clinical investigation, but their DFP was very extensive because of all of their areas of use and would have been very expensive to fund. Hence they did not acquire the necessary financial assurances for a DFP and were restricted to acquiring a used Ga-68 generator of less than 10 mCi in activity. The center was not able to conduct their research in patients as initially planned and was only able to perform research in small animals. It was their radiation safety officer who was the first to succinctly and accurately describe a DFP as “extensive and expensive.” It was extensive as over 170 man-hours were required from the radiation safety office alone to prepare the DFP. This total does not include the large number of man-hours needed from numerous other departments for the preparation of the DFP. It was expensive, as the financial assurances in the form of a bond would need to be purchased to cover the decommissioning expenses of over one million dollars. This expense continues on an annual basis.

The restrictive aspects arising from the current Part 30 regulations are preventing and/or deterring the use of promising Gallium-68 (Ga-68) diagnostic imaging agents for patients due to the decommissioning funding plan burden for its parent Ge-68.

Charge 1: Estimate the number of potential Ge-68/Ga-68 generator licenses affected.

At first glance, this appears to be a reasonable request, one that could be addressed by sending survey-type questionnaires to a sample of licensees so as to extrapolate to a number of licensees nationally. However, given how extensive of an effort it is to prepare a DFP, this actually is a very complex and time consuming effort for each licensee (as illustrated for the licensee discussed above). A DFP is unique to each licensee, and once prepared it is only applicable to that licensee and cannot be used by another licensee. Neither the licensees nor the subcommittee have the time or other resources to conduct and answer such a survey. Most likely the NRC does not either and it is therefore impractical to collect firm numbers on licensees affected.

There are other ways we can estimate the effect of the extensive and expensive components of a DFP on the availability of the Ga-68 DOTAs. As we do know, it has already deterred the use of Ga-68 DOTAs in patients. For example in the case of the DFP on the university-based East Coast medical center discussed above, the impact was to effectively prevent the clinical use of Ga-68 radiopharmaceuticals. It has also been known to deter the use of Ga-68 DOTA radiopharmaceuticals elsewhere.[1]

> "Currently in the US there are only three active sites that are reliably imaging patients with the Ga-68 DOTA radiopharmaceuticals. These sites include the National Institute of Health, Stanford University and the University of California in San Francisco. Three sites total within all of the United States. The current wait for a NET patient is over 2+ months at the NIH."

[1] Personal communication with Josh Mailman, President of the NorCal CarciNet Community, a patient advocacy group for neuroendocrine tumor patients. https://norcalcarcinet.org/

Although the subcommittee cannot project the future impact of the DFP requirement on future of Ga-68 DOTAs, the statement was submitted by one of the largest commercial radiopharmacy companies in the US, Triad Isotopes[2]:

> Triad Isotopes, a leading commercial provider of radiopharmaceuticals, operates over 50 nuclear pharmacies in markets throughout the United States.
>
> Under the current regulations, the complexity and cost of a DFP would potentially hinder our ability to provide Ga-68 radiopharmaceuticals from our nuclear pharmacies to all areas of the country. The net effect is that the DFP regulations would likely limit the availability of this radiopharmaceutical, for several reasons:
>
> - First, economic pressures will impede adoption. The difficulty to compensate for the fixed costs of the DFP will limit the number of radiopharmacies that will be able to offer Ga-68 radiopharmaceuticals.
> - Second, the short half-life of Ga-68 will make this a challenging radiopharmaceutical to distribute. To ensure good usage across the country, the product will need to be available through as many nuclear pharmacies as possible; however, it would be difficult to dispense and deliver through a long spoke-hub model due to that short half-life of 68 minutes.
> - Taking both cost and distribution challenges into account, it is unlikely that nuclear pharmacy networks such as ours would provide Ga-68 related radiopharmaceuticals to all areas of the country if a DFP was initiated; thus, every patient in need would not have equal access to these radiopharmaceuticals, most especially those in smaller and/or more rural markets.

