

TECHNICAL LEAFLET: SUMMARY OF PRODUCT CHARACTERISTICS

1. TRADE NAME OF THE MEDICINAL PRODUCT

PULMOCIS®

Kit for the preparation of technetium [^{99m}Tc] human albumin macroaggregates injection.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

The kit for the preparation of technetium [^{99m}Tc] human albumin macroaggregates injection, (^{99m}Tc-MAA), PULMOCIS®, consists of 5 vials, each containing the following sterile, pyrogen-free, freeze-dried product under nitrogen :

- human albumin as macroaggregates : 2.0 mg
- stannous chloride dihydrate : 0.2 mg
- human albumin : 7.0 mg
- sodium chloride : 8.7 mg

The product contains no antimicrobial preservative.

The macroaggregates number per vial is ranging between 2 and 4 millions.

No macroaggregates has a size higher than 150 µm.

Not more than 10 of them have a size higher than 100µm.

The product is to be used after labelling by the addition of sterile, pyrogen free isotonic sodium pertechnetate [^{99m}Tc] injection, allowing the preparation of Technetium [^{99m}Tc] human albumin macroaggregates injection.

The product is prepared from batches of human albumin but has been screened for hepatitis B surface antigen (HbsAg), antibodies for human immunodeficiency virus (anti-HIV) and antibodies for hepatitis C virus (anti-HCV).

3. PHARMACEUTICAL FORM

Powder for injection.

4. CLINICAL PARTICULARS

4.1. Diagnostic Indications

Pulmonary perfusion scintigraphy.

As secondary indication ^{99m}Tc -albumin macroaggregates may be used for venoscintigraphy.

4.2. Posology and method administration

Recommended activities to be administered intravenously to an adult weighing 70 kg vary between 37 - 185 MBq (1 - 5 mCi). The number of particles per administered dose must be in a range of 60×10^3 - 700×10^3 . The lung test may start immediately after injection.

The activity to be administered in children should be a fraction of the adult activity and should be calculated according to the following equation :

$$\text{Pediatric dose (MBq)} = \frac{\text{Adult dose (MBq)} \times \text{child weight (kg)}}{70 \text{ kg}}$$

Although body weight is the more used factor on which to base the adjustment of the activity administered, in a limited number of cases the body surface area may be considered to be more appropriate.

$$\text{Pediatric dose (MBq)} = \frac{\text{Adult dose (MBq)} \times \text{child surface (m}^2\text{)}}{1.73}$$

In pulmonary scintigraphy, images can be acquired in anterior, right/left oblique, right/left profile and posterior position.

4.3. Contra-indications

There are no specific contra-indications.

4.4. Special warnings and special precautions for use

Radiopharmaceuticals should be used only by authorised persons. Their receipt, use, transfer and disposal are subject to national licensing regulations.

Radiopharmaceuticals should be prepared by the user in a manner which satisfies both radiological safety and pharmaceutical requirements.

The syringe should be 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.

Special care should be exercised when administering ^{99m}Tc -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 -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.

4.5. Interaction with other medicaments and other forms of interaction

Changes in the biological distribution of ^{99m}Tc -MAA are induced by different 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. Pregnancy and lactation

When it is necessary to administer radioactive medicinal products to women of childbearing potential, information should always be sought about pregnancy. Any woman who has missed a period should be assumed to be pregnant until proven otherwise. Where uncertainty exists it is important that radiation exposure should be the minimum consistent with achieving the desired clinical information. Alternative techniques which do not involve ionising radiation should always be considered.

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

Before administering a radioactive medicinal product to a mother who is breast feeding consideration should be given as to whether the investigation could be reasonably delayed until the mother has ceased breast feeding and as to whether the most appropriate choice of radiopharmaceutical has been made, bearing in mind the secretion of radioactivity in breast milk. If the administration is considered necessary, breast feeding should be interrupted for 12 hours and the expressed feeds discarded. Breast feeding can be restarted when the radioactivity level in the milk will not result in a radiation dose to the child greater than 1 mSv.

4.7. Effects on ability to drive and use machines

None are to be expected after use of this product.

4.8. Undesirable effects

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

For each patient, exposure to ionising radiation must be justifiable on the basis of likely benefit. The activity administered must be such that the resulting radiation dose is as low as reasonably achievable bearing in mind the need to obtain the intended diagnostic or therapeutic result.

