



Kevin F. Grant
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April 1, 2022

U.S. Nuclear Regulatory Commission – Region III
Materials Licensing Section
2443 Warrenville Road, Suite 210
Lisle, IL 60532-4352

RE: Request to amend NRC Radioactive Material License 24-32462-01MD
RLS (USA) Inc., 1623 Lotsie Blvd. Overland, MO 63132

Dear Licensing Representative,

Please allow this letter to serve as notice that RLS (USA), Inc wishes to amend Radioactive Materials License 24-32462-01MD as follows:

1. Please remove Anne Siewko, R.Ph. as an Authorized Nuclear Pharmacist (ANP) for RLS (USA) Inc., Overland, MO facility under license Condition 12 (B). Mrs. Siewko is no longer employed by RLS (USA) Inc.
2. Please add the following radionuclide to the Possession and Use Table:

Radionuclide	Chemical / Physical Form	Maximum Possession Limit	Purpose of Use
Yttrium-90	Resin microsphere	2 Ci total	For the preparation and redistribution of SIR-Spheres® for permanent brachytherapy

Should you have any questions or require additional information, please contact me by email at kevin.grant@rls.bio or call Tel. (314) 427-6888.

Sincerely,

Kevin F. Grant, R.Ph.
Radiation Safety Officer
RLS (USA) Inc.

SOP 3.3.11 Y-90 Microspheres Dispensing

I. Purpose

To describe the dispensing of Yttrium-90 Microspheres.

II. Scope

This applies to all Nuclear Pharmacy sites

III. Related Documents/ Websites:

- A. SOP 2.2.6 CRC 25 and 55 Potentiometer Settings
- B. SOP 2.2.7 Atom Lab Potentiometer Settings
- C. <https://www.youtube.com/watch?v=Xdj5acMqVas>

IV. Responsibilities

It is the responsibility of the Pharmacy Manager or designee to oversee policy compliance for personnel under his/her supervision. It is the responsibility of the individuals performing this procedure to comply with these instructions and all relevant safety assessments including personal protective equipment, ergonomics, radiation safety, chemical management, and hazard analysis recognition.

V. Definitions

- A. **Manufacturer's shipping container** – The shield in which the microspheres are shipped from the manufacture to the pharmacy.
- B. **Product Vial** – The immediate container (glass vial) located within the manufacture's shipping container that contains microspheres directly from the manufacture.
- C. **Dispensing Vial shield**- A shielded container specifically designed to shield Y-90 while dispensing.
- D. **Beta Syringe Shield**- A syringe shield made of acrylic or similar material designed to attenuate the beta particles and reduce exposure to the user.
- E. **V- Vial Delivery Shield**- An acrylic shield with lid designed to be used while the dose is being administered to the patient in the surgical suite.
- F. **Final Shipping Container**- A vendor modified W-12 used in conjunction with other components to ship the final product to the customer.
- G. **Beta Emitter** – A radionuclide that decays by emitting a beta particle from the nucleus. The beta particle may be positively or negatively charged.
- H. **Dose Calibrator Dipper**- The device hung inside the dose calibrator used to ensure items being measured in the dose calibrator are done so in a reproducible geometry.
- I. **Calibration Number / Dial Value**- The resistance setting on the dose calibrator used to differentiate between radionuclide energies to determine the activity of the sample.

VI. Equipment and Materials

- A. 1 Product Vial
- B. 1 Dispensing Vial Shield
- C. 1 Beta Syringe Shield
- D. Remote Handling Device
- E. 1 V-Vial
- F. 1 Acrylic V-Vial Shield
- G. Final Shipping Container
- H. Dose Calibrator Model(s) CRC 25R or CRC 55T
- I. 2- 25g needles
- J. 1- 5cc syringe fitted with a 21g needle at least 55 mm in length
- K. G-M Survey Meter with Pancake Probe or Equivalent Instrument

