Pulmocis 2 mg
kit for radiopharmaceutical preparation

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Pulmocis 2 mg kit for radiopharmaceutical preparation

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vial contains 2.0 mg of human albumin as macroaggregates

The radionuclide is not part of the kit.

Less than 0.2 % of the particles are higher than 100 µm. None of the particles has a size higher than 150 µm. The macroaggregates number per vial is ranging between 2 x 10^6 and 4 x 10^6.

Excipient with known effect:
Each vial contains 3.5 mg of sodium.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Kit for radiopharmaceutical preparation.
White pellet.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

This medicinal product is for diagnostic use only.

After labelling with sodium pertechnetate (^{99m}Tc) solution, the suspension of technetium(^{99m}Tc) -albumin macroaggregates (or ^{99m}Tc-MAA) may be used :

- For the pulmonary perfusion scintigraphy.
- And as secondary indication for venoscintigraphy.

4.2 Posology and method of administration

This medicinal product is intended for use in designated nuclear medicine facilities only, and should only be handled by authorised personnel.

Posology

Adult and elderly patients

The recommended activity administered to an adult weighing 70 kg varies between 37 - 185 MBq. The number of particles per administered dose must be in a range of 60 x 10^3 - 700 x 10^3.

Paediatric population

The use in paediatric children and adolescents has to be considered carefully, based upon clinical needs and assessing the risk/benefit ratio in this patient group. The activities to be administered to children and to adolescents may be calculated according to the paediatric Task Group of the EANM (2008). This activity can be calculated from the formula below using a multiplying coefficient based on the patient's body mass (table 1)

Recommended activity [MBq] = 5.6 MBq x Factor (Table 1)

Table 1

Body weight	factor	Body weight	factor	Body weight	factor
3 kg	= 1*	22 kg	= 5.29	42 kg	= 9.14
4 kg	= 1.14*	24 kg	= 5.71	44 kg	= 9.57
6 kg	= 1.71*	26 kg	= 6.14	46 kg	= 10.00
8 kg	= 2.14	28 kg	= 6.43	48 kg	= 10.29
10 kg	= 2.71	30 kg	= 6.86	50 kg	= 10.71
12 kg	= 3.14	32 kg	= 7.29	52-54 kg	= 11.29
14 kg	= 3.57	34 kg	= 7.72	56-58 kg	= 12.00
16 kg	= 4.00	36 kg	= 8.00	60-62 kg	= 12.71
18 kg	= 4.43	38 kg	= 8.43	64-66 kg	= 13.43
20 kg	= 4.86	40 kg	= 8.86	68 kg	= 14.00

*In very young children (up to 1 year) a minimum dose of 10 MBq is necessary in order to obtain images of sufficient quality.

Method of administration

This medicinal product should be reconstituted before administration to the patient.
The radiolabelled solution should be administered intravenously. It is recommended to administer the medicinal product to the patient in the decubitus position.

For patient preparation, see section 4.4.
For instructions on reconstitution of the medicinal product before administration, see section 12.

Image acquisition

The lung test may start immediately after injection.

4.3 Contraindications

Hypersensitivity to the active substance, to any of the excipients listed in section 6.1 or to any of the components of the labelled radiopharmaceutical.

4.4 Special warnings and precautions for use

Potential for hypersensitivity or anaphylactic reactions
The possibility of hypersensitivity including serious, life-threatening, fatal anaphylactic/ anaphylactoid reactions should always be considered. If hypersensitivity or anaphylactic reactions occur, the administration of the medicinal product must be discontinued immediately and intravenous treatment initiated, if necessary. To enable immediate action in emergencies, the necessary medicinal products and equipment such as endotracheal tube and ventilator must be immediately available.

Individual benefit/risk justification
For each patient, the radiation exposure must be justifiable by the likely benefit. The activity administered should in every case be as low as reasonably achievable to obtain the required diagnostic information.

Special care should be exercised when administering ^{99m}Tc albumin macroaggregates (MAA) to patients with significant right to left cardiac shunt. In order to minimise the possibility of microembolism to the cerebral and renal circulations ^{99m}Tc albumin macroaggregates (MAA) should be given by slow intravenous injection and the number of particles reduced by up to 50%. Such precautions are also advised in patients with respiratory failure complicating pulmonary hypertension.

