PharmaLogic
Take The Lead

Q-4

February 23, 2016

Tara L. Weidner
Medical Branch
US NRC Region I
2100 Renaissance Blvd. Suite 100
King of Prussia, PA 19406-2713

Re: NRC RAM License 47-25375-01MD 03034289

Dear Ms. Weidner,

I am requesting an amendment of the above NRC RAM license, as follows:

Please add possession of Germanium68/Gallium 68 (Ge68/Ga68) Generator in any chemical and/or physical form up to a maximum of 900 mCi.

In addition please remove the following:

- Shawn Lorrain as ANP. [redacted]
- Tamiko Ushio as ANP. Tamiko is no longer employed at PharmaLogic.

I have enclosed a copy of our RAM and monograph of the Ge68/GA68 generator.

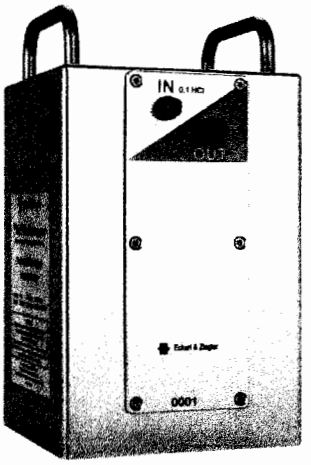
Should you need any additional information I may be reached at rvansant@pharmalogic.info or [redacted]

Regards,

Richard L. Van Sant, PharmD
Director Regulatory Affairs

5903 47

GalliaPharm Radionuclide Generator



GalliaPharm
$^{68}Ge/^{68}Ga$ Generator

Cyclotron-independent production of the positron emitter $^{68}Gallium$

Description

The GalliaPharm $^{68}Ge/^{68}Ga$ Generator from Eckert & Ziegler Radiopharma GmbH is a pharmaceutical product for obtaining the positron emitter $^{68}Gallium$, independent of a cyclotron.

The generator is a closed system consisting of pharmacopoeia grade borosilicate glass column containing a titanium dioxide bed on which ^{68}Ge is adsorbed. ^{68}Ga is continuously produced by decay of its radioactive parent ^{68}Ge and is eluted with sterile, ultra pure 0.1 M HCl. The generator is available with the following activities: 20 mCi, 30 mCi, 40 mCi and 50 mCi.

Output

In practice, the generator requires at least 4 hours to achieve full yield after being eluted. The output, of course, will decrease with decay of the ^{68}Ge parent.

Advantages

The GalliaPharm is produced under GMP conditions ensuring highest quality standards and is designed to minimize both ^{68}Ge breakthrough and metal impurities. No metals are used within the closed system. All components are compliant with the monographs of the European Pharmacopeia (if available) or their suitability for the respective application has been otherwise tested.

Generator Shelf-Life

Expected life of the generator is dependent upon several factors such as frequency of use, volume of elution and others. The useful life of the generator has been investigated in a long-term study. From the data obtained compliance with specification is given over 12 months. Therefore, a shelf-life of 12 months is justified when used according to the Summary of Product Characteristics (SmPC) provided by the manufacturer.

Marketing Authorization

The sterile and GMP compliant GalliaPharm $^{68}Ge/^{68}Ga$ Generator is registered as a medicinal product in several European countries. Furthermore Eckert & Ziegler Radiopharma GmbH is a holder of a Type II Drug Master File (#28741) in the USA.

Quality Control Process

Every GalliaPharm has to pass several tests according to the GMP conditions and tests mentioned in the 'Gallium (^{68}Ga) chloride solution for Radiolabelling' monograph of the European Pharmacopoeia before delivery. Additionally, Eckert & Ziegler also tests sterility of the eluate. Finally the GalliaPharm will be released by a qualified person.

The GalliaPharm eluate complies with the following specifications (excerpt):

Test parameter	Specification
Appearance	Clear, colorless solution
Identity ^{68}Ga	Half-life 62–74 min
Content	> 60 % of nominal activity
Chemical impurity	Fe < 10 µg / GBq Zn < 10 µg / GBq
Radionuclidic purity (γ-emitting impurities)	< 0.001 % of nominal activity
Radiochemical purity	> 95 % free $^{68}Ga^{3+}$
pH	0.5–2.0
Microbiological quality	Sterile
Bacterial endotoxines	< 30 EU / ml