This statement from Triad has added weight in that at four of their sites they do have a DFP in place; hence, they are well aware of how extensive and expensive a DFP can be. Patient access is already clearly hindered in the U.S. by the small number of licensees who can provide Ga-68 DOTAs. Regulatory relief from the DFP is urgently needed to increase patient access to these invaluable radiopharmaceuticals.

[2] Personal communication with Fred Gattas, Director, Quality Control and Safety, Triad Isotopes

Charge 2: Recommend to the Committee on which route of action it believes NRC should pursue to address the decommissioning funding plan issue.

The subcommittee recommends the following language be added as a footnote to Appendix B Part 30 -- Quantities[1] of Licensed Material Requiring Labeling as the most expeditious, cost effective, and practical route to addressing the DFP issues.

> [3]This does not include Ge-68 in a Ge-68/Ga-68 medical use generators (limit less than 10^5 x 2 uCi) that are returned to the manufacturer at end of use.

(Note: Given the title of Appendix B -- Quantities of Licensed Material Requiring Labeling the 2 uCi will be considered a new "labeling" quantity for Ge-68)

This new calculated limit of 200 mCi as a trigger amount for a DFP would only be allowed for Ge-68 in a Ga-68 generator for medical use. This limit would allow for the use of a Ga-68 generator for clinical use and at the end of its one-year shelf-life allow it to be used for research such as in small animals. Regardless of its use, when the licensee is finished using the Ga-68 generator, it would be returned to the manufacturer for final disposal. The new limit would also allow a licensee to possess more than one generator to maintain a higher useful amount of Ga-68 available at all times for the preparation of Ga-68 DOTAs.

In order to maintain a higher useful amount of Ga-68, a licensee may purchase several Ga-68 generators with staggered calibration dates. This would be done much in the same way a radiopharmacy currently maintains a higher useful amount of Tc-99m with the purchase of Tc-99m generators with staggered calibrations dates, the difference being a staggered time interval of only 2-3 days for Tc-99m generators versus ~ 6 months for Ga-68 generators. For example, a licensee who also performs research may have the following Ga-68 generators on-hand if they purchase a new one every six months (Table 1).

Table 1: Activity of Ga-68 Generators -- Use is for both clinical and research

Age	Decay Factor	mCi of Ge-68
new	1	50.0
6 mos	0.63	31.5
12 mos	0.39	19.5
+new	1	50.0
18 mos[1]	0.24	12.2
24 mos[1]	0.15	7.6
Total		170.8

[1] These generators would only be used for research

The three major factors that we believe serve as the basis for this recommendation for this new labeling quantity of Ge-68 are as follow.

1. Under normal operation, the Ge-68 is stably bound within the generator. The design and operation of the Ga-68 generator thus ensures that it will have nearly the same safety profile as a sealed source device.

2. At the end of its use, the generator is returned to the manufacturer for final disposal. This disposal step in essence eliminates any concern at a licensee regarding Ge-68 associated DFP.

3. If Appendix B were to be revised, it would be appropriate to add Ge-68 with a labeling quantity of 10 uCi. *However, the subcommittee currently recommends a more conservative number of only 2 uCi for the purposes of a Direct Final Rulemaking.*

Design and Operation of the Ga-68 Generator

The Ga-68 generator is a device that serves as source of this important radionuclide. Ga-68 decays by positron emission and thus can be used for called positron emission tomography (PET) diagnostic medical imaging procedures. The vast majority of radionuclides used for PET imaging require a large and expensive particle accelerator such as a cyclotron. One of the best advantages of the Ga-68 generator, therefore, is that it provides a PET radionuclide without a cyclotron.

Currently, Ga-68 is used mainly in the preparation of the Ga-68 DOTAs, which have already emerged as the radiopharmaceutical of choice for NETs. The advantages of the Ga-68 DOTAs will greatly enhance the diagnosis and treatment of NET patients across the country.