Paediatric population
For information on the use in paediatric population, see section 4.2.
Careful consideration of the indication is required since the effective dose per MBq is higher than in adults (see section 11).

Patient preparation
The patient should be well hydrated before the start of the examination and urged to void as often as possible during the first hours after the examination in order to reduce radiation.

The syringe should be gently swirled immediately prior to injection to homogenise the injectate. Blood should never be drawn into the syringe because that induces the formation of small clots.

Specific warnings
Pulmocis contains human albumin.
Standard measures to prevent infections resulting from the use of medicinal products prepared from human blood or plasma include selection of donors, screening of individual donations and plasma pools for specific markers of infection and the inclusion of effective manufacturing steps for the inactivation/removal of viruses. Despite this, when medicinal products prepared from human blood or plasma are administered, the possibility of transmitting infective agents cannot be totally excluded. This also applies to unknown or emerging viruses and other pathogens.

There are no reports of virus transmissions with albumin manufactured to European Pharmacopoeia specifications by established processes.

It is strongly recommended that every time that Pulmocis is administered to a patient, the name and batch number of the product are recorded in order to maintain a link between the patient and the batch of the product.

This medicinal product contains less than 1 mmol sodium (23 mg) per dose, i.e. essentially ‘sodium- free’.

Precautions with respect to environmental hazard are in section 6.6.

4.5 Interaction with other medicinal products and other forms of interaction

Changes in the biological distribution of (^{99m}Tc-MAA) are induced by differents drugs.

- Pharmacologic interactions are caused by chemotherapeutic agents, heparin, bronchodilators.
- Toxicologic interactions are caused by heroin, nitrofurantoin, busulfan, cyclophosphamide, bleomycin, methotrexate, methysergide.
- Pharmaceutic interactions are caused by magnesium sulphate.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential
When an administration of radiopharmaceuticals to a woman of childbearing potential is intended, it is important to determine whether or not she is pregnant. Any woman who has missed a period should be assumed to be pregnant until proven otherwise. If in doubt about her potential pregnancy (if the woman has missed a period, if the period is very irregular, etc.), alternative techniques not using ionising radiation (of there any) should be offered to the patient.

Pregnancy
Radionuclide procedures carried out on pregnant women also involve radiation doses to the foetus. Only essential investigations should therefore be carried out during pregnancy, when the likely benefit exceeds the risk incurred by the mother and the foetus.

Breastfeeding
Before administering radiopharmaceuticals to a mother who is breastfeeding consideration should be given to the possibility of delaying the administration of radionuclide until the mother has ceased breastfeeding, and to what is the most appropriate choice of radiopharmaceuticals. If the administration is considered necessary, breastfeeding should be interrupted for 12 hours and the expressed feeds discarded.
Close contact with infants should be restricted during this period.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed.

4.8 Undesirable effects

For safety with respect to transmissible agents, see section 4.4.

Due to the fact that only spontaneous reports could be analysed, no frequency indications could be provided.

Adverse Reactions sorted by System Organ Class

Immune system disorders
Frequency not known: Anaphylactic reaction, hypersensitivity-type reactions, including life-threatening anaphylaxis.

Vascular disorders
Frequency not known: Circulatory collapse

General disorders and administration site conditions
Frequency not known: Chest pain, chills, application site hypersensitivity.

Single or repeated injections of ^{99m}Tc-albumin macroaggregates may be associated with hypersensitive-type reactions, including very rare life-threatening anaphylaxis chest pain, rigor and collapse may occur. Local allergic reactions have been seen at the injection site.

Exposure to ionising radiation is linked with cancer induction and a potential for development of hereditary defects.
As the effective dose is 2.0 mSv when the maximal recommended activity of 185 MBq is administered these adverse events are expected to occur with a low probability.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system.

