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Mattawan, Michigan 49071 USA
Telephone: 269.668.3336
Fax: 269.668.4151

May 21, 2010

Ms. Patricia Pelke
Materials Licensing Branch
U.S. Nuclear Regulatory Commission, Region III
2443 Warrenville Road, Suite 210
Lisle, IL 60532-4352

RE: Materials License 21-11315-02
Request for license amendment to add authorization for a ^{137}Cs sealed calibration source
and a $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ generator

Dear Ms. Pelke,

MPI Research is requesting an amendment to Materials License 21-11315-02, as described in this letter and attachment. The request is for addition of two items to sections 6 - 8 of the license (a ^{137}Cs sealed calibration source and a $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ generator) to support emergent business requirements.

The ^{137}Cs sealed calibration source is a 0.250 mCi Eckert & Ziegler Isotope Products source model RV-XXX, part number RV-137-U250. The SSSR Safety Evaluation is enclosed. This source will be used as a PET scanner calibration source.

The $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ generator is a Covidien Ultra-Technekow DTE, with a maximum ^{99}Mo activity of 16 Ci. The 16 Ci model (Covidien order # N894) would be the maximum activity needed; actual generator sizing would depend on the needs of the specific imaging studies to be performed. MPI Research requests authorization to possess two such generators at any given time, to prevent possible delays in study schedules. Technekow generator information, package insert, and Material Safety Data Sheet are enclosed for your information. Generators using tungsten or depleted uranium shielding will be returned to Covidien after use. Appropriate shielding will be used for elutions.

Please contact me at 269-668-3336 extension 2050, if there are any questions, or if further information is required.

Sincerely,

Richard Granberg, CHP
Radiation Safety Officer
MPI Research, Inc

RECEIVED MAY 25 2010

REGISTRY OF RADIOACTIVE SEALED SOURCES AND DEVICES
SAFETY EVALUATION OF SEALED SOURCE
(CORRECTED PAGE 1 - March 26, 1999)

NO.: CA0406S148S

November 1, 1998

PAGE 1 OF 4

SEALED SOURCE TYPE: Gamma Calibration Source

MODEL: RV-XXX, EG-XXX series LV, EG-XXX series LVM

MANUFACTURER/DISTRIBUTOR: Isotope Products Laboratories
1800 North Keystone Street
Burbank, CA 91504
(818) 843-7000 (voice)
(818) 843-6168 (fax)

ISOTOPE:

Any Gamma Emitter

MAXIMUM ACTIVITY:

10 millicuries

LEAK TEST FREQUENCY: 6 Months

PRINCIPAL USE: (I) Calibration Sources (activity greater than 30 microcuries)

CUSTOM SOURCE: _____ YES X NO

REGISTRY OF RADIOACTIVE SEALED SOURCES AND DEVICES
SAFETY EVALUATION OF SOURCE.
(AMENDED IN ITS ENTIRETY)

NO.: CA0406S148S

DATE: November 1, 1998

PAGE: 2 of 4

SEALED SOURCE TYPE: Gamma Calibration Sources

DESCRIPTION:

The XXX represents nuclide mass, preceded by RV (Reference Volume) or EG (Epoxy Gamma). The series LV and LVM are Large Volume and Large Volume Marinelli, respectively. Model RV-XXX are polyethylene bottles up to 30 milliliters in size and Model EG-XXX series LV are polyethylene bottles up to 1000 milliliters. Model EG-XXX series LVM are polyvinylchloride marinelli beakers of various sizes.

The source consists of a solubilized metal (gamma emitter) salt uniformly dispersed in a epoxy matrix and cast into the appropriate plastic container. The container is then closed with the appropriate cap.

LABELING:

The source is identified with a pressure sensitive label on which is imprinted IPL, nuclide, activity, date of manufacture, serial number a radiation symbol and the words "Caution Radioactive Materials".

