# OncoSil™ System Radiation Safety Guidelines


**Product Name: OncoSil™ System**
**Product Number: OS01**

The following information is a guide only. Refer to local, state and federal regulations governing therapeutic radioactive materials to ensure compliance is met.



OncoSil MEDICAL

# 1 Introduction to the Radiation Safety Guidelines for Oncosil™

Radioactive phosphorous-32 ($^{32}P$) is the active agent in OncoSil™ for treating a solid tumour mass. Consequently, radiation safety is important for OncoSil™ dose preparation, transportation to the endoscopy suite, implantation to patients, and post-implant patient care. The radiation safety programme established within the treatment facility for clinical nuclear medicine should be extended to activities involving the OncoSil™ System.

Clinical radiation safety is best achieved through a positive radiation safety culture represented by overall understanding, attitudes, beliefs, perceptions, and values that employees, supervisors, support staff, and administrators share concerning safety in the medical setting. Professional leadership within the treatment facility and nuclear medicine organisation works to establish positive attitudes toward radiation safety, and the ability to maintain radiation exposure risks to levels as low as reasonably achievable/practicable (ALARA/ALARP) – for employees, patients, and immediate family members - thereby ensuring stakeholder trust.


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# 2 Basics of Radiation Safety



## 2.1 General Radiation Safety is an Important Consideration in the Use of OncoSil™

From the receipt of the radioactive material, to dose preparation and implantation into the patient, and subsequent release of the patient from the treatment facility, there are many radiation safety practices that must be in place and followed by staff, the patient and the patient's family. The management of risks from ionising radiation requires actions based on the fundamental principles of radiation protection and safety and in accordance with the best practices in radiological protection.

## 2.2 Fundamental Principles of Radiation Protection and Safety

**ALARA and ALARP** are regulatory requirements stating that licensees will maintain doses to a level As Low As Reasonably Achievable (ALARA) which means "making every reasonable effort to maintain exposures to ionising radiation as far below the dose limits as practical, consistent with the purpose for which the licensed activity is undertaken, taking into account the state of technology, the economics of improvements in relation to state of technology and benefits to the public health and safety, and other societal and socioeconomic considerations."; or As Low As Reasonably Practicable (ALARP) which arises from UK legislation requiring "Provision and maintenance of plant and systems of work that are, so far as is reasonably practicable, safe and without risks to health".

ALARP is used especially in the UK and is a broader term than ALARA as it is used in fields other than those involving radiation. Three basic principles should always be applied to accomplish this objective – time, distance and shielding.

1. **Time**
   The less time spent exposed to a source of radiation, the lower the dose of radiation you will receive. Plan your work so that tasks can be performed efficiently.

2. **Distance**
   Radiation levels are governed by an inverse square law; therefore, if the distance to the source of radiation is doubled, then the radiation dose levels are reduced to a quarter. Use remote handling devices, such as long tongs to create distance when handling sources of radiation.

3. **Shielding**
   Maintain shielding between the people and the radioactive source. The isotope $^{32}P$ is best shielded at all times, using a low-proton-number shield (Perspex) within, where possible, a lead shield. OncoSil™ may be safely implanted using a Perspex shielded syringe, where the shield is a minimum of 10 mm thick. A shield of this nature will stop exposure to the beta radiation and result in minimal exposure to the hands or fingers of administering medical personnel.

# 2 Basics of Radiation Safety



A system of radiation protection for practices should continue to be based on the principles of **justification** of exposure, **optimisation** of protection and **dose limitation.**

- Justification (benefit must outweigh risk);
- Optimisation (exposure to as few, and as low as possible: dose constraints), and
- Dose limitation (on the individual's level)

The principle of justification requires that any decision that alters a radiation exposure situation should be more beneficial than harmful.

OncoSil Medical and treatment facilities will adopt all dose limitations set by regulatory authorities globally.

The principle of limitation of an individual's risk of harm applies to the total dose to any individual from regulated sources in planned exposure situations.

## 2.3 Standard Units

The SI unit for the amount of radioactivity present in a source is the Becquerel (Bq). The Curie (Ci) is alternative unit where 37 billion Bq (37 GBq) = 1 Ci. One Bq represents the activity of a given quantity of material where one nucleus decays (disintegration) per second. Therefore, the higher the number of Bq (or Ci), the more radiation is produced in a given period.

The SI unit for radiation absorbed dose is the Gray (Gy). A further quantity, derived from the absorbed dose is the equivalent dose, which is the absorbed dose corrected for the type of radiation being absorbed. The equivalent dose is further corrected, with a tissue weighting factor, to obtain the effective dose, for which the SI unit is the Sievert (Sv). Regulatory dose limits and personnel dosimetry reports for staff monitoring are given in Sieverts (Sv), or often in millisieverts (mSv) or microsieverts (μSv).

# 3 Personnel Dosimetry



**Radiation workers who are likely to receive an effective dose greater than 6 mSv per year in the European Union (EU) Member States, or 1 mSv per year in Australia, must have their occupational doses monitored with dosimeters provided by a qualified service.**

**Monitoring services that provide dosimetry read-outs, should be accredited by the responsible national authority.**

## 3.1 Dose Limits

### 3.1.1 Occupational Dose Limits

Occupational dose limits have been established to protect radiation workers. Workers, who may receive intakes of radionuclides and external radiation exposure, must be personally monitored for both internal and external radiation exposures. Treatment facilities often decide to monitor all workers who are likely to be exposed to radioactive materials, however, personnel dosimeters may only be required for workers who are likely to receive an effective dose. The tables below (**Table 1** and **Table 2**) provide the occupational exposures for the applicable regions.

**Table 1: Dose Limits for Occupational Exposure[1]**

| Area of Exposure | Maximum Exposure Limits |
|---|---|
| Whole body<br>Special circumstance (authorised by competent authority)<br>- provided that the average over five consecutive years is 20 mSv | **20 mSv/year**<br>**50 mSv/year** |
| Equivalent dose for lens of the eye | **20 mSv/year** or **100 mSv in any five consecutive years*** |
| Equivalent dose for skin (averaged over 1 $cm^2$) or extremity | **500 mSv/year** |
| Equivalent dose to unborn child | **1 mSv**** |

* Subject to a maximum dose of 50 mSv in a single year, as specified in national legislation
** From time of declaration (according to national legislation) through remainder of the pregnancy

# 3 Personnel Dosimetry



**Table 2: Occupational Dose Limits[2]**

| Area of Exposure | Maximum Exposure Limits |
|---|---|
| Effective dose limit | **20 mSv/year Averaged over a period of 5 consecutive** |
| Effective dose limit in a single year | **50 mSv** |
| Equivalent dose limit: | |
| - In the lens of the eye | **150 mSv/year** |
| - In the skin (averaged over any 1 $cm^2$ regardless of total area exposed) | **500 mSv/year** |
| - In the hands and feet | **500 mSv/year** |

Normal occupational dose limits apply, i.e. a limit on effective dose of 20 mSv/year, averaged over 5 years (i.e. a limit of 100 mSv in 5 years) with the further provision that in any single year:

- The effective dose should not exceed 50 mSv, and
- The equivalent dose should not exceed:
  - 150 mSv for the lens of the eye
  - 500 mSv for the skin (average dose over 1 $cm^2$ of the most highly irradiated area of the skin), and
  - 500 mSv for the hands and feet

Compliance with occupational dose limits is demonstrated by summing the contributions from all authorised practices.