Eckert & Ziegler

GalliaPharm Radionuclide Generator

Technical Specifications

General Data	
Dimensions (W x D x H)	132 x 133 x 230 mm
Weight	14 kg
Time of max. ^{68}Ga accumulation	7 hours
^{68}Ge breakthrough	Not more than 0.001 %
Eluent*	Sterile, ultra pure hydrochloric acid 0.1 mol/l
Elution Speed	2.5 ml/min
Available activities	20 mCi , 30 mCi , 40 mCi and 50 mCi
Decay Characteristics	
Half-life	^{68}Ge: 271 days ^{68}Ga: 68 minutes
Radiation type	Positrons: 1.90 MeV from ^{68}Ga daughter; 89 % abundance Photons: 0.511 MeV positron annihilation radiation; 178 % abundance 1.077 Mev gamma radiation; 3.2 % abundance
Order Information	
Delivery time	3–4 months after receipt of the written purchase order
Additional Information	
Countries of registration	The GalliaPharm has been registered as a medicinal product in the following European countries: AT, BE, DE, DK, ES, FI, FR, IT, NL, NO, PL, SE
Disposal	Additional fees will apply if you want E&Z to take care of the final disposal of the used product.
Accessories	According to the marketing authorization the cassette tube for elution delivered with the generator has a length of 60 cm.

**To keep the warranty and pharmaceutical status it is mandatory to only use the sterile HCl solution provided by Eckert & Ziegler.*

Marketing authorization holder: Eckert & Ziegler Radiopharma GmbH, Robert-Rössle-Str. 10, D-13125 Berlin. Name of medicinal product: GalliaPharm 0,74–1,85 GBq radionuclide generator, radionuclide generator. Active ingredient: germanium (^{68}Ge) chloride as mother nuclide, gallium (^{68}Ga) chloride as daughter nuclide, 0.74–1.85 GBq. Excipients: column (matrix) titanium dioxide (E 171), hydrochloric acid 0.1 mol/l. Indications: Not for direct use in patients. For in vitro radiolabelling of carrier molecules for diagnostic imaging via positron emission tomography (PET). Contra-indications: Hypersensitivity against the active ingredient or the excipients. Side-effects: no side effects known. Warnings: radioactive, handle in accordance with radiation protection requirements. Prescription

Drug Master File in the USA: DMF #28741
Drug Master File holder: Eckert & Ziegler Radiopharma GmbH, Robert-Rössle-Str. 10, D-13125 Berlin
In the USA the FDA regards the ^{68}Ge/^{68}Ga Generator as a drug substance and accordingly Eckert & Ziegler Radiopharma GmbH has submitted a Type II DMF.

Eckert & Ziegler Radiopharma GmbH

Robert-Rössle-Strasse 10
13125 Berlin
Germany
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7132-0025 /Rev.05/ 02.2016

NRC FORM 374

U.S. NUCLEAR REGULATORY COMMISSION

Amendment No. 26

MATERIALS LICENSE

Pursuant to the Atomic Energy Act of 1954, as amended, the Energy Reorganization Act of 1974 (Public Law 93-438), and Title 10, Code of Federal Regulations, Chapter I, Parts 30, 31, 32, 33, 34, 35, 36, 39, 40, and 70, and in reliance on statements and representations heretofore made by the licensee, a license is hereby issued authorizing the licensee to receive, acquire, possess, and transfer byproduct, source, and special nuclear material designated below; to use such material for the purpose(s) and at the place(s) designated below; to deliver or transfer such material to persons authorized to receive it in accordance with the regulations of the applicable Part(s). This license shall be deemed to contain the conditions specified in Section 183 of the Atomic Energy Act of 1954, as amended, and is subject to all applicable rules, regulations, and orders of the Nuclear Regulatory Commission now or hereafter in effect and to any conditions specified below.

Licensee	In accordance with the letter dated January 20, 2015,
1. PharmaLogic WV, Ltd.	3. License No. 47-25375-01MD is amended in its entirety to read as follows:
2. 9 W. Benedum Industrial Park Bridgeport, West Virginia 26330	4. Expiration Date: October 31, 2022
	5. Docket No. 030-34289

6. Byproduct, source, and/or special nuclear material	7. Chemical and/or physical form	8. Maximum amount that licensee may possess at any one time under this license
A. Any byproduct material with atomic numbers 1 through 83, except strontium-89, yttrium-90, molybdenum-99, technetium-99m, iodine-131, xenon-133, and samarium-153	A. Any	A. 200 millicuries per radionuclide and 2 curies total
B. Fluorine 18	B. Any	B. 1 curie
C. Gallium 67	C. Any	C. 500 millicuries
D. Strontium 89	D. Any	D. 80 millicuries
E. Yttrium 90	E. Any	E. 1 curie
F. Molybdenum 99	F. Any	F. 200 curies
G. Technetium 99m	G. Any	G. 200 curies
H. Indium 111	H. Any	H. 300 millicuries
I. Iodine 123	I. Any	I. 50 millicuries
J. Iodine 131	J. Any	J. 5 curies
K. Xenon 133	K. Any	K. 3 curies
L. Samarium 153	L. Any	L. 1.5 curies
M. Thallium 201	M. Any	M. 1 curies