4.9 Overdose

The number of MAA particles per adult patient must not exceed 1.5×10^6.
In the event of the administration of a radiation overdose with ^{99m}Tc-MAA, the absorbed dose to the patient should be reduced where possible by increasing the elimination of the radionuclide from the body by forced diuresis and frequent bladder voiding.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Radiopharmaceutical for diagnostic use.
ATC code: V09EB01

At the chemical concentrations used for diagnostic examinations, ^{99m}Tc-MAA does not appear to have any pharmacodynamic activity.

5.2 Pharmacokinetic properties

Distribution
Following injection into a superficial vein of the systemic venous circulation, the macroaggregates are carried at the speed of this circulation to the first capillary filter, i.e. the capillary tree of the pulmonary artery system.

Organ uptake
The albumin macroaggregate particles do not penetrate the lung parenchyma (interstitial or alveolar) but remain in a temporary occlusive position in the lumen of the capillary. When pulmonary flow distribution is normal, the compound distributes over the entire pulmonary area following physiologic gradients; when district flow is altered the areas of reduced flow are reached by a proportionally smaller amount of particles. The technetium labelled macroaggregates remain in the lungs for variable periods of time, depending of the structure, size and number of particles.

Half-life
The disappearance of activity from the particles in the lungs is governed by an exponential law: the larger aggregate have a longer biological half-life, whereas particles between 5 and 90 µm in diameter have a half-life ranging from 2 to 8 hours.

The decrease in pulmonary concentration is caused by the mechanical break-down of the particles occluding the capillaries, stemming from the systo-diastolic pressure pulsations within the capillary itself.

Elimination
The products of macroaggregate break-down, once recirculated as albumin microcolloid, are quickly removed by the macrophages of the reticuloendothelial system, i.e. essentially the liver and the spleen.

The microcolloid is metabolised with introduction of the radioactive label (^{99m}Tc) into the systemic circulation from which it is removed and excreted in urine.

5.3 Preclinical safety data

Correlation exists between the size of the MAA and their toxic effects.

The pathophysiologic mechanism responsible for toxicity is shown to be the increase of the pulmonary blood pressure. With particles from 10 to 50 µm in diameter the first pulmonary signs of toxicity in dogs (e.g. tachypnea) appear after injection of 20 to 25 mg per kg of body weight.

A sharp increase of the pulmonary blood pressure is noticed when 20 mg of less than 80 µm sized MAA are injected, where no significant pressure changes are recorded with 40 mg of less than 35 µm MAA particles.
With suspension of MAA up to 150 µm diameter, no blood pressure changes appear below 10 mg/kg, while larger diameter suspensions (up to 300 µm) typical blood pressure changes in pulmonary artery appear when the dose exceeds 5 mg/kg.

Doses of 20-50 mg/kg cause sudden death for respiratory failure. A safety factor of 100 is found after injection in dogs of 14 000 ^{99m}Tc-MAA (size: 30-50 µm).

The repeated-dose toxicity studies performed in dogs show no detectable variations in the general behaviour of the animals.

No evidence of pathological changes in the main organs has been detected.

There is no evidence in the literature of teratogenic, mutagenic or carcinogenic effect of the unlabeled product.

This agent is not intended for regular or continuous administration.
Mutagenicity studies, toxicity to reproduction and development studies and long-term carcinogenicity studies have not been carried out.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Human serum albumin
Stannous chloride dihydrate
Sodium chloride
Under nitrogen atmosphere

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products except those mentioned in section 12.

6.3 Shelf life

12 months.
The expiry date is indicated on the outer packaging and on each vial.
Store the labelled product at 2°C – 8°C, and used within 8 hours.

6.4 Special precautions for storage

Store the kit in a refrigerator (2°C – 8°C).
For storage conditions of the radiolabelled medicinal product, see section 6.3.
Storage of radiopharmaceuticals should be in accordance with national regulations on radioactive materials.

6.5 Nature and contents of container

15 mL colourless, European Pharmacopoeia type I, drawn glass vials, closed with rubber stoppers and aluminium capsules.

Packsize: 5 multidose vials.

6.6 Special precautions for disposal and other handling

General warning
Radiopharmaceuticals should be received, used and administered only by authorised persons in designated clinical settings. Their receipt, storage, use, transfer and disposal are subject to the regulations and/or appropriate licences of the competent official organisation.