Regulations require the assessment of occupational intakes of $^{32}P$ when significant amounts are handled; bioassay monitoring is required if exposed workers are likely to or could exceed 10% of applicable limits on intake. Internal radiation doses are determined by measuring concentrations of radioactive material contamination in work areas and assessing internal uptakes by urinalysis.

Since OncoSil™ is administered into the patient by direct intratumoral injection, it is unlikely that any intake of $^{32}P$ by workers should occur in the treatment facility.

# 3 Personnel Dosimetry



### 3.1.2 Public Dose Limits

The public is restricted from general areas where radioactive materials are used, where contamination may exist, and where external exposure rates could result in radiation doses to any member of the public (excluding medical patients) exceeding 1 mSv/yr.

Since $^{32}P$ is a beta-emitter, it is unlikely that members of the public will receive a measurable dose from a patient post-implantation of OncoSil™.

### 3.1.3 Pregnancy and Protecting the Embryo/Foetus

Radiation dose to the embryo/foetus is controlled by limiting the radiation exposure to declared pregnant workers. It is important that the health care worker notifies her employer's Responsible Person (RP) that she is pregnant as soon as possible, however the worker is not legally required to do so, or the worker may choose the make the notification confidential. A risk assessment can then be conducted considering the normal tasks involving radioactive material that the worker performs, and these tasks can be adjusted accordingly to minimise the radiation dose to a pregnant worker. Special considerations govern the protection of pregnant radiation workers and their unborn children in utero [Ref: 1]. Female radiation workers should be informed of the importance of early declaration of pregnancy.

Under normal circumstances, a declared pregnant worker should not be assigned duties with opportunities for radiation exposures, such as preparation of radioactive products.

EU and Australian regulations state that to ensure the protection of the unborn child, the foetus/embryo should be considered a member of the public and afforded the same level of protection. The total dose to the unborn child from occupational exposure of the mother should not exceed 1 mSv from declaration of pregnancy in accordance with national legislation through at least the remainder of the pregnancy. In addition, breastfeeding workers should be aware of the potential for intake of radionuclides that could result in an uptake by the child.

Since OncoSil™ is directly implanted by injection into the tumour, the likelihood of $^{32}P$ uptake by the radiation worker is negligible.

# 4 Regulations Governing Safe Use of Ionising Radiation



**Radiation and radioactive materials are regulated by government authorities in each jurisdiction around the world. The authorities discussed below are examples only and do not represent a complete list of authorities that have jurisdictional control over OncoSil™ System. In Europe, the European Commission, under the Euratom Treaty, is responsible for the protection of people and the environment against the dangers arising from exposure to ionising radiation within EU Member States. The Basic Safety Standards Directive for protection against exposure to ionising radiation is updated and the current directive is 2013/59/Euratom of 5 December 2013** [Ref: 1]**. The Australian Radiation Protection and Nuclear Safety Agency (ARPANSA) is the Australian Government's primary authority on radiation protection and nuclear safety. The National Directory for Radiation Protection, February 2014, provides an overall framework for radiation safety within Australian and the Code of Practice for Radiation Protection in the Medical Applications of Ionizing Radiation (2008) establishes the regulatory requirements for the use of ionising radiation in medicine** [Ref: 3, 5]**. In all Asian countries, a relevant authority has control of radioactive products and radioactivity, for example the National Environment Agency in Singapore.**

## 4.1 Application/Amendment of Radioactive Materials License/Authorisation to Possess

Each EU Member Nation and Australian State and Territory has its own regulatory authority and requirements for the possession and use of radioactive material for medical purposes based upon the documents listed in Regulations Governing Safe Use of Ionising Radiation. Therefore, the specific local, state and federal regulations should be met for the possession and use of OncoSil™ within the treatment facility, including authorisation to possess and use appropriate quantities of $^{32}P$.

## 4.2 Documented Radiation Safety Programme/Management Plan

Regulatory agencies (local, state and federal, as applicable) require radiation safety programmes to be designed for protecting radiation workers, the patient and the public. The treatment facility that handles and implants OncoSil™ should prepare and follow a radiation safety programme document that identifies key personnel (management, authorised users, the accredited radiation personnel and radiation safety support technicians), their responsibilities, duties, and accountabilities for conducting the radiation safety programme. A well-written programme constitutes a valuable tool for management to ensure both safe operations and regulatory compliance.

## 4.3 Accredited Radiation Personnel (ARP)

In EU, the responsibilities of the Radiation Protection Officer (RPO) are given in Article 84 of the Euratom Directive [Ref: 1]. The RPO should be formally educated and trained in all aspects of radiation safety practice.

In Australia, the Responsible Person (RP) is the legal entity that has management responsibility for radioactive sources, radiation-producing equipment, or radiation-associated medical practices. The role and responsibilities of the RP are defined in the *Code of Practice for Radiation Protection in the Medical Applications of Ionizing Radiation (2008)* Chapter 3.1. Whilst some tasks may be delegated to the Radiation Safety Officer (RSO), the ultimate responsibility lies with the RP. The appointment of an RSO is required for the issue of an authorisation by the relevant regulatory authority. An RSO will have sufficient professional and/or technical training to oversee and provide advice on radiation safety within the centre. The tasks normally assigned to an RSO are listed in Safety Guide for Radiation Protection in Nuclear Medicine (2008), Annex B.

## 4.4 Radiation Safety Committee

The treatment facility's Radiation Safety Committee (RSC) comprises a chair, representative of management, Radiation Safety Officer (RSO) / Radiation Protection Officer (RPO) or Responsible Person (RP), a representative from Nursing Services, and one practitioner for each type of activity authorised by the license. The RSC oversees the radiation safety programme to ensure that licensed radioactive materials are used safely within the treatment facility. The RSC also ensures that activities are consistent with a positive safety culture and the philosophy of maintaining personnel radiation exposures as low as reasonably achievable. The RSC oversees the annual audit or review of the radiation safety programme to identify potential problems and implement solutions for improvement.

## 4.5 Training

Radiation protection education, training and information must be provided to potentially exposed workers in accordance with local, state and federal regulations. Training includes initial instruction and annual refresher coursework. Training must be commensurate with worker duties and responsibilities. Training covers formal educational background, work experience, on-the-job training, short courses, and annual refresher courses in radiation protection. Specific topics should include properties of radiation, radiation measurement, facilities standard operating procedures, contamination control, waste control and management, management of patients administered radioactive materials, visitor control, signs and postings, protective clothing, and dosimetry. Records of worker training must be maintained for audits and inspections. OncoSil Medical can provide the treatment facility with specific radiation safety guidance and training for $^{32}$P.

## 4.6 Internal Audit Programme

Annual radiation safety programme reviews and audits must be conducted to ensure compliance. Reviews should include, but are not limited to, radiation safety programme effectiveness, worker compliance, deficiencies and corrective actions, personnel radiation concerns, and programme changes. Records must be maintained for audits and inspections. Reviews should identify potential problem areas: what might happen, how likely is it to happen, and what might be the consequences? Specific action items should be tracked, and corrective changes to the radiation safety programme should be noted. OncoSil Medical will work in conjunction with the treatment facility radiation safety representatives in reviewing raised observations or findings during the audit with relation to $^{32}P$ safety, and will assist with any corrective actions.

