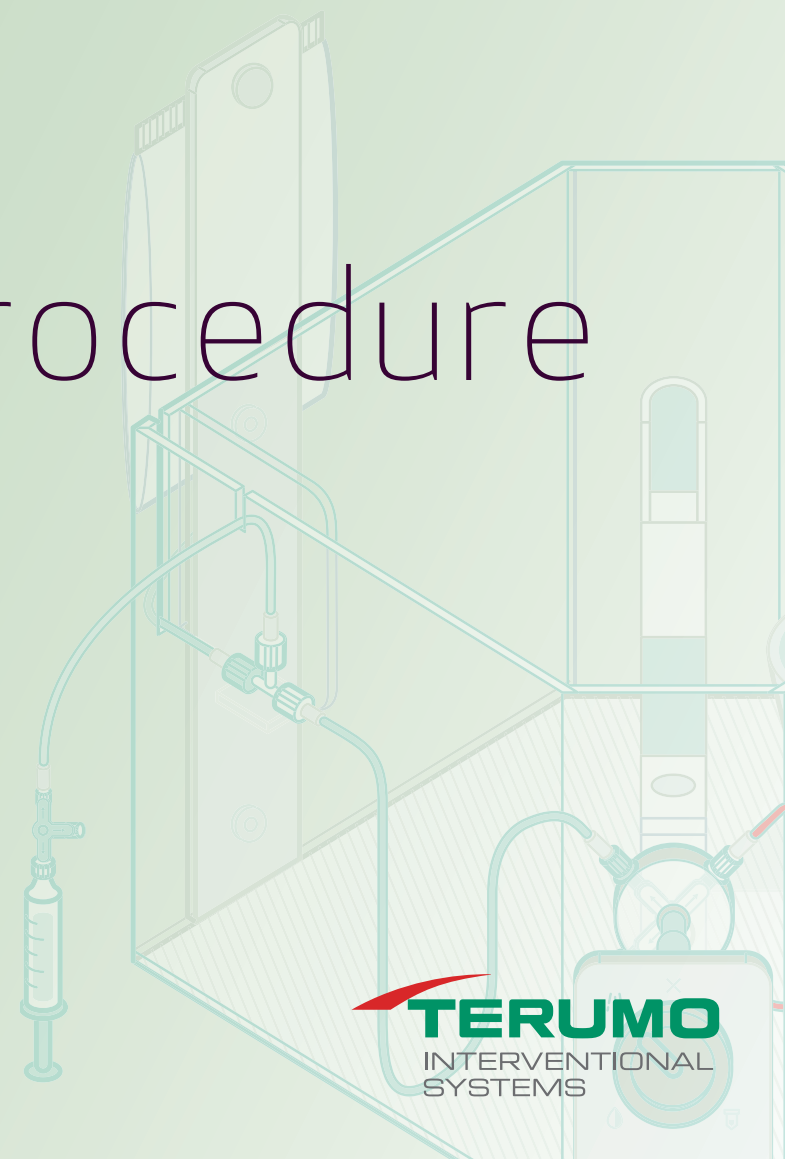


QuiremSpheres™
Holmium-166 Microspheres

QuiremScout™
Holmium-166 Microspheres

Manual Administration Procedure

QuiremSpheres™ customer kit (QS-C001) and
QuiremSpheres™ delivery set (QS-D001)



TERUMO
INTERVENTIONAL
SYSTEMS

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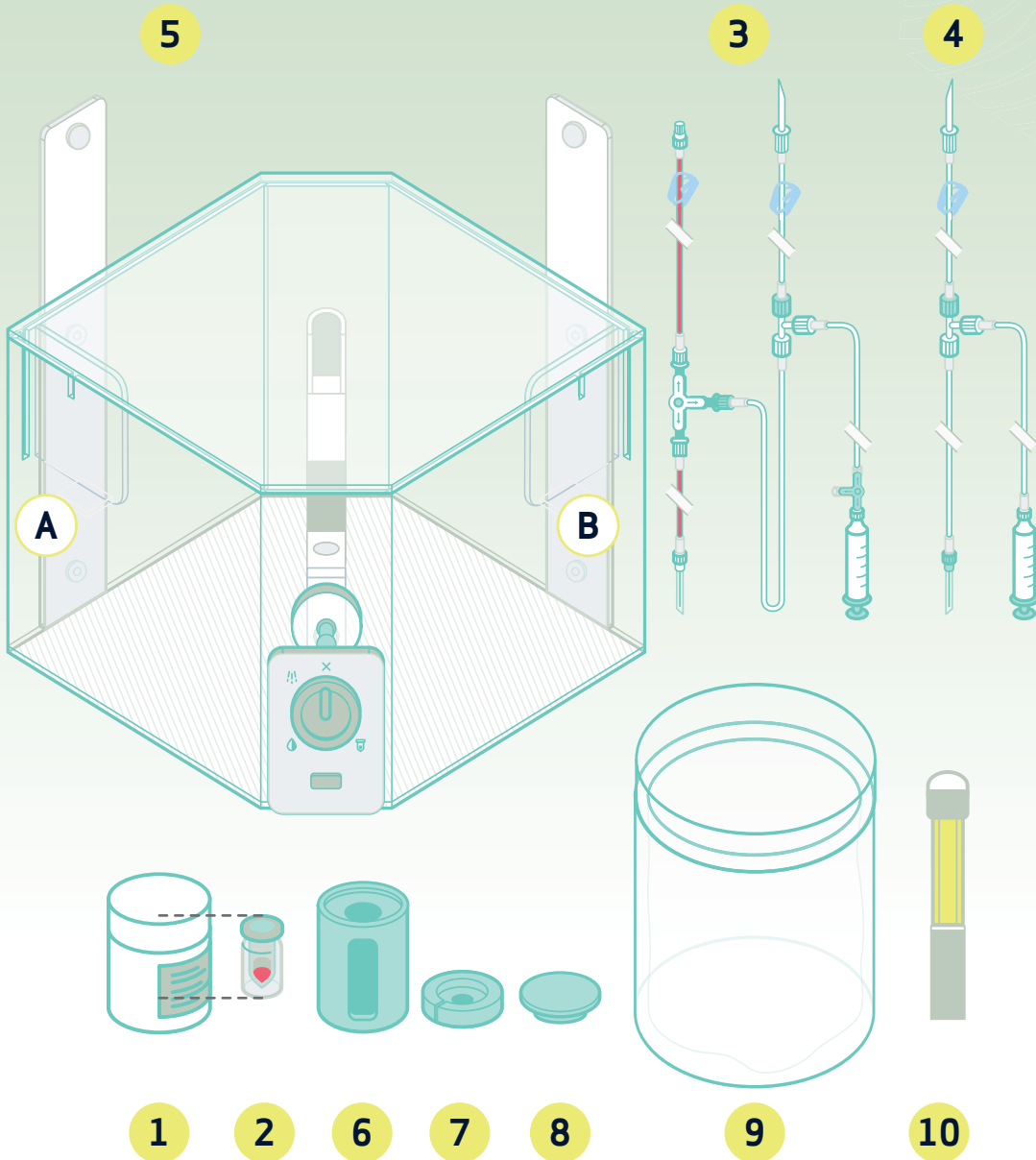
1. General information