In this generator Ge-68 is the parent radionuclide and it has a half-life of 271 days. It decays by electron capture to its daughter radionuclide, Ga-68, which has a half-life of 68 minutes. The generator is a closed system device consisting of a column containing a resin on which the parent radionuclide Ge-is fixed. Ga-68 is continuously produced by the decay of its radioactive parent Ge-68. The Ga-68 is removed from the generator by eluting it off the column with a sterile hydrochloric acid solution. The Ga-68 is soluble in the hydrochloric solution and readily elutes off the column. The Ge-68 is insoluble in the hydrochloric solution and remains fixed on the column and continues to decay to provide additional Ga-68 in future elutions. The Ga-68 generator is a device whose sole purpose is to provide Ga-68. Chemically, the Ga-68 is in the form of gallium chloride ($GaCl_3$) and is used in the preparation of the Ga-68 DOTAs. The Ga-68 as eluted cannot be used directly in patients.

The physical characteristics of both the parent and daughter radionuclides are summarized in Table 2.

Table 2: Physical characteristics of Ge-68 and Ga-68

	Ge-68	Ga-68
Half-live	270.95 days	67.71 minutes
Type of decay	Electron capture	Positron emission
X-rays	9.225 keV (13.1 %) 9.252 keV (25.7 %) 10.26 keV (1.64 %) 10.264 keV (3.2 %) 10.366 keV (0.03 %)	8.616 keV (1.37 %) 8.639 keV (2.69 %) 9.57 keV (0.55 %)
gammas		511 keV (178.28 %), 578.55 keV (0.03 %) 805.83 keV (0.09 %), 1077.34 keV (3.22 %) 1260.97 keV (0.09 %) 1883.16 keV (0.14 %)
beta+		Energy max. Energy 352.60 keV 821.71 keV (1.20 %) 836.00 keV 1899.01 keV (87.94 %)
Data derived from nudat (www.nndc.bnl.gov)		

The Ge-68 is easy to shield as during its decay it has no particulate or penetrating (i.e. high-energy) photon emissions, but only has low energy X-ray emissions. Shielding is, of course, needed for the Ga-68 as it decays by positron emission, with the subsequent production of 511-keV annihilation gamma rays.

A schematic of a generic Ga-68 generator is provided in Figure 2. Note that it has one inlet for the hydrochloric acid eluent and one outlet for the collection of the Ga-68.