# 5 Treatment Facility Requirements



## 5.1 Physical Requirements

All treatment facilities utilising OncoSil™ are subject to physical requirements in relation to safe use of the product. These include secured areas with appropriative signage, radiation monitoring equipment, shielding, trained personnel and controlled documentation.

## 5.2 Designated Areas, Security and Signage

In general, the treatment facility must have areas to safely receive the product, store the product before use, prepare patient doses utilising best practice as prescribed by the OncoSil™ Authorised Trainer (AT), deliver the dose to the patient ensuring safe transport where applicable, care for a patient post-implantation of a radioisotope and dispose of radioactive waste. Any area where OncoSil™ is present should have restricted access limited to authorised staff and no access by the general public. Radioactive material must be secured at all times.

**The Endoscopy Suite:** As the implantation of OncoSil™ is undertaken in the endoscopy suite, it will be necessary to designate the endoscopy suite as a controlled area. This means that any user who enters or works in that area is required to follow special procedures designed to restrict their exposure and prevent or limit the likelihood of radiation contamination or spillage.

There are employees who will need to enter the area and participate in the implantation procedure who are unfamiliar with working with ionising radiation. They must be trained and closely supervised during the entire procedure until the procedure is completed and the area is no longer controlled.

# 5 Treatment Facility Requirements



Protocols provided by the treatment facility for the implantation procedure in the endoscopy suite should ensure the following:

- **Demarcation of Area:** The controlled area needs to be physically demarcated to restrict unauthorised access and the area will be under the direct supervision of competent authorised persons.
- **Radiation Protection Principals:** always remember to consider time, distance and shielding throughout the entire procedure and minimise any exposure or risk of contamination. Containment is essential should a spill/contamination of equipment/personnel occur.
- **Signage:** The area should be marked out at its entry point (or points) by suitable signage including required information, e.g. trefoil sign, nature of the ionising radiation hazard, contact details of the RSO/RPS.
- **Patient Dose:** The dose should not be left in the endoscopy suite without a member of the radiation protection team present and the residual syringe should be returned to Nuclear Medicine in the appropriate equipment by an authorised/trained member of the team.
- **Controlled Entry & Protection of Personnel:** Only those personnel who have been trained and authorised to enter may do so. In order to minimise contamination/exposure risk, staff where possible, should utilise a one-way system in and out of the endoscopy suite.
- **Covering Surfaces & Protection of People & Equipment:** The endoscopy suite must be prepared in advance of the dose arriving in the endoscopy suite to ensure all potential sources of contamination are covered.
- **Dosimetry and Monitoring:** Appropriate equipment for contamination monitoring should be in the endoscopy suite prior to the dose arriving, the spill kit should also be *in situ* and the RPS/RSO should be present. All staff performing manipulations with $^{32}P$ (the Authorised User and the Endoscopist) must wear appropriate extremity dosimeters as defined in their local, state and federal regulations and provided by their RPS/RSO.
- **Post Implantation:** All equipment will be monitored and disposed of depending on its designation. No staff will leave the room until cleared by the delivery team (monitoring of both hands and feet will be undertaken).
- **Endoscopy Suite Controlled Designation Removed:** Once the room and personnel are deemed to be 'clean' after monitoring and have left the endoscopy suite, then the controlled signage can be removed, and the room will revert to its usual designation.

# 5 Treatment Facility Requirements



## 5.3 Radiation Measuring Equipment

The treatment facility will require two different radiation measuring devices:

- Ion chamber for dose verification – the radioactive content of OncoSil™ must be verified using an appropriate ion chamber, which has been calibrated for $^{32}P$. The product is measured for calibration and during patient dose preparation.
- Beta counter/survey meter (GM meter and thin window pancake probe) for daily area surveys (required in areas used to prepare or administer radioactive materials) and contamination detection and clean-up. A beta counter must also be present during the receipt of the OncoSil™ System to the implantation location and remain there for a post-administration area and patient survey.

Staff should be trained in the appropriate use of these instruments and have a clear understanding of the limitations. In addition to required on-going quality assurance, radiation measuring devices must be calibrated annually or after repairs.

## 5.4 Shielding

Appropriate shielding and/or other equipment should be in place to reduce radiation exposure to staff. These include, but are not limited to:

- Syringe shields (minimum wall thickness is 10 mm Perspex)
- Lead transport container for transportation of the dose to the endoscopy suite (ideally this container will be Perspex-lined to reduce the Bremsstrahlung).

All staff handling OncoSil™ should wear protective clothing, including laboratory coat with full-length sleeves. Within the preparation area, handling instruments (long tongs) should be available to increase distance between the fingers and the radioactive source, and staff should be gloved. Only required staff should be present around the radiation source and all staff should maintain maximum distance whenever possible.

## 5.5 Personnel

All personnel that are involved in any aspect of the OncoSil™ procedure must be appropriately qualified. Radiation Workers should be trained annually and in addition, staff must receive specific training for the OncoSil™ System and its use. Training records must be maintained and kept in accordance with local, state and federal regulations.

## 5.6 Documentation

Documentation regarding the use of OncoSil™ within the treatment facility must be maintained in accordance with local, state and federal regulations. Such documents will include, but are not limited to the OncoSil™ System receipt records, patient dose and calibration measurement records, radiation survey records, instrument calibration reports, patient discharge records, and contamination/spill records. We recommend documentation is kept for a minimum of two years or longer as per local protocols.

# 6 Radiation Safety With OncoSil™



**Phosphorous-32 represents a hazard to treatment facility personnel only if unsealed material is assimilated into the body by inhalation, ingestion, or direct skin contact. Protection against potential intakes of $^{32}P$ by others involves limiting:**

- **Skin contaminations, and**
- **Intakes by inhalation or ingestion.**

**In addition, using the fundamental principles of radiation protection and safety will minimise any dose from external exposures.**

**When OncoSil™ is implanted by direct intratumoural injection, the opportunity for direct intakes by others is negligible. Data from preclinical studies, clinical studies and ongoing commercial use of OncoSil™ has shown that administered $^{32}P$ is retained in the target tumour tissue. Negligible amounts are redistributed in the body through blood circulation and excretion. Therefore, significant contamination of urine and faecal excretion is not anticipated, and significant detectable radioactive contamination of toilet facilities is not expected.**

**Special care must be taken to minimise radiation exposure to persons preparing OncoSil™ and treatment facility personnel involved in handling and implanting OncoSil™ to patients. The following sections provide radiation safety guidelines for minimising radiation doses to treatment facility personnel, as well as guidelines for the appropriate release of patients following the OncoSil™ implantation**

## 6.1 General

OncoSil™ contains radioactive $^{32}P$ microparticles Phosphorous-32 emits beta radiation that travel only a few millimetres in tissue and up to 6 meters in air. For beta radiation emissions, the primary radiation hazard to clinical staff is direct skin contact with liquid sources containing $^{32}P$. However, the interaction of beta particles at close range with dense, or high atomic number materials creates X-ray emissions (bremsstrahlung radiation). Therefore, vials and syringes containing $^{32}P$ should be appropriately shielded. Phosphorous-32 decays naturally with a physical half-life of 14.27 days. The physical half-life of a radioactive material is defined as the time it takes for the radioactive material to decay to one-half its original amount. The decay product is Sulphur-32, which is stable and non-radioactive.