The following guidelines are for the administration of QuiremSpheres™ and QuiremScout™ Holmium-166 microspheres. Only clinicians who have received training from Terumo representatives are permitted to deliver QuiremSpheres™ or QuiremScout™ Holmium-166 microspheres to patients. A condensed pictorial version of these guidelines (Quick Reference Guide) is provided with the QuiremSpheres™ customer kit and available from Quirem Medical upon request.

Radiation hygiene principles should be taken into account at all times. In short, this means that dose exposure for clinical staff, nursing staff and unintended dose exposure for the patient should be as low as reasonably achievable (ALARA) by considering the following aspects:

- TIME – Minimize the time of exposure
- DISTANCE – Increase the distance between the radiation source and your body/extremities as much as possible
- SHIELDING – Take appropriate shielding measure

! Note: Wear gloves at all times. After completion of the procedure, all gloves should be regarded as potentially radioactively contaminated and be disposed according to local regulations.



2. Items recommended for the QuiremSpheres™ and QuiremScout™ Holmium-166 microspheres administration procedure

Items provided by Quirem Medical:

QuiremSpheres™ (QS-V001) or QuiremScout™ (QS-S001) Holmium-166 microspheres

- 1 Lead container
- 2 V-vial with microspheres

QuiremSpheres™ delivery set (QS-D001)

- 3 Tube Line (A)
- 4 Tube Line (B)

QuiremSpheres™ customer kit (QS-C001)

- 5 Administration box
- 6 Vial holder
- 7 Tungsten Ring
- 8 Tungsten Cap
- 9 Plastic waste container
- 10 LED-light (2x)

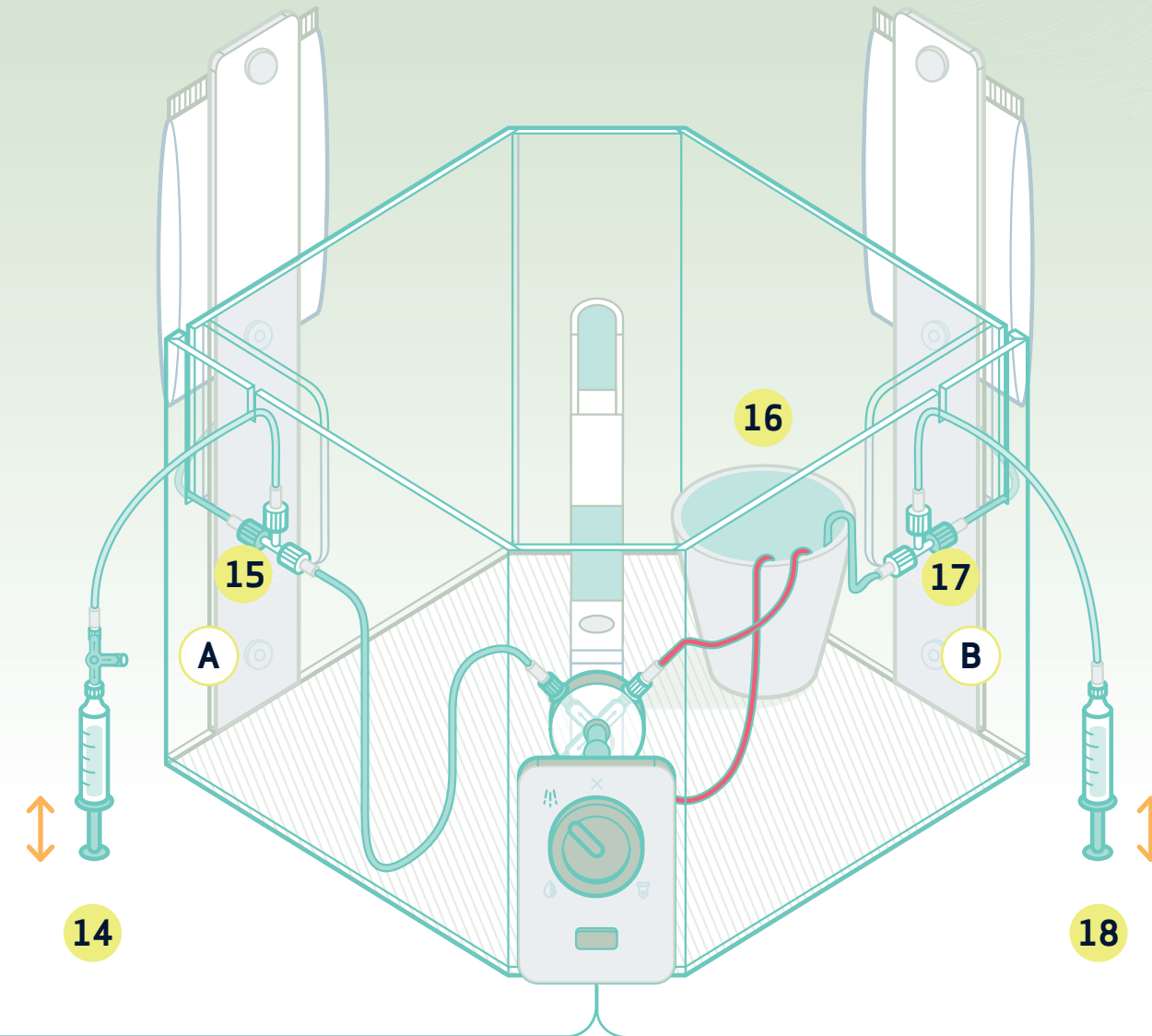
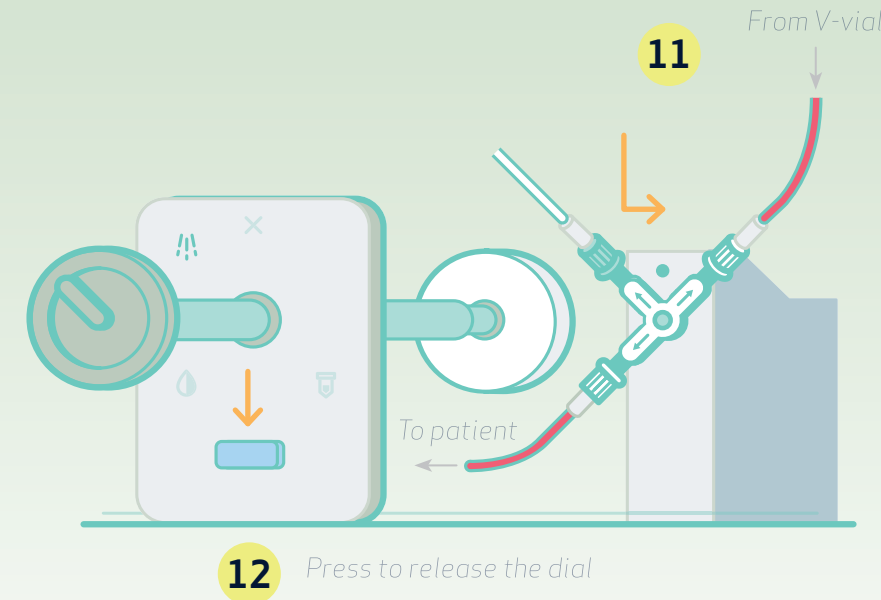
Recommended items, not provided by Quirem Medical:

- Patient prescription
- 2 bags of saline (250 ml each) with possibility of spike connection
- Contrast agent
- Surface radiation contamination meter
- Trolley
- Floor drape placed under the trolley in the angiography suite
- A sterile drape placed on trolley
- On the draped trolley:
 - Scissors
 - Sterile adhesive strips
 - Hemostat
 - Towels
 - Gauze
 - Forceps
 - Alcohol swabs
 - Sterile cup

3. Position the tube lines in the administration box

The following steps can either be performed in a hospital facility for handling radioactive materials (e.g. a nuclear medicine laboratory) or in a hospital facility (e.g. an angiosuite) approved for the QuiremSpheres™ and/or QuiremScout™ Holmium-166 microspheres administration procedure.

- Place the administration box on a draped trolley.
 - Remove the lid of the administration box.
 - Ensure the dial is in the prime position [A] (Fig. 13).
 - Release the dial and shaft by pulling the lever down (Fig. 12).
- ! Note:** Check the expiry date of the QuiremSpheres™ Delivery Set
- Unpack 'Tube Line A' and place it inside the administration box (Fig. 15).
 - Ensure the three-way stopcock is positioned (Fig. 11), following the depicted flow path of the red lined tubing.
 - Push back the shaft and dial until it locks. Ensure the dial can rotate freely to all four positions, providing the sound and feel of a click in each of them.
 - Unpack 'Tube Line B' and place it inside the administration box (Fig. 17).
 - Position a sterile cup in the administration box (Fig. 16).
 - Place both capped needles and the capped catheter connector inside the cup. The vented needle caps should remain on the needles and on the catheter connector to maintain sterility.
 - Hang a bag of saline on the hook at each side of the box.
 - Connect the spikes of both lines to the bags of saline.



4. Prime the tube lines

- Verify that the dial is set to the prime position [A] (Fig. 13).
- Start with 'Tube Line A': Pull and push the plunger of the syringe multiple times to prime the system (Fig. 14). Point the syringe upward to ensure all air is removed from the tube line and fluid flows continuously out of the needle and catheter connector.
- Quickly turn the dial to the [X] position to prevent air re-entering the 'Tube Line A' (Fig. 19).
- Close the clip close to the catheter connection of the 'Tube Line A'.
- Repeat step n for 'Tube Line B' (Fig. 18).
- Remove the sterile cup from the administration box.