DIAGRAM: (See Attachments)

Attachment 1: Model RV-XXX and EG-XXX

Attachment 2: Marinelli Beaker Model EG-XXX series LVM

CONDITIONS OF NORMAL USE:

These gamma sources are designed for use in a laboratory environment for calibration of instruments.

PROTOTYPE TESTING:

Prototype tests have shown the type M sources pass the criteria for calibration sources (greater than 30 microcuries) and have been assigned a classification of ANSI 77C22212 in accordance with ANSI N.542, 1977.

REGISTRY OF RADIOACTIVE SEALED SOURCES AND DEVICES
SAFETY EVALUATION OF SOURCE.
(AMENDED IN ITS ENTIRETY)

NO.: CA0406S148S

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PAGE: 3 of 4

SEALED SOURCE TYPE: Gamma Calibration Sources

EXTERNAL RADIATION LEVELS:

Actual radiation levels will vary with isotope and activity level.

QUALITY ASSURANCE AND CONTROL:

Isotope Products Laboratories maintains a quality assurance and control program which has been deemed acceptable for licensing purposes by the California Department of Health Services. A copy of the program is on file with the California Department of Health Services.

LIMITATIONS AND/OR OTHER CONSIDERATIONS OF USE:

1. The source shall be distributed to persons specifically licensed by the NRC or an Agreement State.
2. Handling, storage, use, transfer, and disposal: To be determined by the licensing authority.
3. Sources which contain greater than 100 μCi of Beta/Gamma emitting material shall be leak tested at intervals not to exceed 6 months using techniques capable of detecting 0.005 microcuries (185 Bq) of removable contamination. Source loadings of less than 100 μCi are exempt from leak testing by the Issuing Agency. Leak testing shall be in accordance with the individual requirements of the radiation control agency which exercises regulatory authority.
4. The source shall not be subjected to conditions that exceed its ANSI 77C22212.
5. This registration sheet and the information contained within the references shall not be changed without the written consent of the California Department of Health Services.

REGISTRY OF RADIOACTIVE SEALED SOURCES AND DEVICES
SAFETY EVALUATION OF SOURCE.
(AMENDED IN ITS ENTIRETY)

NO.: CA0406S148S

DATE: November 1, 1998

PAGE: 4 of 4

SEALED SOURCE TYPE: Gamma Calibration Sources

SAFETY ANALYSIS SUMMARY:

Based on our review of the information and test data cited below, we conclude that the Models RV-XXX, EG-XXX series LV and EG-XXX series LVM sources are acceptable for licensing purposes. They have passed the tests for calibration sources in accordance with ANSI N.542 (1977). Furthermore, this source design has been in use for several years without any known problems.

REFERENCES:

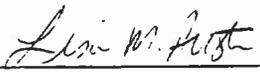
This certificate of registration is based on information and test data contained in the following supporting documents which are hereby incorporated by reference and made part of this registry document:

1. Isotope Products Laboratories application dated March 15, 1985.
2. Isotope Products Laboratories dated August 5, 1985, with attachments thereto.
3. Isotope Products Laboratories dated January 31, 1986, with attachments thereto.
4. Isotope Products Laboratories letter dated April 16, 1998.

ISSUING AGENCY: California Department of Health Services

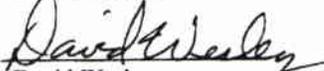
DATE: November 1, 1998

REVIEWED BY:


Lisa M. Austin

DATE: November 1, 1998

CONCURRED BY:


David Wesley

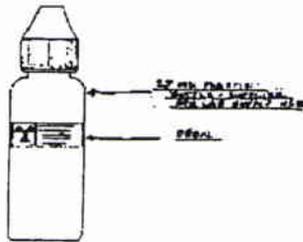
**REGISTRY OF RADIOACTIVE SEALED SOURCES AND DEVICES
SAFETY EVALUATION OF SEALED SOURCE
(AMENDED IN ITS ENTIRETY)**