## 6.2 Clinical Radiation Measurement Programme

The clinical radiation measurement programme includes survey instruments for measuring any contamination, and control of personnel dosimetry to monitor potential occupational exposure.

## 6.3 Portable Survey Instrument

Portable survey instruments must be used for:

A. Area radiation surveys, and

B. Surface contamination monitoring. Area surveys should be completed at the end of each day for all areas where radioactive isotopes were present. Surface contamination monitoring should be performed for all surfaces where $^{32}P$ contamination from OncoSil™ may be present.

## 6.4 Personnel Dosimeters

Radiation dosimeters must be worn by all radiation workers in accordance with local, state and federal regulations who are likely to receive an effective dose. If there is a high reading, contact OncoSil Medical radiation safety personnel in your region.

## 6.5 Exposure Levels and Dose Rates

Since $^{32}P$ is a pure beta-emitting radionuclide, it is generally not possible for persons in the immediate vicinity, including family or other members of the public, to receive measurable radiation doses approaching the public dose limit. The attending health physicist or radiation protection technician may perform periodic surveys for potential radioactive contamination of table surfaces and toilet facilities, but otherwise, no special precautions are needed in the area where $^{32}P$ OncoSil™ is implanted.

Due to the minimal hazard associated with an implantation of OncoSil™, and due to the low potential for either external radiation or external contamination by patient excreta, no physical barriers need to be placed in front of the door to restrict unauthorised access to the patient's room.

During the OncoSil™ implantation procedure, a flush of saline through the catheter and needle into the stomach is required. This is performed after the OncoSil™ dose has been implanted into the tumour. This procedure is performed only to minimise the risk of radioactive contamination of the endoscope during re-sheathing the needle and withdrawal of the endoscope from the patient. No significant $^{32}P$ activity has been found in patient faeces as result of this flushing procedure as the activity level involved is extremely small. No additional precautions are required in relation to patient excreta as a result of this flushing procedure.

The isotope $^{32}P$ does not pose a whole-body an external radiation hazard to healthcare professionals working with the product. Being a pure beta-emitting isotope, the radiation is safely shielded using plexiglass, or Perspex of at least 10 mm thickness. The typical effective dose rates from the OncoSil™ device containing 250 MBq at reference, as received in the Perspex-lined lead pot, are shown in **Table 3** below.

**Table 3: Dose Rates from the OncoSil Microparticles Vial containing 250 MBq at Reference**

| Vial Shield Configuration | Dose Rates (µSv/hour) at a distance of | | | |
|---|---|---|---|---|
| | 1 cm | 10 cm | 20 cm | 30 cm |
| Perspex-lined lead pot (as delivered) | 5.0 | 0.9 | 0.9 | 0.6 |
| Perspex shield (10 mm) only | 1209 | 276 | 87 | 42 |
| Above Perspex shield with the Perspex lid removed | 9099 | 91 | 23 | 10 |
| Product vial unshielded | 75399 | 31699 | 9879 | 4069 |

The OncoSil™ vial containing 250 MBq at reference is only ever unshielded during activity measurements in an ion chamber. During this operation it must only be handled with long (20 cm) forceps and never directly with the fingers.

Once the delivered vial has been diluted to the concentration that the patient dose is drawn from the activity (in the second vial) is 60 MBq. A spare Perspex-lined lead pot is provided in the OncoSil™ System for this secondary vial, and the effective dose rates from this dilution are shown in **Table 4.**

**Table 4: Dose Rates from the OncoSil Microparticles Dilution Vial containing 60 MBq on the Day of Implantation**

| Vial Shield Configuration | Dose Rates (μSv/hour) at a distance of - | | | |
|---|---|---|---|---|
| | 1cm | 10cm | 20cm | 30cm |
| Perspex-lined lead pot (as delivered) | 1.0 | 0.2 | Background | Background |
| Perspex shield (10 mm) only | 183 | 34 | 11 | 4 |
| Above Perspex shield with the Perspex lid removed | 230 | 3 | 0.8 | Background |
| Product vial unshielded | 4959 | 1439 | 455 | 197 |

The OncoSil™ vial containing 60 MBq at reference is only ever unshielded during activity measurements in an ion chamber. During this operation, it must only be handled with long (20 cm) forceps and never directly with the fingers.

When the patient dose is drawn up from the secondary vial, the syringe used must be placed in a suitable Perspex syringe shield. The walls of the shield should be a minimum of 10 mm of Perspex.

If a patient dose of approximately 60 MBq is drawn up (the maximum patient dose permitted with the OncoSil™ dose) then the dose rates (μSv/hour) have been measured as:

- 1 cm from the syringe shield = 65 μSv/hour
- 10 cm from the syringe shield = 3.0 μSv/hour
- 20 cm from the syringe shield = 0.9 μSv/hour
- 30 cm from the syringe shield = background

# 7 Handling The Device



## 7.1 Receipt of Product

Upon receipt of the Type A package containing the OncoSil™ System, the treatment facility's receipt and inspection procedure should be followed, and the product should be visually inspected for any irregularities, or evidence of having been tampered with. The OncoSil™ System is shipped in a tamper-evident Type A package. If there is any evidence that the package has been opened or tampered with, or if the wipe tests demonstrate contamination, OncoSil Medical should be contacted immediately.

As with any radioactive source, handling by staff should be kept to a minimum and the fundamental principles of radiation protection and safety applied. Unless required, the vials containing the $^{32}P$ Microparticles should be kept within the Perspex-lined lead pot. Long handled tongs should be used when handling the unshielded vial, and it should be kept behind appropriate shielding as much as possible. Never handle the unshielded vial directly with fingers and always wear gloves during the inspection.

After inspection, the product should be returned to the Type A package and secured in a Nuclear Medicine Department/Radiopharmacy or other suitably secure location.

## 7.2 Storage of Product

Until the patient dose is prepared, the product should remain within the Type A package and be secured in a shielded area within the Nuclear Medicine Department/Radiopharmacy away from general work areas. The product will be stored at room temperature.

If the patient dose is prepared in advance, then the OncoSil™ suspension vial (housed within the Perspex-lined lead pot) must be stored for decay and the shielded syringe (within a lead transport box) must be stored in a shielded area within the Nuclear Medicine Department/Radiopharmacy until implanted.

The source material must be kept in a secure location.

## 7.3 Radioactive Waste Management and Decay-in-Storage

Radioactive waste is generated during the preparation and administration of OncoSil™. The physical half-life of $^{32}P$ permits flexibility in disposal and eliminates the need for disposal in commercial burial sites. For $^{32}P$ OncoSil™, decay on site is appropriate for any contaminated items due to its 14.27 days half-life and the range of penetration of the beta emissions.

Examples of contaminated wastes may include used syringes and needles, dose vials, gloves, shoe covers, unused radioactive preparations, absorbent surface covers, and wipes from clean-up of spills. Used vials, syringes and other items used in the dose preparation and administrative processes could contain traces of $^{32}P$. These items may require decay in storage prior to disposal through normal waste systems. Other items that may require monitoring are surgical instruments, gloves, gowns and goggles. These items should be surveyed at the conclusion of the procedure.