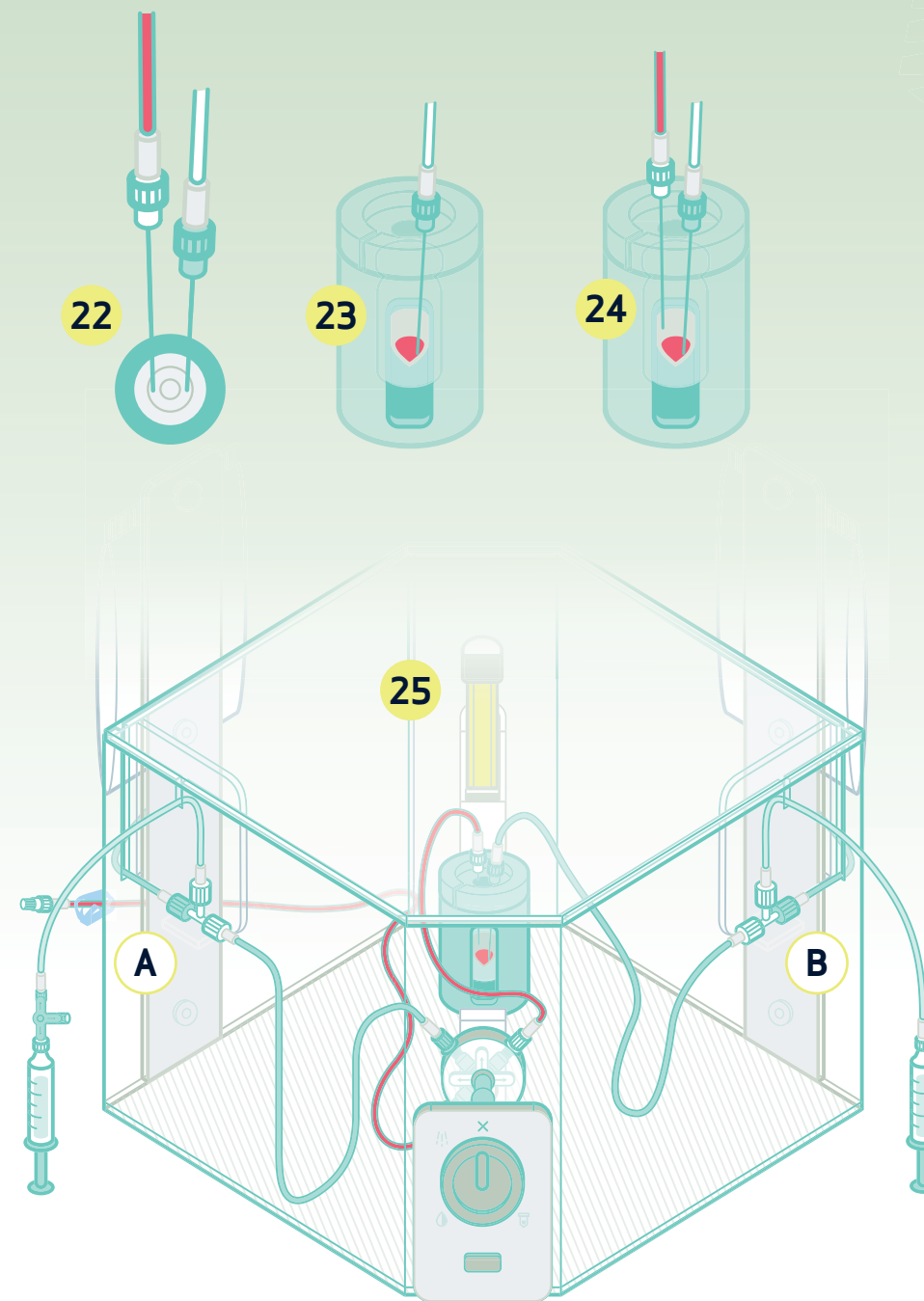
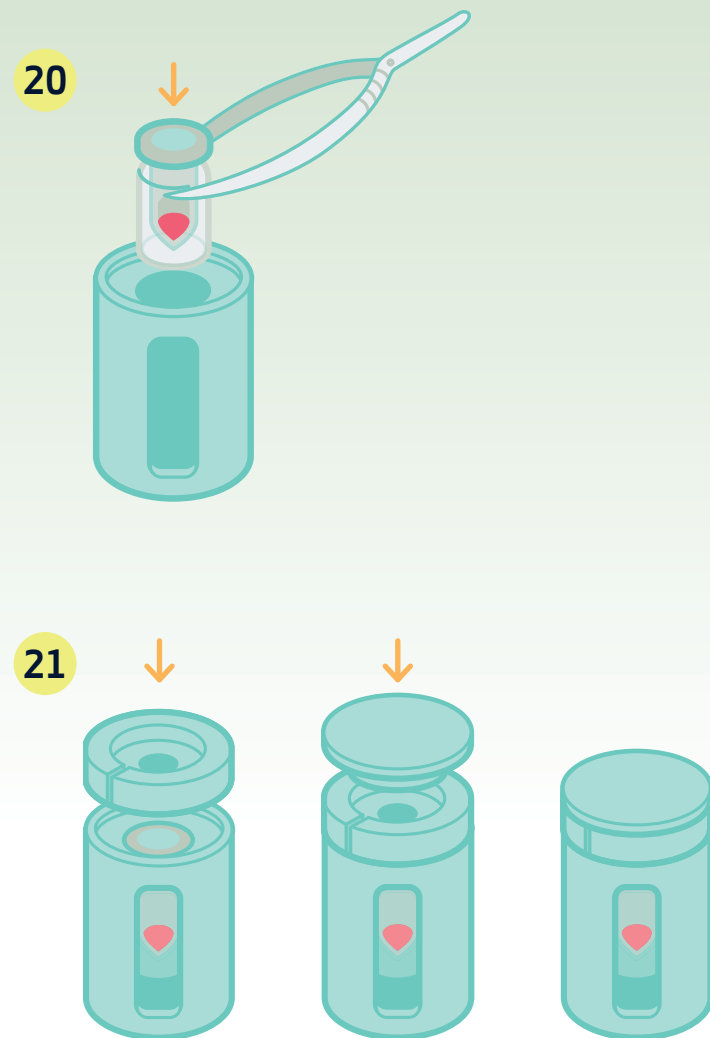
! Note: The dial will never need to return to the prime position after having finished tube priming or during the treatment procedure.



5. Receive QuiremSpheres™ or QuiremScout™ Holmium-166 microspheres and prepare the vial holder

It is recommended that the following steps are performed in a hospital facility for handling radioactive materials (e.g. a nuclear medicine laboratory).

- Open the V-vial transport box and take out the plastic bucket.
- Confirm the microspheres “Activity at the moment of calibration” printed on the label of the plastic bucket. This is the activity recorded in the hotlab at the time of calibration and might deviate from the actual patient prescription.
- Take one peel-off label from the plastic bucket and put it in the patient file.
- Optional: Put the other peel-off label on the side wall of the vial holder for identification.
- Position the lead transport container and vial holder side by side on a trolley or table.
- Remove the aluminum seal of the V-vial to reveal the septum.
- Wipe the rubber septum with an alcohol swab using forceps.
- Take the V-vial out the lead transport container and quickly place it in the vial holder. Use forceps to maintain the distance from your hands to the V-vial (Fig. 20).
- Place the tungsten ring and tungsten cap on the vial holder (Fig. 21).
- Tilt the vial holder back and forth with rotating wrist movements. Swirl the vial holder around and gently tap the bottom of the vial holder on a horizontal surface. This should wet any microspheres on the septum and disperse microspheres stuck to the bottom of the V-vial.