Radiopharmaceuticals should be prepared in a manner which satisfies both radiation safety and pharmaceutical quality requirements. Appropriate aseptic precautions should be taken.

Content of the vial is intended only for use in the preparation of the suspension of technetium(^{99m}Tc) -albumin macroaggregates and are not administered directly to the patient without first undergoing the preparative procedure.

For instructions on extemporaneous solution of the medicinal product before administration, see section 12.

If at any time in the preparation of this product the integrity of this vial is compromised it should not be used.

Administration procedures should be carried out in a way to minimise risk of contamination of the medicinal product and irradiation of the operators.

The content of the kit before reconstitution is not radioactive. However, after sodium pertechnetate (^{99m}Tc) solution is added, adequate shielding of the final preparation must be maintained.

The administration of radiopharmaceuticals creates risks for other persons from external radiation or contamination from spill or urine, vomiting, etc. Radiation protection precautions in accordance with national regulations must therefore be taken.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

CIS bio international
RN 306 - Saclay
B.P.32
F-91192 Gif sur Yvette Cedex

8 MARKETING AUTHORIZATION NUMBER

Country specific

9 DATE OF FIRST AUTHORIZATION/RENEWAL OF AUTHORIZATION

Country specific

10 DATE OF REVISION OF THE TEXT

12/2017

11. DOSIMETRY

Technetium (^{99m}Tc) is produced by means of a (^{99}Mo/^{99m}Tc) generator and decays with the emission of gamma radiation with a mean energy of 140 keV and a half-life of 6.02 hours to technetium (^{99}Tc) which, in view of its long half-life of 2.13 x 10^5 years can be regarded as quasi stable.

According to ICRP 80 the radiation doses absorbed by the patients are the following:

	DOSE ABSORBED PER ACTIVITY ADMINISTERED (mGy / MBq)				
Organ	**Adult**	**15 year old**	**10 year old**	**5 year old**	**1 year old**
Adrenals	6.8E-03	8.8E-03	1.3E-02	1.9E-02	3.1E-02
Bladder	8.7E-03	1.1E-02	1.4E-02	1.6E-02	3.0E-02
Bone surfaces	5.1E-03	6.4E-03	9.1E-03	1.4E-02	2.6E-02
Brain	9.2E-04	1.2E-03	2.0E-03	3.2E-03	5.5E-03
Breast	5.0E-03	5.6E-03	9.9E-03	1.4E-02	2.1E-02
Gall bladder	5.6E-03	7.0E-03	1.0E-02	1.6E-02	2.4E-02
GI-tract					
Stomach	3.7E-03	5.2E-03	8.0E-03	1.2E-02	2.0E-02
SI	2.0E-03	2.6E-03	4.3E-03	6.8E-03	1.2E-02
Colon	1.9E-03	2.6E-03	4.3E-03	6.9E-03	1.2E-02
(ULI	2.2E-03	2.9E-03	5.0E-03	8.3E-03	1.4E-02
(LLI	1.6E-03	2.1E-03	3.3E-03	5.0E-03	9.5E-03
Heart	9.6E-03	1.3E-02	1.8E-02	2.5E-02	3.8E-02
Kidneys	3.7E-03	4.8E-03	7.2E-03	1.1E-02	1.8E-02
Liver	1.6E-02	2.1E-02	3.0E-02	4.2E-02	7.4E-02
Lungs	6.6E-02	9.7E-02	1.3E-01	2.0E-01	3.9E-01
Muscles	2.8E-03	3.7E-03	5.2E-03	7.7E-03	1.4E-02
Oesophagus	6.1E-03	7.7E-03	1.1E-02	1.5E-02	2.2E-02
Ovaries	1.8E-03	2.3E-03	3.5E-03	5.4E-03	1.0E-02
Pancreas	5.6E-03	7.5E-03	1.1E-02	1.7E-02	2.9E-02
Red marrow	3.2E-03	3.8E-03	5.3E-03	7.2E-03	1.2E-02
Skin	1.5E-03	1.7E-03	2.7E-03	4.3E-03	7.8E-03
Spleen	4.1E-03	5.5E-03	8.3E-03	1.3E-02	2.2E-02
Testes	1.1E-03	1.4E-03	2.2E-03	3.3E-03	6.2E-03
Thymus	6.1E-03	7.7E-03	1.1E-02	1.5E-02	2.2E-02
Thyroid	2.5E-03	3.3E-03	5.7E-03	9.0E-03	1.6E-02
Uterus	2.2E-03	2.8E-03	4.2E-03	6.0E-03	1.1E-02
Remaining organs	2.8E-03	3.6E-03	5.0E-03	7.4E-03	1.3E-02
Effective dose (mSv/MBq)	**1.1E-02**	**1.6E-02**	**2.3E-02**	**3.4E-02**	**6.3E-02**