All contaminated items should be bagged, labelled, and stored according to local, state and federal regulations. Decay-in-storage may be accomplished in >10 half-lives (142 days), after which the radioactive materials will have decayed away to stable products; such waste may then be disposed of as regular (nonradioactive) waste if the residual radioactive counts meet local, state and federal regulations.

## 7.4 Contamination Procedures

The treatment facilities contamination procedures should be well defined, and spills should be cleaned-up as soon as possible and in accordance with treatment facility procedures. The ARP should be notified of any spills and appropriate records maintained.

OncoSil Medical does not recommend the use of commercial cleaning agents, such a Radiac wash, to decontaminate surfaces. Such products may be used, once the area has been decontaminated of any Phosphorous ($^{32}P$), as a final clean of the surface.

### Decontamination Spill Steps

**a. Steps for Contained Spills (e.g. in the spill tray lined with absorbent material)**

i. Using gloved hands, carefully fold the absorbent finer on the tray so that the spill remains contained within the liner.
ii. Place the liner in the contaminated waste receptacle together with the gloves being worn.
iii. Check the spill tray for contamination using the radiation monitor, and if counts are registered above background wipe the tray using a demineralised water moistened absorbent pad.
iv. Place the moistened pad in the contaminated waste receptacle and recheck the tray for contamination.
v. Repeat this procedure as necessary until no further contamination is detected.
vi. Reline the tray with a new absorbent plastic backed sheet and proceed with the dose preparation.
vii. Before leaving the contaminated area, ensure all personnel involved in the spillage or decontamination operation are monitored for radiation.
viii. Complete any required documentation on the spill and clean-up process.

**b. Steps for Non-Contained Spills (e.g. spill is on a hard bench surface outside of the spill tray)**

i. Mark a suitable area around the spill using the trefoil tape and write on the tape that the contamination is from Phosphorous-32 ($^{32}P$).
ii. Using gloved hands, moisten an absorbent pad with demineralised water and wipe up the spill starting from the outside (at the taped off area) and working inwards to the centre. Use as many pads as required placing each one in the contaminated waste receptacle.
iii. Check the surface with the radiation monitor and repeat as necessary to reduce the detected contamination to background.
iv. Cut a piece of the contact adhesive sheet to sufficiently cover the area marked off, or as much of the area as possible with one sheet and use further sheets to complete the coverage of the area.
v. Peel the backing paper from the sheet and press the adhesive side onto the hard surface making sure there are no air bubbles in the sheet.
vi. Carefully peel the sheet off the surface making sure it does not tear. Fold the sheet together to trap any contamination and place the sheet, and the gloves, in the contaminated waste receptacle.
vii. Check the surface again for contamination and repeat the above process as necessary if counts above background are still detected.
viii. Before leaving the contaminated area, ensure all personnel involved in the spillage or decontamination operation are monitored for radiation.
ix. Contact the RSO and complete any required documentation on the spill and clean-up process.

# 8 Radiation and Dose Preparation



## 8.1 Control of External Radiation Exposure

Estimates of the effective doses to staff handling OncoSil™ have been performed based on dose rate measurements in a laboratory setting at each major step in the dose preparation procedure. **Table 5** below has the dose rates measured at each critical step, plus an estimate of the time taken to perform the step and finally the estimate of the extremity doses that could result. These figures should be viewed as a guide only and all sites should measure the extremity doses incurred by operators using established procedures, for example with the use of dosimeter rings.

**Table 5: Extremity Dose Estimates in the Dose Preparation of OncoSil™ Microparticles**

| Activity (MBq) | Step Description | Shield Description | Step Time (minutes) | Dose Rate (μSv/hour) | Total Dose (μSv) |
|---|---|---|---|---|---|
| 250 | Using 20cm tongs to remove the Perspex shield lid and wipe the septum with a sterile wipe | Perspex | 0.5 | 90.0 | 0.8 |
| 250 | Adding diluent to the first vial | Perspex (above the lid at 10 cm) | 1.0 | 91.0 | 1.5 |
| 250 | Mixing the first dilution by inverting the Perspex-lined lead pot | Perspex-lined lead pot | 1.0 | 5.0 | 0.1 |
| 250 | Removing the 1.7 ml aliquot from the first dilution vial | Perspex (above the lid at 10 cm) | 2.0 | 2.0 | 0.1 |
| 60 | Mixing the second dilution by inverting the Perspex-lined lead pot | Perspex-lined lead pot | 1.0 | 5.0 | 0.1 |
| ≈58 | Draw up of a patient dose containing ≈8.8 ml | Perspex syringe shield | 2.0 | 31.3 | 1.0 |

It should be noted that the tip of any syringe containing an OncoSil™ suspension is a point where the Perspex shield tapers down to less than 10 mm. Syringe shields should always be handled at the thickest (10 mm) body part and not at the tip.

Using the total dose figures quoted above in **Table 5**, the estimated occupational dose to the fingers of an operator is 3.6 μSv for one dose preparation.

## 8.2 Control of Internal Radiation Exposure

The radiation safety programme protects against inadvertent intakes of $^{32}P$ by inhalation, ingestion, and skin contamination, although such events will be highly unlikely. Rules for working with radioactivity in the clinical environment to prevent intakes of the materials include, but are not limited to, the following:

- Always work in pre-designated areas for handling, dispensing, and administering radioactive materials. Work closely with the radiation safety staff to understand the rules for working in radiation areas.
- Never open sealed bottles or vials in open areas. Preparation of OncoSil™ must take place behind Perspex or Lucite, suitable for shielding from beta particles, under a fume hood. This procedure should **not** be performed under a laminar flow hood, which directs airflow towards the operator, risking exposure to radioactive material.
- Work areas and other surfaces should be covered with plastic or absorbent paper to catch spills and prevent spread of contamination.
- All procedures involving the handling, transfer, dilution, administration, or clean-up of radioactive materials should be planned to increase awareness of potential problems.
- Treatment facility staff should not eat, drink, chew gum, apply cosmetics or smoke in areas where unsealed radionuclides are used or stored.
- Clearly label all containers with radionuclide identity, form, date and radioactivity.
- Do not pipette materials by mouth.
- Wear protective clothing and gloves while working with radioactive materials.
- Dispose of the gloves before leaving the radiation or contamination area.
- Do not wear protective clothing in general or public areas.
- Maintain high standards of cleanliness in the laboratory, clinic, imaging suites, and patient rooms.
- Plan the preparation with all equipment ready for the dispensing process to ensure that time spent when dispensing in kept to a minimum.
- Conduct special surveys after work activities that might result in radioactive material contaminations. Properly monitor for contamination, promptly clean-up spills, and dispose of wastes according to established procedures.
- Notify the RSO or RPO if ingestion or skin contamination occurs. The facility RSO will direct decontamination procedures in accordance with local, state and federal regulations for example, skin decontamination can involve washing with soup and plenty of water, no abrasive cleaners, and no harsh scrubbing.

In particular, staff should be trained on emergency procedures in the event of a major incident, spill, or radiation exposure.

# 9 Radiation and Implantation Procedure



## 9.1 Precautions and Endoscopy Suite Set Up for Implantation of OncoSil™

Universally accepted precautions and good practices for radiation protection should be observed during implantation of OncoSil™. Persons who implant OncoSil™ must avoid direct skin contact with the radioactive materials. Containment procedures should be followed to prevent contamination of significant areas in the event of an inadvertent spill. Shielded syringes should be used to limit and minimise exposure to treatment facility staff. Persons implanting OncoSil™ should wear a laboratory coat, gloves, goggles and personnel dosimeters. All personnel involved in the implantation and handling of OncoSil™ or nurses caring for patient must receive radiation safety training prior to participating in the procedure.