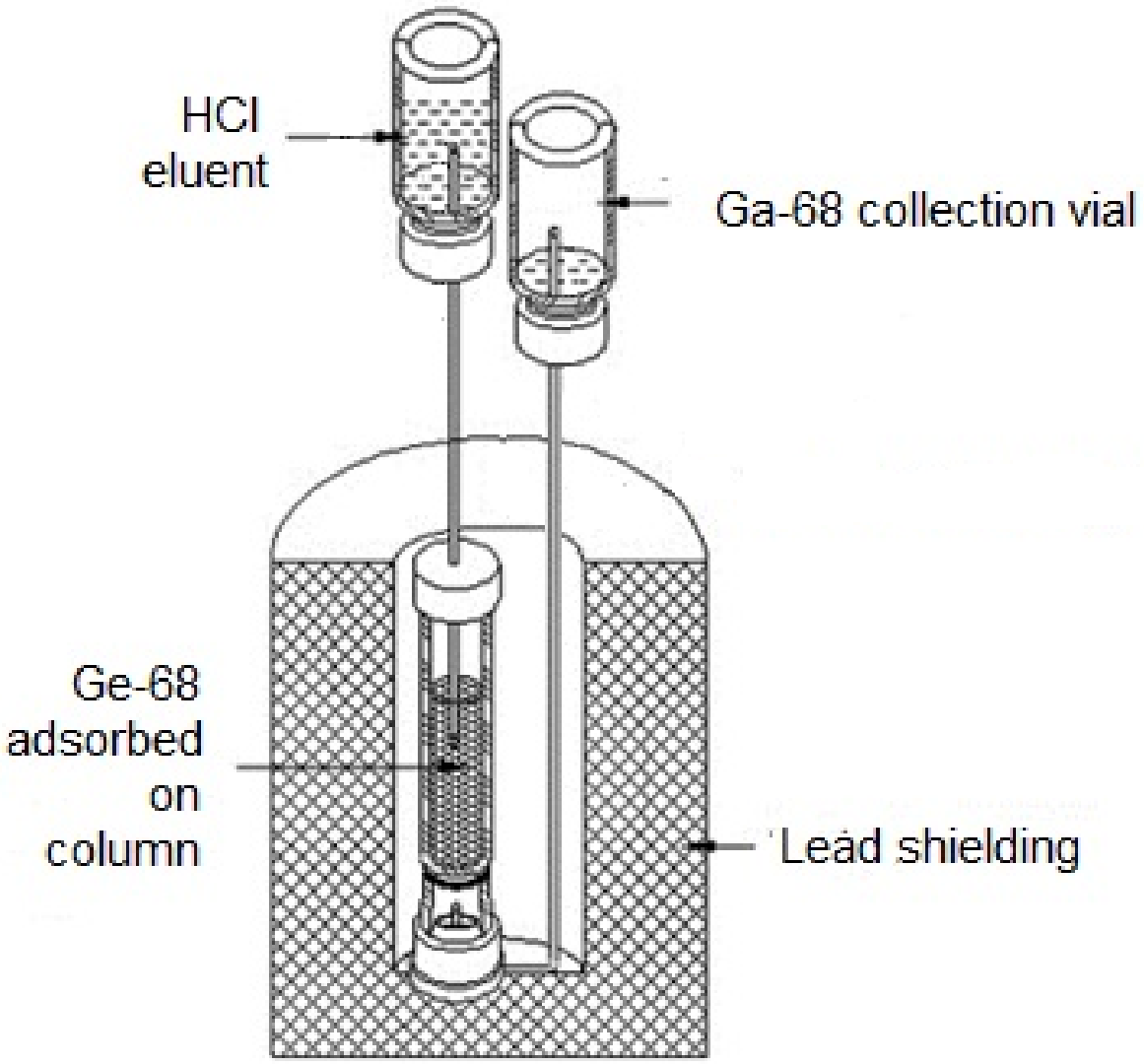

Figure 2.

It is a simple device that has no moving parts. The Ge-68, as a solid, is fixed onto the resin within the column by the chemical process of adsorption and thereby remains entirely within the generator and its heavy lead shielding.

The first Ga-68 generator manufactured in accordance with a Drug Master File for use in the United States is the Galliapharm by Eckert and Ziegler. It is a relatively small and compact device measuring 9 inches x 5.2 inches x 5.2 inches (H x W x D). It weighs approximately 31 pounds. See Figures 3-5. Again note the simplicity of the device, with only one inlet port and one outlet port and no moving parts.