6. Introduce needles into the V-vial

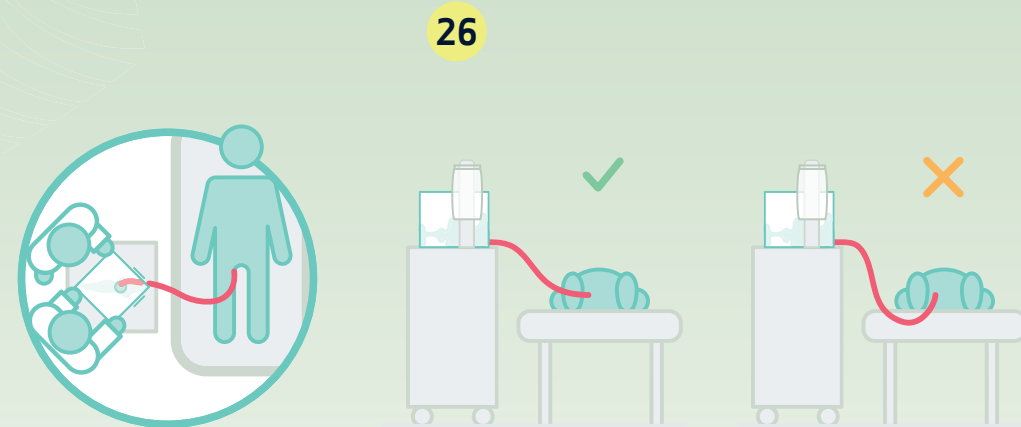
The following steps should be performed in a hospital facility (e.g. an angiosuite) approved for the QuiremSpheres™ and/or QuiremScout™ Holmium-166 microspheres administration procedure.

- Place the vial holder inside the dedicated vial holder slot in the administration box and remove the tungsten cap.
- Turn on the LED light and place the LED light in the dedicated slot (Fig. 25) and verify good alignment between the lead glass windows of the vial holder and the LED lighting.
- Observe the top view of the vial septum. Both needles should be placed in the first ring of the septum in diametrically opposite positions (Fig. 22).
 - Note:** Care must be taken when handling and inserting the needles so as not to compromise sterility. If sterility may have been compromised, discard the QuiremSpheres™ delivery set and use a new one.
- Remove the needle cap of the colorless ‘Tube Line ②’. Push the needle through the septum (Fig. 23). The needle must be placed near the bottom of the V-vial.
 - Note:** Only pierce the septum once.
- Remove the needle cap of the red ‘Tube Line ①’. Push the needle through the septum opposite to the first needle (Fig. 24). The needle must be placed immediately below the surface of the liquid.
 - Note:** Only pierce the septum once.
- Visually verify the position of the needles inside the V-vial against Fig. 24.
- Visually verify the final assembly of the administration box against the figure of the box on the left.
- Close the lid of the box.

7. Connect to the patient

- Remove the vented cap from the catheter connection.
- Connect the catheter connection to the catheter. Avoid allowing the tube to the catheter connection to become slack (Fig. 26).
- Open the clips on the tube lines. Massage the clipped part of the tube lines by rolling it between your thumb and index finger to straighten any dents in the tube line that might be caused by the clips.
- Optional: position the ceiling mounted light of the angio suite above the box for additional visibility of the flow of microspheres in the tube lines during implantation.

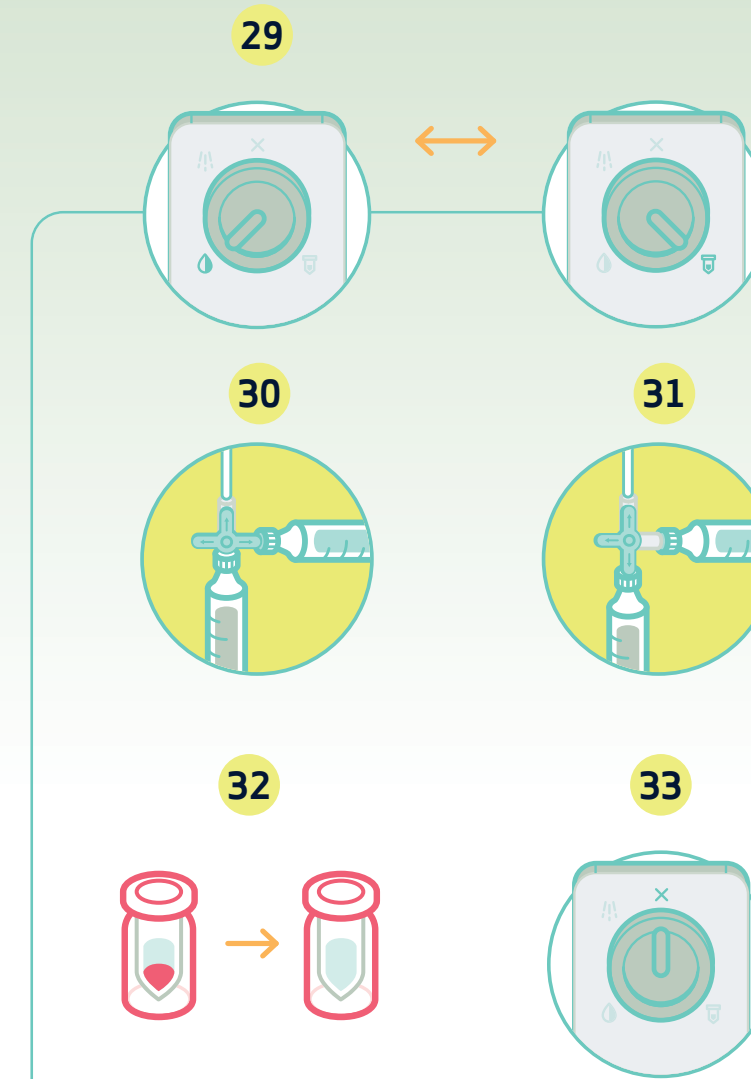
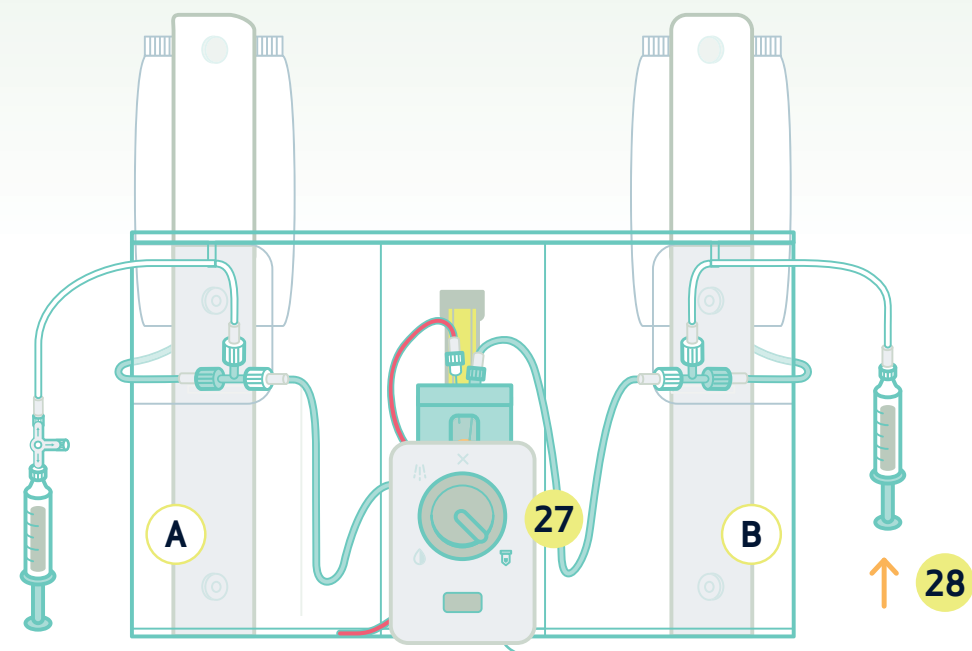
! **Note:** While administering the microspheres, ensure you position yourself such that the administration box shields you from the unexposed tubeline connected to the catheter.