Exposure to ionising radiation is linked with cancer induction and a potential for development of hereditary defects. For diagnostic nuclear medicine investigations the current evidence suggest that these adverse effects will occur with low frequency because of the low radiation doses incurred.

For most diagnostic investigation using a nuclear medicine procedure the radiation dose delivered (EDE) is less than 20 mSv. Higher doses may be justified in some clinical circumstances.

4.9. Overdose

Overdose, as commonly intended (i.e., excessive quantity in weight) is not expected, but overdose may be understood as the administration of a very high number of particles. The number of MAA particles per adult patient must not exceed 1.5×10^6 .

The dangers to be expected relating to the inadvertent administration of excess radioactivity may be reduced by promoting a diuresis and frequent voiding of urine.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

^{99m}Tc -MAA, when administered in usual doses, show no pharmacodynamic effects detectable clinically and/or analytically.

5.2. Pharmacokinetic properties

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. 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.

The disappearance of activity from the particles in the lungs is governed by a 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.

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.

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 unlabelled product.

5.4. Radiation dosimetry

Technetium [^{99m}Tc] decays with the emission of gamma radiation with energy of 140 keV and a half life of 6 hours to technetium [^{99}Tc] which can be regarded as quasi stable.

For this product the effective dose equivalent resulting from an administered activity of 185 MBq is typically 2.2 mSv (per 70 kg individual).

According to ICRP 53 (1988) the radiation doses absorbed by the patients are the following:

ABSORBED DOSE PER UNIT ADMINISTERED (mGy / MBq)					
Organ	Adult	15 years	10 years	5 years	1 year
*Adrenals	$5.8 \cdot 10^{-3}$	$8.7 \cdot 10^{-3}$	$1.3 \cdot 10^{-2}$	$1.9 \cdot 10^{-2}$	$3.1 \cdot 10^{-2}$
*Bladder wall	$1.0 \cdot 10^{-2}$	$1.3 \cdot 10^{-2}$	$1.9 \cdot 10^{-2}$	$2.8 \cdot 10^{-2}$	$5.1 \cdot 10^{-2}$
Bone surfaces	$3.5 \cdot 10^{-3}$	$4.4 \cdot 10^{-3}$	$6.4 \cdot 10^{-3}$	$9.7 \cdot 10^{-3}$	$1.9 \cdot 10^{-2}$
Breast	$5.6 \cdot 10^{-3}$	$5.5 \cdot 10^{-3}$	$1.0 \cdot 10^{-2}$	$1.4 \cdot 10^{-2}$	$2.2 \cdot 10^{-2}$
GI-tract					
Stomach wall	$4.0 \cdot 10^{-3}$	$5.2 \cdot 10^{-3}$	$7.8 \cdot 10^{-3}$	$1.2 \cdot 10^{-2}$	$2.0 \cdot 10^{-2}$
Small intest	$2.1 \cdot 10^{-3}$	$2.6 \cdot 10^{-3}$	$4.3 \cdot 10^{-3}$	$7.0 \cdot 10^{-3}$	$1.3 \cdot 10^{-2}$
ULI wall	$2.2 \cdot 10^{-3}$	$2.9 \cdot 10^{-3}$	$5.0 \cdot 10^{-3}$	$8.4 \cdot 10^{-3}$	$1.5 \cdot 10^{-2}$
LLI wall	$1.6 \cdot 10^{-3}$	$2.1 \cdot 10^{-3}$	$3.5 \cdot 10^{-3}$	$5.4 \cdot 10^{-3}$	$1.0 \cdot 10^{-2}$
Kidneys	$3.7 \cdot 10^{-3}$	$4.8 \cdot 10^{-3}$	$7.2 \cdot 10^{-3}$	$1.1 \cdot 10^{-2}$	$1.8 \cdot 10^{-2}$
*Liver	$1.6 \cdot 10^{-2}$	$2.1 \cdot 10^{-2}$	$3.0 \cdot 10^{-2}$	$4.3 \cdot 10^{-2}$	$7.5 \cdot 10^{-2}$
Lungs	$6.7 \cdot 10^{-2}$	$9.9 \cdot 10^{-2}$	$1.4 \cdot 10^{-1}$	$2.1 \cdot 10^{-1}$	$4.0 \cdot 10^{-1}$
Ovaries	$1.8 \cdot 10^{-3}$	$2.3 \cdot 10^{-3}$	$3.7 \cdot 10^{-3}$	$5.9 \cdot 10^{-3}$	$1.1 \cdot 10^{-2}$
*Pancreas	$5.8 \cdot 10^{-3}$	$7.5 \cdot 10^{-3}$	$1.1 \cdot 10^{-2}$	$1.7 \cdot 10^{-2}$	$2.9 \cdot 10^{-2}$
Red marrow	$4.4 \cdot 10^{-3}$	$6.2 \cdot 10^{-3}$	$8.3 \cdot 10^{-3}$	$1.1 \cdot 10^{-2}$	$1.7 \cdot 10^{-2}$
*Spleen	$4.4 \cdot 10^{-3}$	$5.6 \cdot 10^{-3}$	$8.3 \cdot 10^{-3}$	$1.3 \cdot 10^{-2}$	$2.2 \cdot 10^{-2}$
Testes	$1.1 \cdot 10^{-3}$	$1.4 \cdot 10^{-3}$	$2.3 \cdot 10^{-3}$	$3.7 \cdot 10^{-3}$	$7.1 \cdot 10^{-3}$
Thyroid	$2.0 \cdot 10^{-3}$	$3.3 \cdot 10^{-3}$	$5.5 \cdot 10^{-3}$	$9.0 \cdot 10^{-3}$	$1.6 \cdot 10^{-2}$
Uterus	$2.4 \cdot 10^{-3}$	$2.9 \cdot 10^{-3}$	$4.6 \cdot 10^{-3}$	$7.1 \cdot 10^{-3}$	$1.3 \cdot 10^{-2}$
Other tissue	$2.9 \cdot 10^{-3}$	$3.6 \cdot 10^{-3}$	$5.2 \cdot 10^{-3}$	$7.8 \cdot 10^{-3}$	$1.4 \cdot 10^{-3}$
Effective dose equivalent (mSv/MBq)	$1.2 \cdot 10^{-2}$	$1.8 \cdot 10^{-2}$	$2.5 \cdot 10^{-2}$	$3.8 \cdot 10^{-2}$	$6.9 \cdot 10^{-2}$