Sectional view of the Galliapharm radionuclide generator

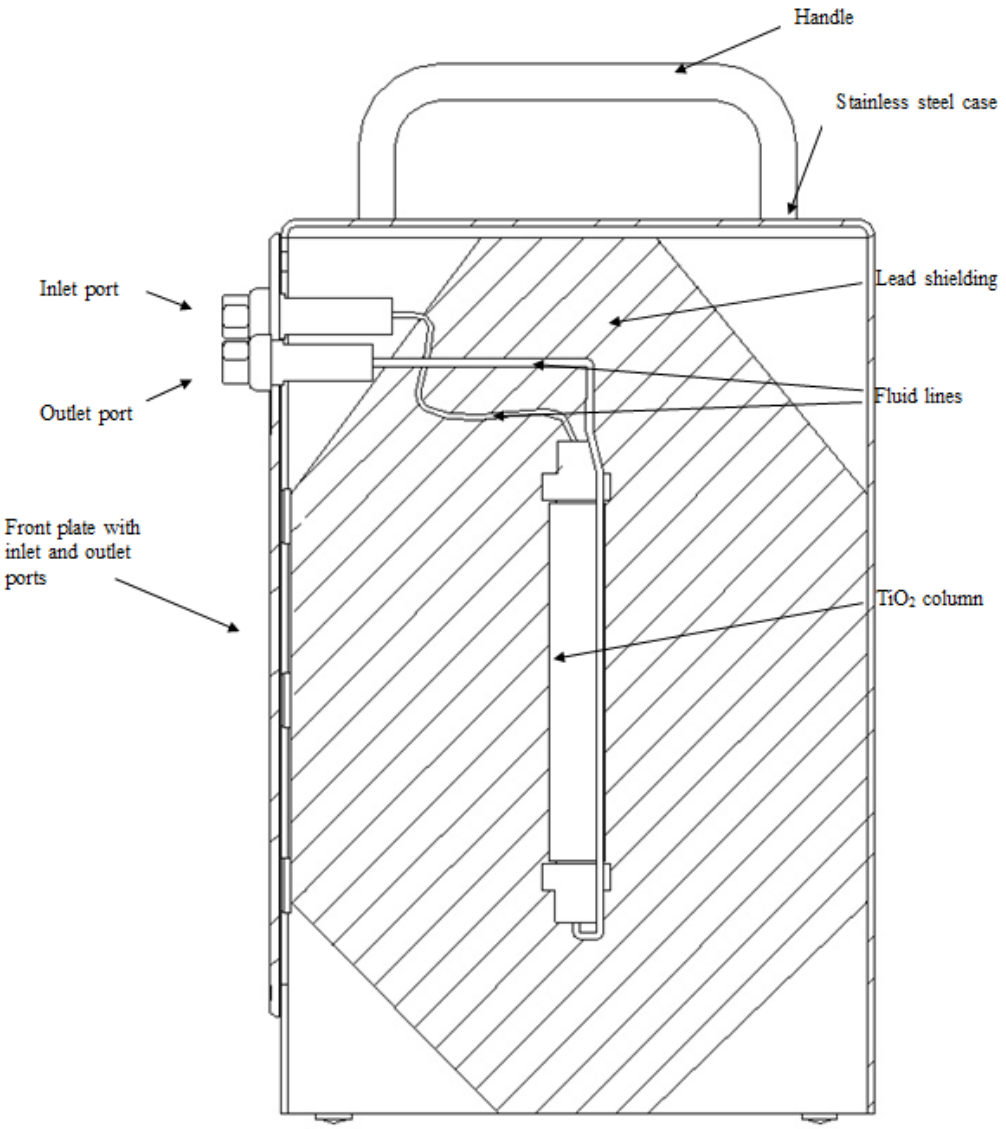

Figure 3.