### Endoscopy Suite Set-Up

- **Demarcation of Area:** The controlled area will have been set up in advance and is physically demarcated to restrict unauthorised access and the area will be under the direct supervision of competent authorised persons. A 'diagram' of the endoscopy suite could be utilised to support planning of where personnel/staff/equipment will be placed including essential items such as the decontamination kit and monitors.
- **Radiation Protection Principals:** Always remember to consider time, distance and shielding throughout the entire procedure and minimise any exposure or risk of contamination. Containment is essential should a spill/contamination of equipment/personnel occur.
- **Signage:** The area will be marked out at its entry point (or points) by suitable signage including required information , e.g. Trefoil' sign, nature of the ionising radiation hazard, contact details of the RSO/RPS.
- **Controlled Entry & Protection of Personnel:** Only those personnel who have been trained and authorised to enter may do so. In order to minimise contamination/exposure risk, staff where possible should utilise a one-way system in and out of the endoscopy suite. All personnel should ensure they maintain the maximum distance to the source and administration of the OncoSil™ must only be performed by appropriately licenced and trained staff.
- **Washing & Changing Facilities:** Where there is risk of contamination (i.e. in any area where unsealed sources of ionising radiations are used) then adequate washing facilities should be supplied. In general, this will mean hand wash sinks both sides of the barrier (or other suitable demarcation points).
- **Covering Surfaces & Protection of People & Equipment:** The endoscopy suite must be prepared in advance of the dose arriving in the endoscopy suite to ensure all potential sources of contamination are covered. This will include the area surrounding the patient bed, the administration/cleaning & disposal area, the EUS monitor, trolleys and any other applicable equipment. All staff must wear disposable overshoes and gloves, with double gloving for all operations involving handling of $^{32}P$. Gloves should be changed immediately if contamination is suspected, and hands should be monitored after removal of gloves. When administering radioactive materials, a disposable apron should be worn. Appropriate PPE (as per site protocol) must be utilised.

# 9 Radiation and Implantation Procedure



- **Dosimetry and Monitoring:** Appropriate equipment for contamination monitoring should be in the endoscopy suite prior to the dose arriving, the spill kit should also be *in situ* and the RPS/RSO should be present. All staff performing manipulations with $^{32}P$ (the AU and the Endoscopist) must wear appropriate extremity dosimeters as defined in their local rules and provided by their RPS/RSO.
- **Equipment:** The following should be in the endoscopy suite in advance of the implantation procedure: Absorbent protectors for the room as applicable, containers for flushing contaminated items, clinical and non-clinical waste receptacles, radioactive waste receptacles, $^{32}P$ sharps containers, PPE, monitors, dosimeters, water/saline, syringes, absorbent pads, syringe shields, three-way taps, long tongs, Luer locks, extension tubing, lead transport container, trolleys, spill kit.
- **Implantation:** EUS is performed – suction is applied to ensure critical structures are avoided. However the suction will be turned off once the needle has been inserted for implantation and prior to administration of the OncoSil™ suspension. The actual volume/dose given should be recorded along with any other pertinent information related to the procedure.
- **Post Implantation:** All equipment will be monitored and disposed of depending on its designation. Once the scope is cleaned/decontaminated, it can be sent to be cleaned in the usual manner. No staff will leave the room until cleared by the delivery team (monitoring of both hands and feet will be undertaken). Ward/recovery room discharge staff must be notified that the patient has been treated with $^{32}P$ and details of the procedure and contact names and numbers must be in the patient's notes. The Nuclear medicine (NM) staff will organise timing/transport for the post-implant localisation scan.
- **In the Event of a Spillage of $^{32}P$ in the ES:** The NM staff/RPS/RSO will initiate the process for decontamination. Containment is the priority. The area around the spill must be cordoned off to prevent spread. Staff not involved in decontamination process or care of the patient will be asked to leave following contamination monitoring to ensure no spread of contamination. All contaminated non-injured persons whose footwear is/may be contaminated should exchange their footwear for overshoes, placing contaminated items into an impermeable bag. They should then proceed to a suitable area where monitoring and washing facilities are available. Contaminated clothing should be removed and placed into an impermeable bag. Tongs will be used where possible to minimise distance to the operator performing the decontamination procedures. Dose rate measurements should be provided and information such as time/date of spillage. Any items contaminated must be removed/isolated to enable estimation of activity involved, minimise dose & keep background as low as possible to aid in decontamination. Spillage over a small area should be cleaned up using decontamination solution and a suitable cloth/wipe to minimise spread.
- **Endoscopy Suite Controlled Designation Removed:** Once the room and personnel are deemed to be 'clean' after monitoring and have left the endoscopy suite, then the controlled signage can be removed, and the room will revert to its usual designation.

## 9.2 Estimates of Effective Doses Received During the Implantation Procedure

Estimates of the effective doses to the healthcare professionals handling the OncoSil™ suspension during the implantation procedure have been performed based on dose rate measurements in a laboratory setting for both the endoscopist (locating the tumour) and the authorised User (nuclear medicine physician depressing the plunger).

### Radiation Dose Received by the Endoscopist during the Implantation Procedure

- The effective dose to the skin of an endoscopist's hand who is holding the endoscope tube during an implant was estimated.
- The only time the fingers or hand will receive a dose of radiation is when the OncoSil™ suspension flows down the catheter to the FNA needle and passes the point where the fingers are holding the endoscope.
- The estimated time the suspension flows down the catheter to the needle is 30 seconds, and holding the endoscope for that time the practitioner's fingers or hand will receive:
  - An effective dose of ≈0.3 mSv when implanting the maximum patient dose of 60 MBq. This allows for in excess of 1500 procedures of 60 MBq per year before approaching the annual extremity limit.
  - An effective dose of ≈0.15 mSv when implanting the typical patient dose of 30 MBq. This allows for in excess of 3000 procedures of 30 MBq per year before approaching the annual extremity limit.
- During the implantation, if the implantation step is unduly delayed or paused while the suspension is in the catheter, the endoscope should be held with tongs, or a suitable remote handling device.

## 9.3 Radiation Dose Rates from the Patient Following Implantation

OncoSil™ has assessed the OH&S dose rates through measurements about a water phantom that contained a simulated dose of OncoSil™. From these measurements, assuming the maximum patient dose of 60 MBq has been implanted, the dose rate is approximately 9.5 µSv/hour at the external skin **surface** of the patient closest to the pancreas. At a distance of 15 cm from the skin surface, the dose rate was less than 1 µSv/hour. If the patient dose is less than the maximum of 60 MBq, then these dose rates will be proportionately less.

Using a dose limit of 1 mSv for a member of the public, a person would have to stand at the skin **surface** of a patient for 100 hours to approach the limit. However, please note that the 1 mSv public limit is to the whole body.

# 9 Radiation and Implantation Procedure



## 9.4 Record Keeping

Records must be kept in accordance with local, state and federal regulations. These include, but are not limited to, prescriptions, procedures for prescriptions, radiation surveys for ambient exposure rate, contamination surveys, and instructions to patient for release, basis for authorising the release of patient, and training documents. All dosimetry records should be retained permanently or until authorised by the regulatory authority for dispositioning.