The effective dose resulting from the administration of a (maximal recommended) activity of 185 MBq of ^{99m}Tc-MAA for an adult weighing 70 kg is about 2.0 mSv.

For an administered activity of 185 MBq the typical radiation dose to the target organ, lungs, is 12.2 mGy and the typical radiation dose to the critical organs, adrenals, bladder, liver, pancreas, spleen, are 1.26, 1.61, 2.96, 1.04 and 0.76 mGy respectively.

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

Withdrawals should be performed under aseptic conditions. The vials must not be opened before disinfecting the stopper. The solution should be withdrawn via the stopper using a single dose syringue fitted with suitable protective shielding and a disposable sterile needle.

If the integrity of this vial is compromised, the product should not be used.

Method of preparation of the suspension of technetium (^{99m}Tc) human albumin macroaggregates injection, (^{99m}Tc)-MAA)

Sodium pertechnetate (^{99m}Tc) injection should comply with European Pharmacopoeia specifications.

Usual precautions regarding sterility and radioprotection should be respected.

Take a vial from the kit and put it in an appropriate lead shielding.

Using a hypodermic syringe, introduce through the rubber stopper 2.5 to 10 ml of sterile and pyrogen-free sodium pertechnetate (^{99m}Tc) injection, radioactivity varying as a function of the volume from 92.5 to maximum 3700 MBq.

Do not use a breather needle as the contents is under nitrogen : after introduction of the volume of sodium pertechnetate (^{99m}Tc) injection, without removing the needle, withdraw an equivalent volume of nitrogen in order to avoid excess pressure in the vial.

Shake for about 2 minutes and wait for 15 minutes before use.

The vial should be shaked before each withdrawal in order to homogenise the suspension.

The obtained preparation is a whitish homogeneous suspension, with a pH ranging between 5.0 and 7.0.

The syringe should be swirled immediately prior to injection to homogenise the injectate.

The homogeneousness of the suspension after preparation, pH, radioactivity and gamma spectrum should be checked before use.

The vial should never be opened and must be kept inside its lead shielding. The suspension should be removed aseptically through the stopper with a sterile lead protected syringe.

<u>Determination of volume and activity of pertechnetate in relation with the number of MAA particles per dose.</u>

In order to take into account the number of MAA particles per dose in the determination of volume and radioactivity of pertechnetate to prepare the radiopharmaceutical, charts have been performed and are described hereafter.

The proposed figures in the following tables are calculated from a mean value of 3 millions of MAA particles per vial.

- The first step allows to determine the volume of labeling of the vial as a function of the volume and the number of MAA particles to inject per dose. The used formula is as follows :

$$\text{Volume of labeling} = \frac{\text{Number of MAA particles per vial} \times \text{Volume to inject}}{\text{Number of MAA particles to inject per dose}}$$

The tables 1 and 2 show examples for volumes to inject of 0.5, 0.8 and 1 ml.

- The second step allows to know the radioactivity to add in the vial for the labeling as a function of the radioactivity to inject and the previously set parameters. The used formula is as follows:

$$\text{Total radioactivity of the vial} = \frac{\text{Radioactivity to inject} \times \text{Volume of labelling}}{\text{Volume to inject}}$$

The total radioactivity of the vial is calculated for radioactivities to inject of 37, 74, 111 and 148 MBq. See tables 3,4,5 and 6.