8. Perform implantation procedure

The control dial on the administration box has dedicated positions for administering microspheres and for injecting contrast or flushing the catheter with saline. Always rotate the dial to the position matching the specific stage of the procedure.

- ! **Note:** Always flush residual contrast fluid from the tube and catheter with saline prior to injecting microspheres. Residual contrast fluid in the tube line or catheter can lead to increased pressure build-up in the vial, impeding the administration of QuiremSpheres™ and QuiremScout™ Holmium-166 microspheres.
- ! **Note:** Never push the plunger of the 'Tube Line ②' syringe if the stopcock is not in the administration position.
- Rotate the stopcock control dial to the administration position. [Ⓜ] (Fig. 27)
 - Ensure that the syringe that is connected to the 'Tube Line ②' is filled with saline.
 - Administer the microspheres **slowly** by pushing the plunger of the 'Tube Line ②' syringe (Fig. 28). Infuse 2.5 ml of saline in a pulsed manner with 0.1 ml per push per second.



9. Administer contrast agent

- ! **Note:** Never push the plunger of the 'Tube Line ①' syringe if the stopcock is not in the contrast position.
- Rotate the stopcock control dial to the contrast position [Ⓛ] (Fig. 29).
 - Flush with 2.5 ml of saline from the 'Tube Line ①' syringe with 0.1 ml per push per second to administer the loaded microspheres in the tube line to the patient. Ensure that the syringe that is already connected to the 'Tube Line ①' is refilled with 5 ml saline.
- ! **Note:** If the syringe connected to 'Tube Line ①' is empty prior to administering the contrast, attempting to refill it with saline after the contrast has been administered will result in it being filled with a contrast-saline mixture, instead of pure saline.
- Fill a syringe with 2.5 ml contrast.
 - Connect the syringe with the 'Tube Line ①' and turn the stopcock (Fig. 30).
 - Infuse the contrast agent in a pulsed manner with 0.1 ml per push per second.
 - Perform the fluoroscopy.
- ! **Note:** When performing the fluoroscopy, take into account that there is approximately 2 ml dead space in the tube line before the contrast reaches the liver.
- Prior to administering the microspheres, flush the tubing and catheter with 5 ml saline by turning the stopcock (Fig. 31). Infuse saline in a pulsed manner with 0.1 ml per push per second.
- ! **Note:** Flushing the tube with saline ensures that the loaded microspheres are administered and clears the contrast agent in the tube line. The high viscosity of the contrast remaining in the tube and catheter can hinder the flow of microspheres and may cause pressure build-up in the vial.

10. Finalize implantation

- Wait 5 sec for the suspension in the V-vial to settle.
- Visually verify that no microspheres remain in the V-vial and tube lines by checking the V-vial bottom for any settling of microspheres (Fig. 32). If the V-vial or tube lines are not clear of microspheres, repeat step 8 and 9 of the administration procedure.
- Rotate the stopcock control dial to the closed position (Fig. 33).