MATERIALS LICENSE SUPPLEMENTARY SHEET

License No. 47-25375-01MD

Docket No. 030-34289

Amendment No. 26

6. Byproduct, source, and/or special nuclear material	7. Chemical and/or physical form	8. Maximum amount that licensee may possess at any one time under this license
N. Any byproduct material permitted by 10 CFR 35.400	N. Sealed sources (Bard Brachytherapy Inc. Model STM 1251; IsoAid L.L.C. Model IAI-125A; North American Scientific Model MED 3631, or MED 3633; Theragenics Model 200; Best Medical Models 2301-2308, 2309-2316, or 2331-2335)	N. 0.5 curies
O. Any byproduct material permitted by 10 CFR 31.11	O. Prepackaged units for *in vitro* diagnostic tests	O. 100 millicuries
P. Any byproduct material permitted by 10 CFR 35.65(a)	P. Sealed sources (International Isotopes Idaho Inc. Model BM06E series, BM06S series, BM03-XXA and BM03-XXL series; North American Scientific Inc. Model Med 3503, MED 3550, MED 3400 or MED 3402; Isotopes Product Laboratories Model RV-XXX series, EG-XXX series, and GF Type R Series)	P. 100 millicuries
Q. Depleted Uranium	Q. Metal	Q. 400 kilograms

9. Authorized use:

A. - M. Preparation and distribution of radioactive drugs, production of technetium 99m pertechnetate, compounding of iodine 131 and distribution of unused and used molybdenum 99/technetium 99m generators to authorized recipients in accordance with 10 CFR 32.72 and to authorized recipients for non-medical use.

N. Redistribution of sealed sources to authorized recipients in accordance with 10 CFR 32.74 and to authorized recipients for non-medical use.

O. Redistribution to specific licensees or general licensees pursuant to 10 CFR 31.11 provided the packaging and labeling remain unchanged.

P. Calibration and checking of the licensee's instruments. Redistribution of sealed sources initially distributed by a manufacturer licensed pursuant to 10 CFR 32.74 to authorized recipients and to authorized recipients for non-medical use.

Q. Shielding for molybdenum-99/technetium-99m generators.

MATERIALS LICENSE SUPPLEMENTARY SHEET

License No. 47-25375-01MD

Docket No. 030-34289

Amendment No. 26

CONDITIONS

10. Licensed material may be used or stored only at the licensee's facilities located at 5842B Davis Creek Road, Barboursville, West Virginia and 9 W. Benedum Industrial Park Road, Bridgeport, West Virginia.

11. Licensed material shall be used by, or under the supervision of:

    A. A pharmacist working or designated as an authorized nuclear pharmacist in accordance with 10 CFR 32.72(b)(2)(i) or (4).

    B. Authorized nuclear pharmacists: James Cordonier II, R.Ph., Steven C. Green, R.Ph., Shelby Griffith, R.Ph., Kevin Hart, R.Ph., Garth Kistner, R.Ph., Shawn Lorrain, R.Ph., Glen Palmer, R.Ph., Laurie Stallings, R.Ph., BCNP, Richard Sucese, R.Ph., Timothy Summers, R.Ph., Dana Suttle, R.Ph., Tamiko Ushio, R.Ph., Zonker White, R.Ph., and Anna K. Wierzbicki, R.Ph.

12. The Radiation Safety Officer for this license is Steven C. Green, R.Ph.

13. In addition to the possession limits in Item 8, the licensee shall further restrict the possession of licensed material to quantities below the minimum limit specified in 10 CFR 30.35(d) for establishing decommissioning financial assurance.

14. This license does not authorize commercial distribution of licensed material to persons exempt from licensing pursuant to 10 CFR 30.14 through 30.21, inclusive, or equivalent regulations of any Agreement State.

15. A. Sealed sources shall be tested for leakage and/or contamination at intervals not to exceed six months or at the intervals specified in the certificate of registration issued by the U. S. Nuclear Regulatory Commission under 10 CFR 32.210 or under equivalent regulations of an Agreement State.

    B. Notwithstanding Paragraph A of this Condition, sealed sources designed to primarily emit alpha particles shall be tested for leakage and/or contamination at intervals not to exceed three months.

    C. In the absence of a certificate from a transferor indicating that a leak test has been made within the intervals specified in the certificate of registration issued by the U. S. Nuclear Regulatory Commission under 10 CFR 32.210 or under equivalent regulations of an Agreement State, prior to the transfer, a sealed source received from another person shall not be put into use until tested and the test results received.