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VII. Procedure

A. Dispensing Procedure

1. Document the product activity as reported by the manufacturer on Attachment A (Y-90 Microspheres Dose Calculation worksheet) and calculate the activity at time of compounding.
Please note that your dose calibrator should be calibrated for Y-90 potentiometer setting in accordance with SOP 2.2.6 or 2.2.7 prior to manipulating this product.
2. Enter in the predetermined calibration number utilizing the attachment designated for the dose calibrator being used.
3. In a properly prepared hood while wearing sterile gloves, wipe down the external surfaces of all equipment, and products involved in the dispensing process with sterile IPA prior to introducing it into the laminar flow hood.
4. Agitate the product vial for 30 seconds.
5. Utilizing a remote handling device, immediately remove the product from its shield, place it in the dose calibrator and record the activity on Attachment A.
6. Remove the product from the dose calibrator using remote handling device and place into the bottom half of the dispensing vial shield.
7. Remove the vial aluminum seal and appropriately disinfect the septum with a sterile alcohol swab.
8. Place the lid to the dispensing vial shield and tighten until secure.
9. Complete all calculations required to obtain the volume needed for dispensing the product.
10. Remove the center of aluminum seal from sterile v-vial.
11. Mark the v-vial on opposite sides of the v-vial.
12. Place the v-vial in the acrylic shield and then place the acrylic shield into bottom half of the shipping container.
13. Appropriately disinfect the septum of the v-vial with a sterile alcohol swab.
14. Insert a short 25-gauge needle through the septum of the v-vial at one marks until it just pierces the septum to create a vent. Ensure that the needle will not touch the fluid once introduced, a filter needed may be preferred.
15. Shake the dispensing vial containing the product vigorously to disperse the SIR-Spheres microspheres
16. Insert a 25-gauge needle through the septum of the manufacture's shipping vial to create a vent, ensuring the needle is well clear of the contents in the shipping vial.
17. Use a shielded 5ml syringe with a 21-gauge hypodermic needle at least 50mm long to puncture the septum of the shielded product vial, and quickly draw back and forth several times to mix the microspheres thoroughly.
18. Quickly withdraw the pre-calculated volume, while pulling back a small quantity of air to clear the needle, before the product settles.
19. Pierce the v-vial next to the opposite hash mark leaving approximately 2 mm between the vent needle and the dispensing needle.
20. Verify the patient dose in the v-vial by re-measuring the activity in the product vial. If applicable adjust the activity by adding or removing microspheres as needed.
Please note if there are too many microspheres in the original transfer, the contents removed from the v-vial to achieve the required activity must be returned to the product vial to properly determine the activity dispensed.
21. Once the proper activity is obtained through reference of the product vial, qs the volume in the v-vial to a minimum of 3 mls not to exceed 5 mls.
22. Using remote handling devices remove the v-vial from the acrylic shield and directly measure the v-vial in the dose calibrator utilizing the Y-90 Sir Spheres v-vial calibration number previously calculated.

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23. If the v-vial measures within $\pm 10\%$ of the ordered activity record the activity displayed on both the form 48 and Attachment A.
24. Verification by trained personnel will include review of dispensed activity, prescribed activity, and selection of the dose proper dose calibrator setting, while the dose is in the dose calibrator.
25. Place the v-vial back into the acrylic shield, utilizing remote handling devices, secure the lid and plug on the acrylic shield.
26. Place the shielded v-vial in the pass through for proper DOT packaging.
27. Survey yourself, the hood, equipment and surrounding area for contamination with a G-M Survey Meter with Pancake Probe or Equivalent Instrument.

VIII. Training

Employees performing this procedure shall be trained on this procedure.

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List of Attachments

Attachment A: Y-90 Microspheres Dose Calculation Worksheet

Attachment B: Y-90 Decay Factor Chart

Attachment C: CRC®-25 Selecting the Calibration Number

Attachment D: CRC®-55 Selecting the Calibration Number

Document History		
Version	Date	Brief Description of Change
1	1 June 2020	New document
1.1	1 Nov 2021	Administrative

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Attachment A: Y-90 Microspheres Dose Calculation Worksheet

Vial Lot Number: _____ Calibration Activity: _____ mCi

Calibration Date: _____ Manufacturer Calibration Time: _____ Eastern Time Zone

Calibration Time Adjusted for Local Time Zone: _____ Time of assay: _____

Difference in Time Zone Cal Time/Assay Time in Hours: _____

* Be sure to account for time zone differences if applicable

Calculate Current Activity of Vial:

Use Decay Chart to calculate current activity of dose: = _____ mCi [A]

*Use the decay factor that correlates to the hours column in the chart and multiply by the calibration activity

Dose Calibrator Assay of Vial: = _____ mCi [B]

Time of Dose Calibrator Assay: _____ [M]

Are [A] and [B] within +/- 10%? _____ if no, recalculate current activity and re-assay. If activity still does not correspond, contact RSO.

From this point forward, only Dose Calibrator activity will be used

Preparation of Dose:

Assay Activity divided by volume: = [B] / 5 mL = _____ mCi/mL [C]

Prescribed Activity: _____ mCi [D]

Volume to be drawn from Shipping Vial: = [D] / [C] = _____ mL

After dose is drawn, measure residual activity in Shipping Vial: _____ mCi [E]

Patient syringe activity = Initial Activity – Residual Activity = [B] - [E] = _____ mCi [F]

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Attachment B: Y-90 Decay Factor Chart

Hours	Decay Factor
0.5	0.995
1	0.989
2	0.979
3	0.968
4	0.956
5	0.947
6	0.937
7	0.927
8	0.917
9	0.907
10	0.898
11	0.888
12	0.878
36	0.678
24	0.772
48	0.595
72	0.459