For an administered activity of 185 MBq, the typical radiation dose to the target organ, lungs, is 12.3 mGy and the typical radiation dose to the critical organs (*), adrenals, bladder wall, liver, pancreas, spleen, are 1.07, 1.85, 2.96, 1.07 and 0.81 mGy respectively.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Human albumin
Stannous chloride dihydrate
Sodium chloride

6.2. Incompatibilities

None known.

6.3. Shelf life

The expiry date for this kit is 12 months from the day of manufacture.
The expiry date is indicated on the outer packaging and on each vial.
The expiry date for the labelled product is 8 hours after labelling.

6.4. Special precautions for storage

The kit should be stored at a temperature ranging between +2 °C and +8 °C.

The labelled product should be stored at a temperature ranging between +2 °C and +8 °C.

6.5. Nature and contents of container

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

6.6. Instructions for use / handling

Method of preparation

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 (from 2.5 to maximum 100 mCi).

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

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 shaken before each withdrawal in order to homogenise the suspension.

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.

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

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 labelling 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 :

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

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 labelling 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 (1,2,3 and 4 mCi). See tables 3,4,5 and 6.

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

TABLE 1**DETERMINATION OF THE LABELLING 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		







-  Labelling 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 LABELLING VOLUME OF THE VIAL AND THE VOLUME TO INJECT AND CONSIDERING A VIAL CONTAINING 3 MILLIONS MAA PARTICLES

VOLUME OF LABELLING (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

-  Labelling 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 LABELLING VOLUME, THE VOLUME AND THE RADIOACTIVITY TO INJECT AND CONSIDERING A VIAL CONTAINING 3 MILLIONS MAA PARTICLES



	37 MBq			74 MBq			111 MBq			148 MBq		
	0.5	0.8	1	0.5	0.8	1	0.5	0.8	1	0.5	0.8	1
3	222	139	111	444			666			888		
4	296	185	148	592	370		888	555		1184	740	
5	370	231	185	740	462	370	1110	694	555	1480	925	740
6	444	277	222	888	555	444	1332	832	666	1776	1110	888
7	518	324	259	1036	647	518	1554	980	777	2072	1295	1036
8	592	370	296	1184	740	592	1776	1110	888	2368	1480	1184
9	666	416	333	1332	832	666	1998	1249	999	2664	1665	1332
10	740	462	370	1480	925	740	2220	1387	1110	2960	1850	1480