- The third step will describe the decrease calculation taking into account the time of labeling and the time of injection. The decay table of (^{99m}Tc) is presented in table 7.

TABLE 1

DETERMINATION OF THE LABELING VOLUME FROM VOLUME AND NUMBER OF MAA PARTICLES TO INJECT AND CONSIDERING A VIAL CONTAINING 3 MILLIONS MAA PARTICLES

NUMBER OF MAA PARTICLES TO INJECT PER DOSE	VOLUME TO INJECT (mL)		
	0.5	0.8	1
600 000	2.5	4	5
500 000	3	4.8	6
480 000	3.1	5	6.3
428 000	3.5	5.6	7
400 000	3.75	6	7.5
375 000	4	6.4	8
343 000	4.4	7	8.7
330 000	4.5	7.3	9
300 000	5	8	10
267 000	5.6	9	
250 000	6	9.6	
240 000	6.25	10	
215 000	7		
188 000	8		
167 000	9		
150 000	10		

Labeling volume (mL)
Injected volume (mL)
Number of MAA particles to inject / dose

TABLE 2

DETERMINATION OF THE NUMBER OF INJECTED MAA PARTICLES AS A FUNCTION OF THE LABELING VOLUME OF THE VIAL AND THE VOLUME TO INJECT AND CONSIDERING A VIAL CONTAINING 3 MILLIONS MAA PARTICLES

VOLUME OF LABELING (ml)	VOLUME TO INJECT (mL)		
	0.5	0.8	1
3	500 000		
4	375 000	600 000	
5	300 000	480 000	600 000
6	250 000	400 000	500 000
7	215 000	343 000	428 000
8	188 000	300 000	375 000
9	167 000	267 000	330 000
10	150 000	240 000	300 000

Labeling volume (mL)

Injected volume (mL)

Number of MAA particles to inject/dose

TABLES 3, 4, 5 and 6

DETERMINATION OF THE RADIOACTIVITY TO ADD TO THE VIAL AS A FUNCTION OF THE LABELING VOLUME, THE VOLUME AND THE RADIOACTIVITY TO INJECT AND CONSIDERING A VIAL CONTAINING 3 MILLIONS MAA PARTICLES

	37 MBq			74 MBq		
	0.5	**0.8**	**1**	**0.5**	**0.8**	**1**
3	222	139	111	444		
4	296	185	148	592	370	
5	370	231	185	740	462	370
6	444	277	222	888	555	444
7	518	324	259	1036	647	518
8	592	370	296	1184	740	592
9	666	416	333	1332	832	666
10	740	462	370	1480	925	740

Table 3 **Table 4**

	111 MBq			148 MBq		
	0.5	**0.8**	**1**	**0.5**	**0.8**	**1**
3	666			888		
4	888	555		1184	740	
5	1110	694	555	1480	925	740
6	1332	832	666	1776	1110	888
7	1554	980	777	2072	1295	1036
8	1776	1110	888	2368	1480	1184
9	1998	1249	999	2664	1665	1332
10	2220	1387	1110	2960	1850	1480