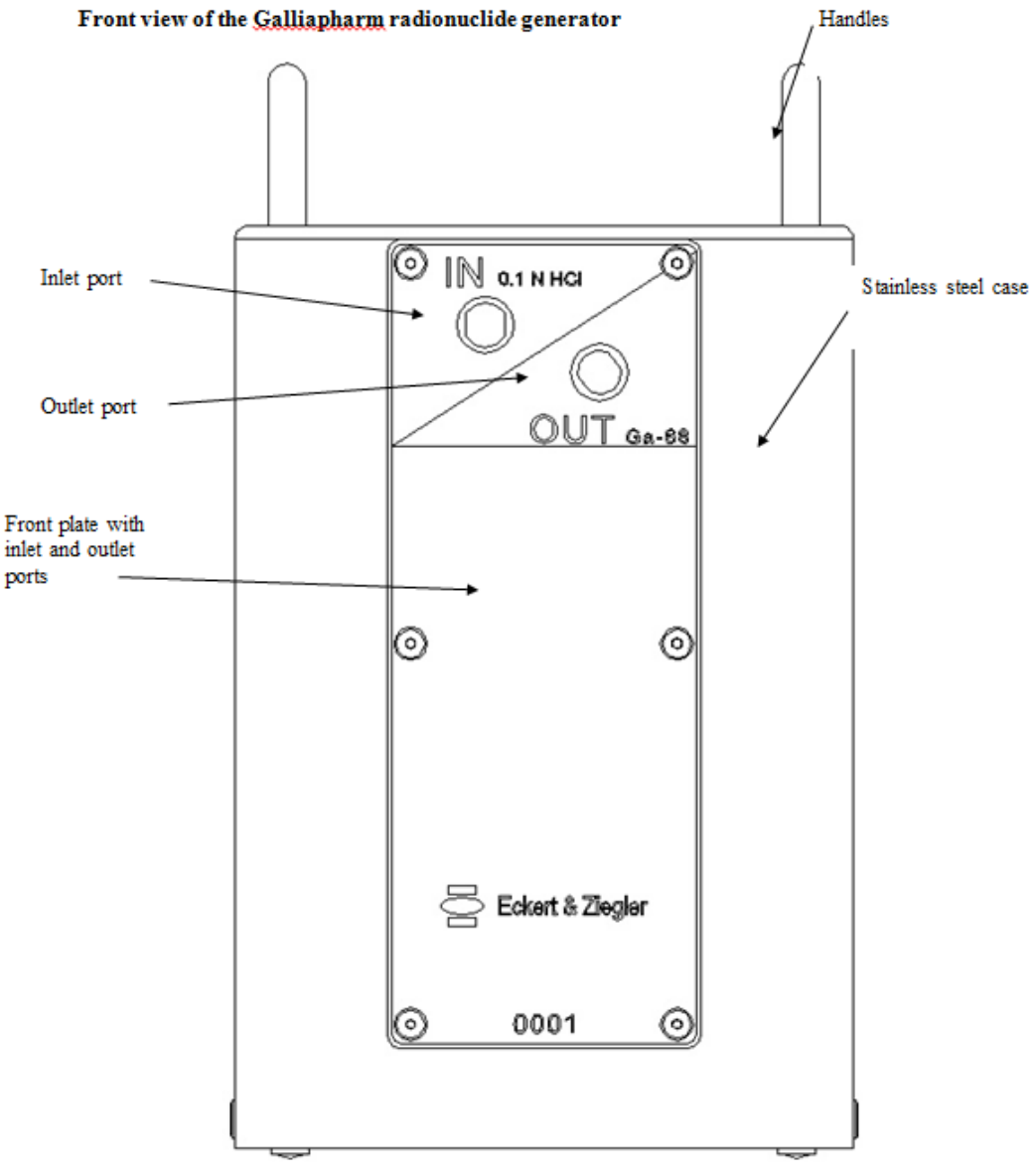

Figure 4.

Once the generator is placed in position in the nuclear medicine facility, it is not moved but simply remains in place for its entire lifetime. Due to its compact size, the generator and the associated chemistry module are typically placed together in the same hot cell. This close placement also has a chemistry advantage; by keeping the outlet line connecting the generator to the chemistry module as short as possible, the yields of the syntheses of the drug product are maximized.

The inlet line has a customized thread on its fitting to avoid a miss-connection; that is, it will only connect to the inlet port. Likewise, the outlet line will only connect to the outlet port. Because the generator remains in place once positioned, there are no mechanical stresses that could potentially lead to a leakage of activity.

Figure 5.

During the normal elution process of the Ga-68 generator, a very small amount of Ge-68 measured in nanocuries does get displaced from the column; this is known as parent breakthrough and is a phenomenon associated with all radionuclide generators. Ge-68 breakthrough is expressed as a percentage of total Ga-68 activity eluted from the column, corrected for decay. The specification for Ge-68 breakthrough is not more than 0.001% of the eluted Ga-68 activity. The breakthrough for this generator typically begins as low as 0.0001% when the generator is new and may rise slightly with the number of elutions. To minimize the breakthrough, it is recommended that the generator should be eluted at least once per working day. When used accordingly, the breakthrough should remain below the 0.001% limit for 12 months. The volume of the elution is ~ 5 mL, and the recommended rate of elution no greater than 2 mL/min. The breakthrough amounts are so low that unlike other medical use generators (i.e., Tc-99m or Rb-82 generators) the breakthrough cannot be measured with a dose calibrator. More sensitive equipment must be used to measure the amount of Ge-68 in a Ga-68 elution.

If an elution is not used for a Ga-68 radiopharmaceutical preparation, (i.e., was performed for maintenance of the column to minimize breakthrough), these unused elutions may be collected into a small waste vial and then stored for a day for decay (21 half-lives). For final disposal, since it is an acid solution it may need to be placed into a chemical waste container or, depending on a site's location one may be able to dispose of it in the sanitary sewer via a sink.

For example, for this latter scenario, with a breakthrough of 0.0001% when the generator is new and at its highest activity of 50 mCi the Ge-68 activity would only be a small amount of 0.03 µCi (or 30 nCi) of Ge-68 (= 50 mCi x 60% elution yield x 0.0001% breakthrough) per elution. The limits for disposal in sewerage are specified in § 20.2003 Disposal by release into sanitary sewerage and its associated Appendix B, see table 3.