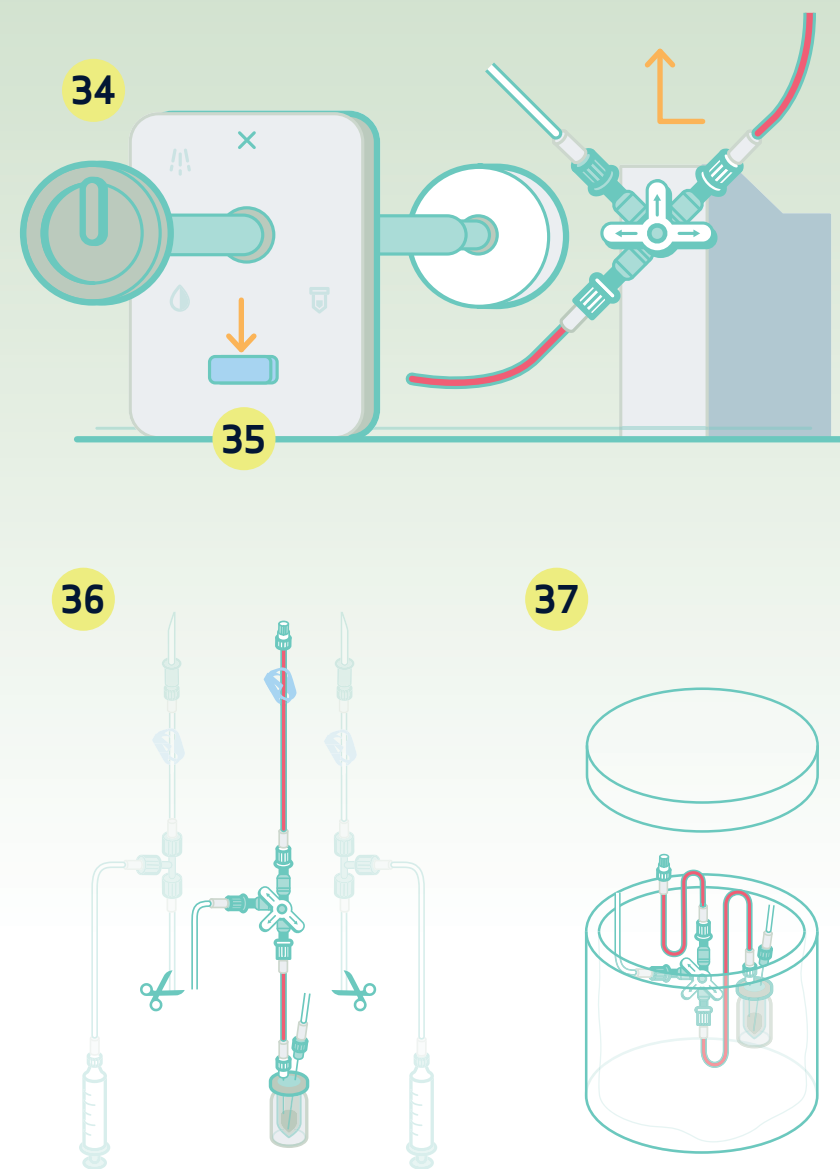
11. Disassembly and clean-up

! **Note:** Tubing marked with a red line has come into contact with microspheres during the procedure and should be regarded as radioactive waste material.

- k) Verify that the stopcock control dial is set to the closed position (Fig. 34).
- l) Release the dial and shaft by pulling the lever down (Fig. 35).
- m) Close the clips located near the saline bags in both tube lines.
- n) Remove the lid of the administration box.
- o) Cut the tube lines as indicated (Fig. 36).
- p) Remove the tungsten ring.
- q) As a whole, wrap the tubing, vial and catheter in a drape and put it inside the plastic waste container (Fig. 37).
- r) Put the lid on the waste container.
- s) Turn off the LED light.

12. Disposal of radioactive waste

The QuiremSpheres™ delivery set, V-vial, catheters and other single-use disposables will contain small residual quantities of microspheres and require monitoring for radioactivity. These items should be disposed of according to local procedures. This may involve storage to decay prior to disposal through the usual facility waste system. All gowns and surgical gear must be monitored at the end of each procedure. Contaminated items should be bagged, labelled and returned to the medical physics department or another designated area for decay until safe for laundering or disposal.



13. ABORT procedure

If the procedure needs to be abandoned prematurely, execute the following steps:

- a) Rotate the control dial to the closed position.
- b) Using a hemostat, close the tube near the catheter connector of the 'Tube line (A)'.
- c) Uncouple the tube line spikes from the bags with saline.
- d) As a whole, wrap the tubing, vial and catheter in a blue drape and put it inside the plastic waste container.
- e) Record the time at which administration of microspheres was aborted.
- f) Record the number of flushes used to administer the microspheres.
- g) Turn off the LED light.

14. Cleaning Instructions

Administration box

General cleaning guidelines:

Clean the PMMA material with a mild detergent suitable for cleaning PMMA material, such as Burnus antistatic plastic cleaner. For cleaning, do not use corrosive cleaners as they can harm the life and usability of the delivery box. To clean the dial and shaft, release it by pressing the lever. Clean the components using a mild detergent in lukewarm water and a soft cloth.

Disinfection guidelines:

To disinfect the box after cleaning, spray an alcoholic solution onto the box and immediately dry with a soft cloth.

In case of radioactivity contamination:

Store the delivery box in a place suitable for storing gamma- and beta-radiation emitting materials for at least 8 days. At regular intervals, check again for contamination. If no contamination is detected, clean the box according to abovementioned instructions.

Vial Holder

General cleaning guidelines:

Use a mild detergent in lukewarm water and a soft cloth. Remove any residual detergent using lukewarm water and a clean soft cloth. Leave all components to dry separately. For cleaning, do not use corrosive or alcoholic cleaners, as they can harm the life and usability of the vial holder significantly. Specially in case of radioactive contamination, the use of a volatile (alcohol) detergent might cause extra risk.

Disinfection guidelines:

To disinfect the vial holder after cleaning, spray an alcoholic solution onto the box and immediately dry with a soft cloth.

In case of radioactivity contamination:

Store the vial holder in a place suitable for storing gamma- and beta-radiation emitting materials for at least 8 days. After 8 days, check again for contamination. If no contamination is detected, clean the vial holder according to above mentioned instructions.

Required items

Items provided by Quirem Medical:

- QuiremScout™ (QS-S001) or
QuiremSpheres™ (QS-V001)
Holmium-166 microspheres
- Lead container
 - V-vial with microspheres

- QuiremSpheres™ delivery set (QS-D001)
- Tube Line Ⓐ
 - Tube Line Ⓑ

- QuiremSpheres™ customer kit (QS-C001)
- Administration box
 - Vial holder
 - Tungsten vial holder cap
 - Plastic waste container
 - LED-light (2x)