Table 5 **Table 6**

Injected activity (MBq) **Injected volume (mL)**

Total activity (MBq) **Labeling volume (mL)**

TABLE 7

^{99m}Tc (HALF-LIFE : 6.02 hours) DECAY TABLE												
H Min	%	H Min	%	H Min	%	H Min	%	H Min	%	H Min	%
0 05	99.05	2 05	78.67	4 05	62.49	6 05	49.64	8 05	39.43	10 05	31.32
0 10	98.10	2 10	77.92	4 10	61.89	6 10	49.16	8 10	39.05	10 10	31.02
0 15	97.16	2 15	77.18	4 15	61.30	6 15	48.69	8 15	38.68	10 15	30.72
0 20	96.23	2 20	76.44	4 20	60.72	6 20	48.23	8 20	38.61	10 20	30.43
0 25	95.32	2 25	75.71	4 25	60.14	6 25	47.77	8 25	37.94	10 25	30.14
0 30	94.41	2 30	74.99	4 30	59.56	6 30	47.31	8 30	37.58	10 30	29.85
0 35	93.50	2 35	74.27	4 35	58.99	6 35	46.86	8 35	37.22	10 35	29.57
0 40	92.61	2 40	73.56	4 40	58.43	6 40	46.41	8 40	36.87	10 40	29.28
0 45	91.73	2 45	72.86	4 45	57.87	6 45	45.97	8 45	36.51	10 45	29.00
0 50	90.85	2 50	72.16	4 50	57.32	6 50	45.53	8 50	36.17	10 50	28.73
0 55	89.98	2 55	71.47	4 55	56.77	6 55	45.10	8 55	35.82	10 55	28.45
1 00	89.12	3 00	70.79	5 00	56.23	7 00	44.66	9 00	35.48	11 00	28.18
1 05	88.27	3 05	70.12	5 05	55.69	7 05	44.24	9 05	35.14	11 05	27.91
1 10	87.43	3 10	69.45	5 10	55.16	7 10	43.82	9 10	34.80	11 10	27.64
1 15	86.60	3 15	68.78	5 15	54.64	7 15	43.40	9 15	34.47	11 15	27.38
1 20	85.77	3 20	68.13	5 20	54.11	7 20	42.98	9 20	34.14	11 20	27.12
1 25	84.95	3 25	67.48	5 25	53.60	7 25	42.57	9 25	33.82	11 25	26.86
1 30	84.14	3 30	66.83	5 30	53.09	7 30	42.17	9 30	33.49	11 30	26.60
1 35	83.33	3 35	66.19	5 35	52.58	7 35	41.76	9 35	33.17	11 35	26.35
1 40	82.54	3 40	65.56	5 40	52.08	7 40	41.36	9 40	32.86	11 40	26.10
1 45	81.75	3 45	64.94	5 45	51.58	7 45	40.97	9 45	32.54	11 45	25.85
1 50	80.97	3 50	64.32	5 50	51.09	7 50	40.58	9 50	32.23	11 50	25.60
1 55	80.20	3 55	63.70	5 55	50.60	7 55	40.19	9 55	31.92	11 55	25.36
2 00	79.43	4 00	63.09	6 00	50.12	8 00	39.81	10 00	31.62	12 00	25.12

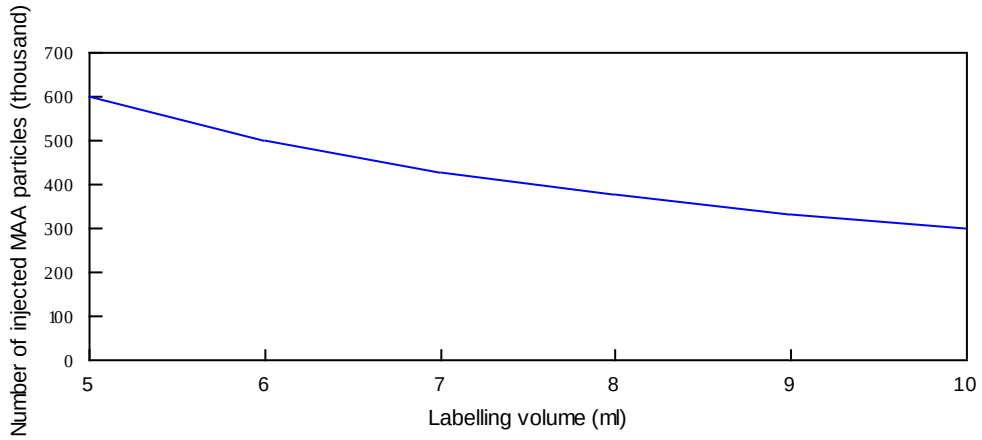
EXAMPLE FOR AN INJECTED VOLUME OF 1 mL

The following table and curve allow to determine the number of MAA particles injected when volumes of labeling are 5 to 10 mL and when the volume to inject is 1 mL.