    D. Sealed sources need not be tested if they contain only hydrogen-3; or they contain only a radioactive gas; or the half-life of the isotope is 30 days or less; or they contain not more than 100 microcuries of beta- and/or gamma-emitting material or not more than 10 microcuries of alpha-emitting material.

MATERIALS LICENSE SUPPLEMENTARY SHEET

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E. Sealed sources need not be tested if they are in storage and are not being used; however, when they are removed from storage for use or transferred to another person and have not been tested within the required leak test interval, they shall be tested before use or transfer. No sealed source shall be stored for a period of more than 10 years without being tested for leakage and/or contamination.

F. The leak test shall be capable of detecting the presence of 0.005 microcurie (185 becquerels) of radioactive material on the test sample. If the test reveals the presence of 0.005 microcurie (185 becquerels) or more of removable contamination, a report shall be filed with the U. S. Nuclear Regulatory Commission in accordance with 10 CFR 30.50(c)(2), and the source shall be removed immediately from service and decontaminated, repaired, or disposed of in accordance with Commission regulations.

G. Tests for leakage and/or contamination, including leak test sample collection and analysis, shall be performed by the licensee or by other persons specifically licensed by the U. S. Nuclear Regulatory Commission or an Agreement State to perform such services.

H. Records of leak test results shall be kept in units of microcuries and shall be maintained for five years.

16. Sealed sources or detector cells containing licensed material shall not be opened or sources removed from source holders by the licensee.

17. The licensee shall conduct a physical inventory every six months, or at other intervals approved by the U. S. Nuclear Regulatory Commission, to account for all sources and/or devices received and possessed under the license. Records of inventories shall be maintained for five years from the date of each inventory and shall include the radionuclides, quantities, manufacturer's name and model numbers, and the date of the inventory.

18. The licensee is authorized to hold byproduct material with a physical half-life of less than or equal to 120 days for decay-in-storage before disposal without regard to its radioactivity if the licensee:

A. Monitors byproduct material at the surface before disposal and determines that its radioactivity cannot be distinguished from the background radiation level with an appropriate radiation detection survey meter set on its most sensitive scale and with no interposed shielding; and

B. Removes or obliterates all radiation labels, except for radiation labels on materials that are within containers and that will be managed as biomedical waste after they have been released from the licensee; and

C. Maintains records of the disposal of licensed materials for three years. The record must include the date of disposal, the survey instrument used, the background radiation level, the radiation level measured at the surface of each waste container, and the name of the individual who performed the disposal.

MATERIALS LICENSE SUPPLEMENTARY SHEET

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19. The licensee is authorized to retrieve, receive and dispose of radioactive waste from its customers limited to radiopharmacy supplied syringes and vials and their contents.

20. The licensee is authorized to transport licensed material in accordance with the provisions of 10 CFR Part 71, "Packaging and Transportation of Radioactive Material."

21. Except as specifically provided otherwise in this license, the licensee shall conduct its program in accordance with the statements, representations, and procedures contained in the documents, including any enclosures, listed below. The U. S. Nuclear Regulatory Commission's regulations shall govern unless the statements, representations, and procedures in the licensee's application and correspondence are more restrictive than the regulations.

A.	Application dated April 26, 2012	[ML12122A214]
B.	Letter dated June 19, 2012	[ML12178A539]
C.	Letter dated September 6, 2012	[ML12263A215]
D.	Application dated November 16, 2012	[ML1234A305]
E.	Letter dated January 10, 2013	[ML13029A564]
F.	Letter dated January 23, 2013	[ML13024A257]
G.	Letter dated January 20, 2015	[ML15048A157]
H.	Letter received March 20, 2015	

For the U. S. Nuclear Regulatory Commission

Original signed by Tara L. Weidner

Date March 30, 2015 By _____

Tara L. Weidner
Medical Branch
Division of Nuclear Materials Safety
Region I
King of Prussia, Pennsylvania 19406

Monday, March 30, 2015 10:21:31

This is to acknowledge the receipt of your letter/application dated

February 23, 2016, and to inform you that the initial processing which includes an administrative review has been performed.

Amendment (47-25375-01MD)

☒ There were no administrative omissions. Your application was assigned to a technical reviewer. Please note that the technical review may identify additional omissions or require additional information.

☐ Please provide to this office within 30 days of your receipt of this card

_____.

A copy of your action has been forwarded to our License Fee & Accounts Receivable Branch, who will contact you separately if there is a fee issue involved.

Your action has been assigned **Mail Control Number** 590347.
When calling to inquire about this action, please refer to this control number.
You may call us on (610) 337-5398, or 337-5260.

NRC FORM 532 (RI)
(6-96)

Sincerely,
Licensing Assistance Team Leader