## 9.5 Prescription

A prescription must be provided by the radiation medical practitioner before the OncoSil™ implantation. In the U.S., the prescription is called the Written Directive, and in Europe and Australia it is called a Written Referral. This prescription should contain the patient's name, the radioactivity (or permissible range) to be administered, the route of administration and the name of the radioactive material, as well as any other information required by local, state and federal regulations. Prior to implantation, the study participant's identity must be verified as well as the amount and dosage of the radioactive material. Persons performing the administration must verify that the administration was given in accordance with the prescription. A permanent record must be maintained for each administration. To ensure that requirements are met, a procedure for OncoSil™ implantation must be implemented, and maintained. It should be noted that calculation of the patient dose is based on the tumour volume. It is the responsibility of the practitioner to ensure the tumour volume has been calculated within 6 weeks of the implantation procedure to ensure the correct dose is administered to the patient.

## 10.1 General

After implantation of OncoSil™ into the patient tumour, the patient becomes a source of radiation, but, the radiation source remains in the patient and negligible radiation is emitted from the patient. That is because $^{32}P$ is a pure beta-emitter, and beta particles are absorbed internally. Only a small fraction of the beta energy is emitted externally as bremsstrahlung X-rays; therefore, the exposures (and subsequent risks) to staff, other patients and family members from external radiation exposure are negligible. Previous clinical trials using OncoSil™ show that $^{32}P$ remains in the tumour, and only a small fraction of the injected activity could leave the tumour, redistribute in extracellular fluids, and be excreted (urine and faeces). The biokinetic data shows that OncoSil™ is safe both for the patient and for family members. It therefore follows that OncoSil™ is also safe for the medical staff.

Although the radiation risks through the patient's bodily excretions are negligible, good radiation safety practices should be followed by all staff, the patient, and others to minimise the trace contamination that may result by direct contact with excreted $^{32}P$ on potentially contaminated surfaces. Patients must be provided with written instructions upon their release from the treatment facility containing radiation safety guidelines. Verbal instruction should also be provided. Local, state and federal regulations may over-ride these general guidelines in **provided in Section 11**.

# 11 Patient Care Pre-Release



## 11.1 General

Given the low activities of $^{32}P$ administered to the patient with the OncoSil™ therapy, the nearly total retention in the tumour, and the lack of significant external radiation from $^{32}P$, the post-implantation radiation dose to staff and others will be negligible, or not measurable, that is, below the limit of detection. In the general care of patients, good radiation safety practice should be followed by staff. As the primary clearance pathway, the small amount of $^{32}P$ not retained within the tumour is urinary excretion. Staff should instruct the patient on good radiation safety practices to minimise trace contamination that may result when a patient uses bathroom facilities.

OncoSil Medical also provides a jurisdictional compliant Take-Home Information for OncoSil™-Treated Patients and Families, to guide on radiation safe bathroom practices following implantation of the OncoSil™ device. An implant of OncoSil™ represents a low external radiation risk. Consequently, only a few restrictions are recommended after administration of OncoSil™ with regards to patient care and release, close physical contact with family members and other persons, and travel on public transport.

Guidelines for these few restrictions and for special situations involving breast-feeding and sexual intimacy are provided in the Take-Home Information for OncoSil™-Treated Patients and Families.

## 11.2 Accommodation Post-Implantation

Following OncoSil™ implantation, the patient may be moved to a recovery room where they may be observed for four hours (a qualified study member should remain with the patient to monitor for complications with regular observations of consciousness, vital signs as clinically indicated, and answer any questions that the patient may have). Potential exposures to medical staff, other patients and accompanying family members will be negligible.

## 11.3 Excretion or Expulsion of $^{32}P$ from a Patient Post-Implantation

The primary clearance pathway for $^{32}P$ is via excretion; biological, pharmacokinetic, and dosimetry data for OncoSil™ show that the levels of radioactivity in blood, urine, and faeces of the treated patient are negligible and do not represent any significant source of radiation to healthcare personnel, other patients and family members. The primary radiation safety concern for the staff and the public will be trace $^{32}P$ contamination of fluids and surfaces. Protection measures for trace contamination levels are as follows:

- Gloves should be worn when changing dressings.
- All contaminated products (including bed linen/clothing) should be bagged for radioactive waste disposal.
- Non-contaminated bed linen, rubbish or items of clothing may be washed or disposed of normally.
- Catheter bags or drainage bags can be safely changed by staff wearing gloves and be discharged into a fluid collection system (and held for approximately 114 to 142 days through complete $^{32}P$ decay).

Vomiting is a known side effect of the endoscopy procedure. It is therefore possible that some of the administered $^{32}P$ may be present in the stomach after the line flush. If a patient implanted with the OncoSil™ device vomits shortly after the implantation procedure, the ARP should be notified immediately and should coordinate the clean-up procedure with post-op personnel. Affected materials (clothing, bed sheets, towels, etc) should be considered potentially contaminated with $^{32}P$. These items may be bagged and monitored with an appropriate survey meter. If contamination is found, they should be held for complete decay (five months), then disposed of as regular trash or laundered as desired. Surfaces such as floors, tables, and bathroom fixtures should be washed as per standard hospital procedure. Used cleaning supplies should be surveyed and, if contaminated, disposed of as radioactive waste. The surfaces should be monitored for any residual activity and washed until background levels are obtained.

## 11.4 Bathroom Hygiene

Patients should be instructed on good radiation safety practices by treatment facility staff. This guidance should include at a minimum, instructions for patients to wash hands thoroughly and flush toilets twice after use. Toilet seats and handles should be wiped with a disinfecting wipe (Clorox or similar) folding it inside to itself. Spills should be promptly cleaned up whilst wearing gloves. Restrooms should be checked over by staff after use by patients.

## 11.5 Staff Precautions

Individual monitoring of staff is generally a requirement in accredited treatment facilities and is recommended for staff handling OncoSil™. All staff should wear film badges or some form of dosimeter including ring badges for preparing the OncoSil™ dose in accordance with Local, state and federal regulations.

Nursing care and ward cleaning requirements will be at the discretion of the treatment facilities radiation safety procedures.

# 12 Patient Release Procedure



## 12.1 Patient Release Criteria

The treatment facility implanting OncoSil™ should refer to local, state and federal regulations regarding patient release criteria involving $^{32}P$ to ensure all regulatory requirements are met.

## 12.2 Patient Release Information

Please refer to the Take-Home Information for OncoSil™-Treated Patients and Families.

## 12.3 Patient Death after OncoSil™ Therapy

In the event that a patient dies within the treating facility while still containing a therapeutic amount of $^{32}P$ radioactive material, procedures for handling deceased patients and follow-up surveys of mortuaries and crematoriums are the responsibility of the facility that treated the patient with the OncoSil™ device.

The treatment facility ARP shall ensure all Local, State and Federal regulations are met including notifying regulatory authorities.

In the event of a patient death within three months post-implantation of OncoSil™, the patient's treating physician is advised to contact the coroner and provide contact details for the ARP at the treatment facility. The coroner shall contact the ARP immediately and without delay to determine what (if any) precautions are necessary with regards to performing an autopsy on a patient with radioactivity ($^{32}P$). It is critical to ensure that Local, State and Federal regulations governing therapeutic radioactive materials are met.