The proposed figures in the following tables are calculated from a mean value of 3 millions of MAA particles per vial.
The formula used is:

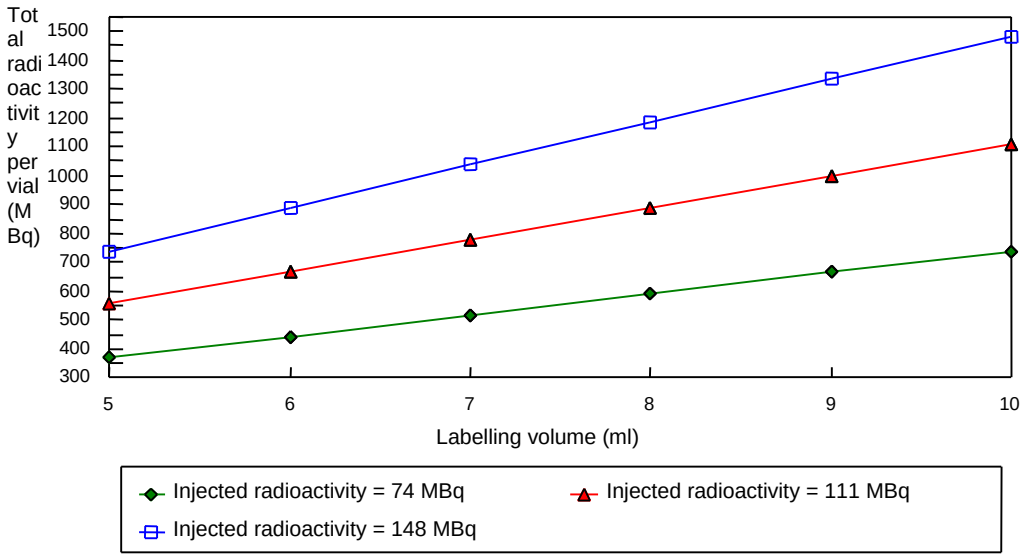
$$\text{Number of injected MAA particles} = \frac{\text{Total number of MAA particles} \times \text{Injected volume}}{\text{Labeling volume}}$$

Volume of labeling (mL)	Number of injected MAA particles
5	600 000
6	500 000
7	428 600
8	375 000
9	333 300
10	300 000



The following table and graph allow to deduce **the total radioactivity to add to the vial** when the radioactivities to inject are 74, 111 or 148 MBq with a injected volume of 1 mL and considering a vial containing 3 millions particles.

Volume of labeling (mL)	**Total radioactivity per vial (MBq) with a radioactivity to inject of**		
	74 MBq	**111 MBq**	**148 MBq**
5	370	555	740
6	444	666	888
7	518	777	1036
8	592	888	1184
9	666	999	1332
10	740	1110	1480



Quality control

The quality of labeling (radiochemical purity) could be checked according to the following procedure:

Method

Non-filterable radioactivity.

Materials and methods

1. Polycarbonate membrane filter 13 mm to 25 mm in diameter, 10 µm thick and with circular pores 3 µm in diameter.
2. 0.9 % sodium chloride solution.
3. Miscellaneous: syringes, needles, 15 ml glass vials, appropriate counting assembly.

Procedure

1. Fit the membrane into a suitable holder.
2. Place 1 ml of the injection on the membrane, filter and collect in a vial (A).
3. Rinse the membrane with 2 ml of 0.9% sodium chloride solution and collect in the vial (A).
4. Measure the radioactivity of the filter (X) and the radioactivity of the vial A (Y), using an appropriate detection apparatus.
5. Calculations:

Calculate the percentage of technetium (^{99m}Tc) human albumin macroaggregates as follows :

$$\frac{X}{X + Y} \times 100$$

The radioactivity remaining on the membrane should be not less than 90 % of the total radioactivity of the injection.

The administration of radiopharmaceuticals creates risks for other persons from external radiation or contamination from spill or urine, vomiting, etc. Radiation protection precautions in accordance with national regulations must therefore be taken.

The residues may be put in a ordinary waste bin insofar as the activity of vials and syringes does not exceed that of background when measured with a low level radiation detector.
Any unused product or waste material should be disposed of in accordance with local requirements.