Table 3

Table 4

Table 5

Table 6

 **Injected activity (MBq)**
 **Total activity (MBq)**



 **Injected volume (ml)**
 **Labelling volume (ml)**

TABLE 7

^{99m}Tc (HALF-LIFE : 6.02 hours) DECAY TABLE											
H	%	H	%	H	%	H	%	H	%	H	%
Min		Min		Min		Min		Min		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

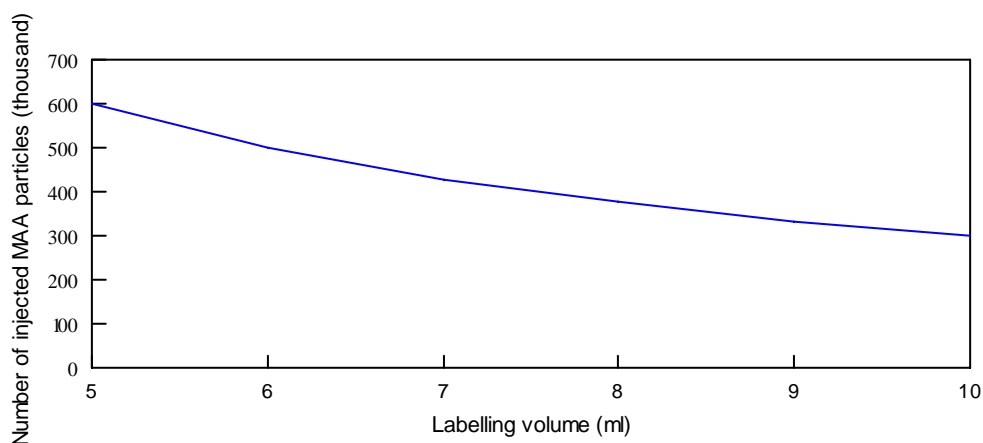
The following table and curve allow to determine the number of MAA particles injected when volumes of labelling are 5 to 10 ml and when the volume to inject is 1 ml.

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 :

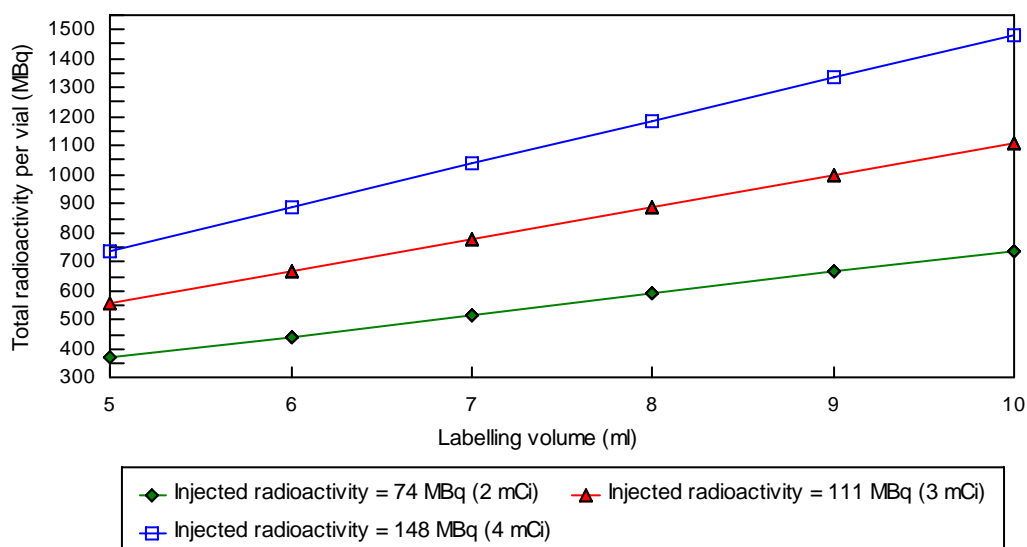
$$\text{Number of injected MAA particles} = \frac{\text{Total number of MAA particles} \times \text{Injected volume}}{\text{Labelling volume}}$$

Volume of labelling (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 (2, 3 or 4 mCi) with a injected volume of 1 ml and considering a vial containing 3 millions particles.

Volume of labelling (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 labelling (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. Waste must be disposed of according to national regulations.

7. MARKETING AUTHORISATION HOLDER

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