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Attachment C: CRC®-25 Selecting the Calibration Number

1. Press the **MENU** key.
2. Press **4** to select setup. The setup menu will appear.
3. Press **4** to select other. The “Enter Password” prompt will appear.
4. Input your password and press the enter key. The other menu will appear.
*The password is the last three digits of the serial number and is located on the laminated sheet for your convenience.
5. Press **4** to select nuclides. The nuclides menu will appear.
6. Press **3** to select “New Cal Num.” The “choose Nuclide” Prompt will appear.
7. Press NUCL key. The “Specify Nuclide” Prompt will appear.
8. For Y-90 input 990, then press the **ENTER** key. The “Change Cal #?” prompt will appear.
9. Press **9** for Yes. The “Enter Calibration #” prompt will appear.
10. Reference the laminated sheet on the hood in which the dose calibrator you are using resides and type in the calibration number for the radionuclide and container type you wish to measure and press the **ENTER** key.
11. The “New Cal # OK” Prompt will appear press **9** yes if the number is correct. Press **6** for No and re-enter the calibration number.
12. Once you have pushed **9** for Yes press the **MENU** Key Twice. The other menu will then be displayed.

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Attachment D: CRC®-55 Selecting the Calibration Number

1. Touch the **Home** button.
2. Touch the **SETUP** button. The setup screen will appear.
3. Touch the **ADVANCE CHAMBER** button. The “Please Enter Password” Prompt will appear with a key pad.
4. Input your password and touch the **ACCEPT** button.
*The password is the last Three digits of the serial number you can find it on the laminated sheet attached to the hood.
5. Touch the **SETUP CALNUM** button. The Setup CalNum screen will appear.
6. Touch the Nuclide: field box. The “Please Select Nuclide” screen will appear.
7. Touch the Down Arrow() button to scroll down the list until Y-90 is displayed in the list.
8. Touch the Y-90 and the entire line for the selected nuclide will become highlighted and an **ACCEPT** button will appear. Touch the **ACCEPT** button to select the highlighted nuclide.
9. Touch the **User R Cal#:** Field box. The “Please enter R Cal #” Key pad will appear.
10. Reference the laminated sheet on the hood in which the dose calibrator you are using resides and type in the calibration number for the radionuclide and container type you wish to measure and touch the **ACCEPT** button. You only need to enter a number in the R cal column leave the P column blank.
11. Touch the **Home** button.
12. Once the nuclide has been added it can be accessed by touching the currently displayed nuclide and then selecting Y-90 from the list then pressing the ACCEPT button. The selected nuclide will now be displayed on the chamber measurement screen.

Pavon, Martha

From: Kevin Grant <kevin.grant@rls.bio>
Sent: Friday, April 1, 2022 7:25 AM
To: Parker, Bryan
Subject: [External_Sender] RLS St Louis license amendment for Y-90 microspheres
Attachments: RLS SOP 3.3.11 Y-90 Microspheres Dispensing.pdf; RLS St Louis Amendment Letter 1April2022.pdf

Mr. Parker,

As per our phone conversation on March 16th, I am submitting a license amendment adding Sirtex Y-90 microspheres to radioactive materials license 24-32462-01MD. Attached is the signed amendment letter and a copy of the relevant RLS procedures regarding the handling and dispensing of Y-90 microspheres to ensure safe practices will be followed.

The reason for the addition stems from customer concerns regarding sterility due to the proposed changes in USP 825. When a patient is determined to receive Y-90 microsphere therapy, the hospital will schedule the dose with the pharmacy. The pharmacy would procure Y-90 microspheres from Sirtex and either send the vial directly to the hospital or re-suspend and draw the calculated dose per physician order. The microspheres would then be sent to the hospital where trained physicians can prep and administer to the patient.

I will be working the early shift next week and usually end my shift around 9:30 am in case you need to reach out to me for any additional information.

Best regards,



Kevin Grant, PharmD
Radiation Safety Officer

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Pavon, Martha

From: Tomczak, Tammy
Sent: Monday, April 4, 2022 7:12 AM
To: Pavon, Sandy; Pavon, Martha
Subject: FW: Please open an action
Attachments: [External_Sender] RLS St Louis license amendment for Y-90 microspheres

Good morning, Sandy and Martha 😊

Please add the attached to ADAMS.

Thank you!!
Tammy

From: Parker, Bryan <Bryan.Parker@nrc.gov>
Sent: Friday, April 01, 2022 7:39 AM
To: Tomczak, Tammy <Tammy.Tomczak@nrc.gov>
Subject: Please open an action

Hey Tammy,

Please open an action with the attached request from RLS (USA).

Thanks.

Bryan