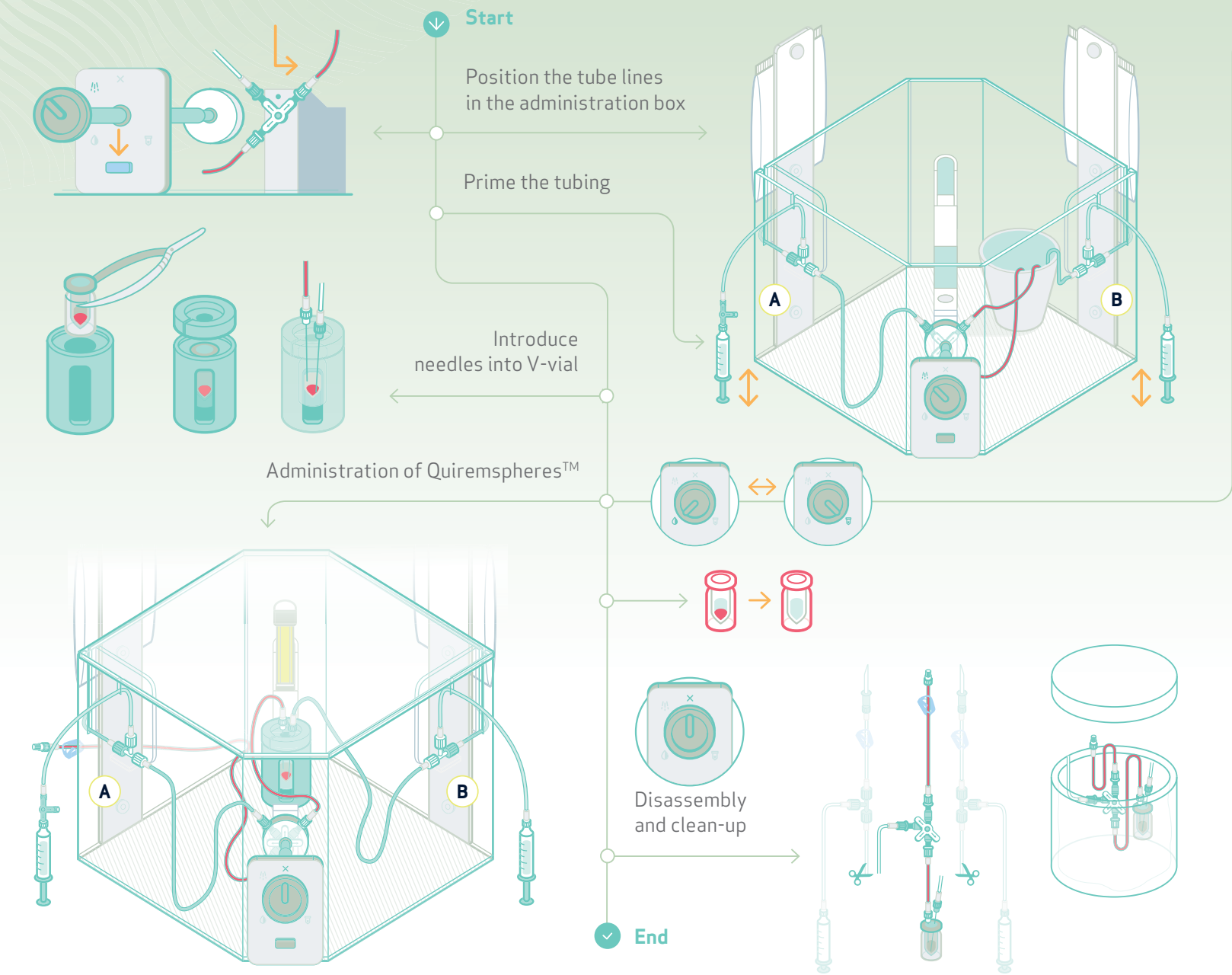
Recommended items,
not provided by Quirem Medical:

- Patient prescription
- 2 bags of saline (250 ml) with possibility of spike connection
- Contrast agent
- Surface radiation contamination meter
- Trolley
- Floor drape placed under the trolley in the angiography suite
- A sterile drape placed on trolley
- On the draped trolley:
 - o Scissors
 - o Sterile adhesive strips
 - o Hemostat
 - o Towels
 - o Gauze
 - o Forceps
 - o Alcohol swabs
 - o Sterile cup

Quick Reference Guide

Administration of QuiremScout™ and QuiremSpheres™ Holmium-166 microspheres

QuiremSpheres™
QuiremScout™
Holmium-166 Microspheres



	Injection	Dial	Syringe	Technique	Purpose
1.	Saline (left syringe)	Ⓢ	5.0 ml	Pulsed injection (0.1 ml per push)	Flush 'Tube Line Ⓐ' to clear viscous contrast agent remaining in the tube and catheter. Refill the syringe with saline directly after flushing.
2.	Microspheres (right syringe)	Ⓢ	2.5 ml	Pulsed injection (0.1 ml per push)	Create a swirling effect to bring the microspheres into a homogeneous suspension. The resulting pressure build-up will push the suspension out of the vial and into 'Tube Line Ⓐ'.
3.	Saline (left syringe)	Ⓢ	2.5 ml	Pulsed injection (0.1 ml per push)	Flush to administer the loaded microspheres into 'Tube Line Ⓐ' to the patient.
4.	Contrast agent (left syringe)	Ⓢ	2.5 ml	Pulsed injection (0.1 ml per push)	The contrast agent allows visualization of flow. After administering contrast agent, flush with saline before fluoroscopy since there is approximately 2 ml dead space in 'Tube Line Ⓐ' before the contrast reaches the liver.
5.	Cycle through steps 1, 2, 3 and 4 until the vial is empty. Wait 5 seconds to allow for any remaining microspheres to settle in the vial. Visually verify that no microspheres remain in the vial and tube lines by checking the vial bottom for any settling of microspheres.				
6.	If visually confirmed the vial to be empty, flush with 20 ml saline (right syringe) to ensure all microspheres are administered to the patient. Ensure that the central dial is in the [Ⓢ] position.				



Customer Kit Manufacturer

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Quirem Medical B.V. is a Terumo Company



Delivery Set Manufacturer

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Juri-Gagarin-Ring 4
19370 Parchim
Germany





At Terumo Interventional Systems, we imagine what better outcomes can be. Together with you, we push boundaries to achieving them.

PUSHING BOUNDARIES

That is why we embrace challenges in interventional medicine and relentlessly pursue excellence in all that we do. By continuously refining our products and solutions, we strive to set new expectations for procedures and support interventionalists with the best experiences possible.



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