Germanium-68

Atomic No.	Radionuclide	Class	Table 1 Occupational Values			Table 2 Effluent Concentrations		Table 3 Releases to Sewers
			Col. 1	Col. 2	Col. 3	Col. 1	Col. 2	
			Oral Ingestion ALI (µCi)	Inhalation		Air (µCi/ml)	Water (µCi/ml)	Monthly Average Concentration (µCi/ml)
				ALI (µCi)	DAC (µCi/ml)			
32	Germanium-68	D, see ^{66}Ge	5E+3	4E+3	2E-6	5E-9	6E-5	6E-4
		W, see ^{66}Ge	-	1E+2	4E-8	1E-10	-	-

Table 3.

This limit is calculated by dividing the amount of 0.03 µCi of Ge-68 by the concentration limit of 0.0006 µCi/mL (from the appendix), which equals 50 mL of required sewerage volume to meet the monthly average concentration.

In other words, less than two ounces (i.e., ¼ cup) of sewerage are needed for dilution for each elution disposed of to maintain the concentration of Ge-68 below the sewerage limits of § 20.2003. These conditions can easily be achieved if the elution is first held for one day for the decay of the Ga-68 and then disposed of in the sewerage.

Despite these nanocurie amounts of Ge-68 that come off the column with each elution, the Ga-68 generator could be considered for all practical purposes a sealed source device. As such it would be exempt from any DFP requirement pursuant to § 30.35 Financial assurance and recordkeeping for decommissioning.

While the small footprint and the simplistic ease of use of a Ga-68 generator are significant advantages over a cyclotron in producing a PET radionuclide it does have one limitation: the relatively small quantity of Ga-68 that it is able to produce compared, for example, to the output of a cyclotron. The relatively small output of a Ga-68 generator (i.e., mCi vs. Ci) and Ga-68's relatively short half-life will result in a radiopharmacy having a much smaller distribution area for Ga-68 radiopharmaceuticals than that for F-18 and/or Tc-99 radiopharmaceuticals. Therefore, there will be a need for a large number of radiopharmacies across the country to have the capability to prepare Ga-68 DOTA to provide equitable access for all patients nationwide.

Disposal of the Ga-68 Generator

Disposal by the licensee is very simple; at the end of its useful lifetime the generator is returned to the manufacturer for final disposal. Final disposal by the manufacturer in essence eliminates any concern regarding Ge-68 in regards to a DFP for the licensee. See, for example, the letter below from Eckert & Ziegler (Figure 6).

Eckert & Ziegler

Eckert & Ziegler Radiopharma GmbH, Robert-Rössle-Straße 10, D-13125 Berlin

TO WHOM IT MAY CONCERN

Eckert & Ziegler
Radiopharma GmbH

Robert-Rössle-Straße 10
D-13125 Berlin
www.ezag.de

Alina Hue
Sales & Customer Support

Telefon +49 (0)30 94184-280
Telefax +49 (0)30 94184-470
e-mail radiopharma@ezag.de

Berlin, 16.07.2015

Return ^{68}Ge / ^{68}Ga GalliaPharm generator

Herewith we, **Eckert & Ziegler Radiopharma GmbH**, located at Robert-Rössle-Str. 10, 13125 Berlin, Germany, confirm that we are obliged to keep back the used ^{68}Ge/^{68}Ga Pharmaceutical Grade Generator (GalliaPharm).

Additional service fees will apply, if you want E&Z to take care of the final disposal of the used product.

Best regards,

A. Hue

Eckert & Ziegler
Radiopharma GmbH
Robert-Rössle-Straße 10
13125 Berlin-Germany

Alina Hue
Sales & Customer Support

Figure 6.

Propriety of current default labeling quantity of 0.1 uCi for Ge-68

The subcommittee reviewed the radionuclides currently listed in Appendix B. Table 4 below contains all of the radionuclides from Appendix B that have a labeling quantity of 10 uCi and a half-life greater than 120 days in order to assess the impact of changing the labeling quantity for Ge-68 from 0.1 uCi to 2 uCi.