# 13 Patients Undergoing Surgical Resection with Curative Intent

**Reassessment and subsequent surgical resection with curative intent (e.g. Whipple procedure) in patients following implantation with the OncoSil™ device is based on the clinical judgement of the patient's medical team. There are several important factors in the area of occupational radiation protection and safety that OncoSil Medical, as the device manufacturer, advises treatment facilities to consider during planning for the resection of tumours implanted with the OncoSil™ device.**

- There is limited prior experience with the OncoSil™ device in patients who subsequently undergo surgical resection regarding occupational radiation dosimetry. The OncoSil Medical RSO is available for discussions in relation to occupational radiation dosimetry during planning for patient resections if required.
- Localisation of the Microparticles within the tumour coupled with the knowledge of the date and activity implanted creates the means by which the activity that will be present in tissue at the time of resection can be calculated. Beta radiation (as emitted by $^{32}P$) is not considered a significant hazard, except when handled at close proximity, for example when a surgeon is handling treated tissue with the fingers. Calculation of the remaining activity and an estimate of the time that the surgeon will be handling the treated tissue allows an assessment of any radiation doses to the fingers.
- **Table 6** below shows the relative activity of Phosphorous-32 remaining from an implanted dose after the elapsed time.

**Table 6:** Relative Activity of Phosphorous-32 Remaining from an Implanted Dose After the Elapsed Time

| Time from Implant (weeks) | Implant Activity Remaining (%) |
|---|---|
| 4 | **25.7** |
| 8 | **6.6** |
| 10 | **3.3** |
| 12 | **1.7** |
| 16 | **0.4** |

# 13 Patients Undergoing Surgical Resection with Curative Intent

- As guidance for the surgical team planning a resection the following scenario and subsequent dose rate estimates are provided [**Ref: 7**]:
  - **Activity implanted:** Assuming the maximum possible activity of OncoSil Microparticles implanted, which is 60 MBq.
  - **Tumour volume:** Assuming the tumour is the largest treated with the OncoSil™ device, which is 114 mL.
  - **Decay time:** Assuming that the time between implantation and planned resection (which represents the decay time) is 12 weeks.
  - **Distance from the source:** Assume that there is 3 mm between the surgeon's skin and the source due to the surgical gloves warn, and the fact that the Microparticles are implanted inside the tumour.
  - The dose rate to a contiguous highest-exposed skin area of 10 $cm^2$ is estimated to be 4.3 mGy per hour.
  - If a surgeon has close contact with the implanted tissue for a total of 1 hour during a resection operation, then this will deliver a total dose of 4.3 mGy per operation.
  - If the annual limit on extremity doses for a surgeon is 500 mSv, and it is assumed that the radiation and tissue weighing factors are 1.0, then a given surgeon can perform 116 hours of close contact surgery with a treated tumour annually, under the conditions shown above.
  - These figures are provided as a guide only, and it must be verified by the site RSO that the figures are applicable to the site where the resection is being performed.
- Another potential consideration is contamination of areas of a treatment facility that are not normally under radioactive materials control procedures. Guidance on practices and procedures should be obtained in this regard from the site RSO, or delegate, before the surgery is performed. OncoSil Medical can advise the site RSO if required in relation to radiation safety practices to avoid contamination of the operating theatre.

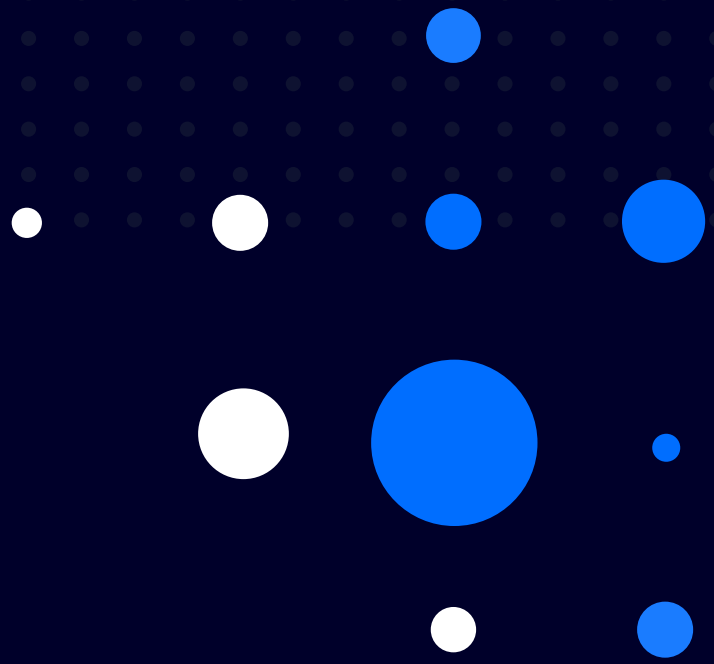
OncoSil Medical requests that the company is informed prior to any planned operative intervention in patients who have received the OncoSil™ device in order for the company's Radiation Safety Officer, where required or requested, to work with the relevant site radiation safety and treatment teams (including laboratory and pathology staff) to ensure the risks of any of these hazards are minimised.

# 14 References


1. The Council Directive 2013/59/EURATOM of 5 December 2013.
2. National standard for limiting occupational exposure to ionising radiation (2002) Schedule 1.
3. Australian Radiation Protection and Nuclear Safety Agency (ARPANSA).
4. IRPA, 2014; 2013/59/Euratom, Fundamentals For Protection Against Ionizing Radiation, 2014.
5. The Code of Practice for Radiation Protection in the Medical Applications of Ionizing Radiation (2008) Schedule A (lists the requirements for an Australian Radiation Safety Management Plan).
6. Ionising-Radiations-Regulations-2017-Approved-Code-of-Practice-and-Guidance, HSE, UK.
7. VARSKIN Version 6.1 (Hamby DM and Mangini CD, "A Computer Code for Skin Contamination Dosimetry", NUREG/CR-6918, Rev. 3, U.S. Nuclear Regulatory Commission, Rockville, Maryland).

# 15 Glossary

| Description | Definition |
|---|---|
| **OncoSil™ System** | The delivered package containing one sealed can containing:<br>• One Perspex-lined lead pot with the 250 MBq of OncoSil Microparticles at 12:00 CET/CEST on the day of reference<br>• Two vials of OncoSil™ Diluent; one sterile spare vial; one spare Perspex-lined lead pot; and one Instructions for Use |
| **AD** | Authorised Dispenser |
| **ALARA** | As Low As Reasonably Achievable |
| **ALARP** | As Low As Reasonably Practicable |
| **ARP** | Accredited Radiation Personnel |
| **AT** | Authorised Trainer (for OncoSil™ System dose preparation and implantation) |
| **AU** | Authorised User |
| **Becquerel (Bq)** | The SI Unit of Radioactivity: 1 Bq = 1 disintegration per second |
| **Curie (Ci)** | An older unit of radioactivity: 1 Ci = $3.7 \times 10^{10}$ Bq |
| **RP** | Responsible Person |
| **RSC** | Radiation Safety Committee |
| **RSO/RPS** | Radiation Safety Officer/Radiation Protection Supervisor |
| **Sievert (Sv)** | The SI Unit of Effective Dose (mSv = $1 \times 10^{-3}$ Sv) |

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