What is quite surprising from this review are the number of radionuclides with substantially longer half-lives than Ge-68 but with a labeling quantity that is 100x greater than the current value for Ge-68 of 0.1 uCi.

Licensed Material	Quantity (µCi)	Half-Life*	Decay Mode*
Sb-125	10	2.76 y	β-
Ba-133	10	10.6 y	EC
Ca-45	10	162.6 d	β-
Cs-135	10	2.3e6 y	β-
Cs-137	10	30.1 y	β-
Cl-36	10	3.01e5 y	EC+, β+, β-
Eu-155	10	4.75 y	β-
Gd-153	10	240 d	EC
Fe-55	10	2.74 y	EC
Mn-54	10	312 d	EC, β-
Ni-63	10	101 y	β-
Nb-93m	10	16.1 y	IT
Pr-147	10	2.62 y	β-
Rb-87	10	4.81e10 y	β-
Sm-151	10	90 y	β-
Tl-204	10	3.78 y	EC, β-
Tm-170	10	129 d	EC, β-
Tm-171	10	1.92 y	β-
Zn-65	10	244 d	EC+, β+

Licensed Material	Quantity (µCi)	Half-Life*	Decay Mode*
Zr-93	10	1.61e6 y	β-
Ge-68	0.1	217 d	EC

* http://www.nndc.bnl.gov/mird/

Table 4.

In the past 27 years, Appendix B has not been revised, and Ge-68 may not have been included initially as the NRC did not have regulatory authority over it. Subsequently, in 1992-1994, Appendix C but not Appendix B added a labeling quantity for Ge-68. This occurred even though the NRC still did not have authority over Ge-68. Unfortunately, when the NRC did gain authority over Ge-68 in 2007, a revision of Appendix B was deemed "beyond the scope" of that action and did not occur.

If a revision of Appendix B had ever taken place, it appears that Ge-68 would easily have been included among the group of radionuclides with a labeling quantity of 10 uCi. Our proposed labeling quantity of 2 uCi is thus conservative as it would still offer a five-fold "safety factor" versus a labeling quantity of 10 uCi, (i.e., a 200-mCi trigger limit versus a 1,000-mCi limit for a DFP). This new quantity would thus not adversely impact the safety or the ability of a licensee to decommission a Ge-68/Ga-68 generator.

Relationship of the proposed rulemaking to NRC's Strategic Plan

The proposed rule supports NRC's 2013-2018 Strategic Plan by supporting its Regulatory Effectiveness Strategy 1: Proactively identify, assess, understand, and resolve safety and security issues. The proposed rule supports these activities in the following ways:

- Resolve generic safety and security issues and ensure implementation of enhancements within timeframes commensurate with their risk significance.

  The use of a more up- to-date value for labeling unsealed Ge-68 for limited use in Ge/Ga-68 generators used for medical use and returned to the manufacturer poses no decommissioning safety risk. The lack of decommissioning risk warrants the special circumstance of doing a direct final rule in order to minimize the significant risk of preventing patient access to the medical benefits received from Ga-68 radiopharmaceuticals.

- Emphasize the importance of developing and maintaining an effective nuclear-safety culture for all NRC-regulated activities and for activities regulated by the Agreement States.

The 27-year-old labeling value used to require a DFP which for Ge-68 has resulted in the unintended regulatory impediment for medical use of the Ge/Ga-68 generator. Immediate correction of this unintended regulatory impediment will demonstrate NRC's support of medical safety culture.

The subcommittee's recommendation to the Committee is that the following language be added as a footnote to Appendix B Part 30 -- Quantities[1] of Licensed Material Requiring Labeling.

> [3]This does not include Ge-68 in a Ge-68/Ga-68 medical use generators (limit less than 2 uCi x 10^5) that are returned to the manufacturer at end of use.

The subcommittee believes this recommendation has strong basis to support this regulatory change through the Direct Final Rulemaking process. This process should be initiated as soon as possible by the NRC to eliminate the deleterious effect the DFP process is having on patient access to Ga-68 radiopharmaceuticals.