NO.: CA0406S148S

DATE: November 1, 1998

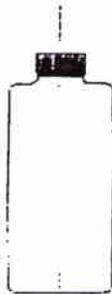
ATTACHMENT: 1

SEALED SOURCE TYPE: Gamma Calibration Source



Model RV-XXX

ISOTOPE PRODUCTS LABORATORIES		
Reference Source		
Model	RV-XXX	Label No. 500
Date	11/1/98	Lot No.
REFERENCE SOURCE FOR ISOTOPE CALIBRATION		
Activity		Activity at Date
		11/1/98



Model EG-XXX

ISOTOPE PRODUCTS LABORATORIES		
Reference Source		
Model	EG-XXX	Label No. 500
Date	11/1/98	Lot No.
REFERENCE SOURCE FOR ISOTOPE CALIBRATION		
Activity		Activity at Date
		11/1/98

REGISTRY OF RADIOACTIVE SEALED SOURCES AND DEVICES
 SAFETY EVALUATION OF SEALED SOURCE
 (AMENDED IN ITS ENTIRETY)

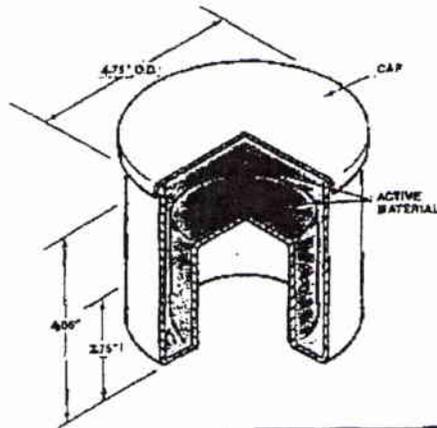
NQ: CA0406S148S

November 1, 1998

ATTACHMENT: 2

SEALED SOURCE TYPE: Gamma Calibration Source

MARINELLI BEAKER



ISOTOPE PRODUCTS LABORATORIES <small>(BURBANK, CALIFORNIA 91504)</small>		
CODE	APPROVED BY	DRAWN BY
DATE DEC 85		REV TO DO
MARINELLI BEAKER		
MODEL B6 JXXX SERIES LVM		352



Ultra-Technekow™ DTE Technetium Tc 99m Generator

The Ultra-Technekow dry-top eluting (DTE) generator is prepared with fission-produced Mo 99 absorbed onto alumina in a lead shielded column. This generator provides a closed system for the production of sterile metastable technetium 99m (Tc 99m), which is produced by the decay of Mo 99. These solutions should be clear, colorless, and free from any particulate matter.

A four day production schedule and variety of size offerings afford the flexibility needed to meet most departments' activity requirements on the days you need it the most. Designed to provide enhanced radiation protection, the Ultra-Technekow DTE generator, through the use of tungsten and depleted uranium (DU) shielding

in our larger activity offerings, aids in decreasing the occupational exposure to you and your staff. Sterile, non-pyrogenic isotonic solutions of sodium pertechnetate Tc 99m can be obtained conveniently by periodic aseptic elution of the generator.

Important Safety Information

Allergic reactions including anaphylaxis have been reported infrequently following the administration of sodium pertechnetate Tc 99m. Radiation risks associated with the use of sodium pertechnetate Tc 99m are greater in pediatric patients than in adults and, in general, the younger the patient the greater the risk owing to greater absorbed radiation doses and longer life expectancy. These greater risks should be taken firmly into account in all benefit/risk assessments involving pediatric patients. Each eluate of the generator should be tested and should not contain more than the USP limit of 0.15 microcuries of molybdenum 99 per millicurie of technetium 99m per administered dose at the time of administration. Use link to package insert for full prescribing information.

*On order information, abbreviation indicates type of internal shielding available: (L=Lead, T-Tungsten, DU=Depleted Uranium). Tungsten and depleted uranium shields are required to be returned. Please contact your local sales representative for return program training.

**On order information, each unit comes with an option of a 10mL or 20mL accessory pack (indicate with order).

Order Information

Description	Qty	Unit	Size	Order #	11 Digit NDC
Generator, Mo99 (DU)*	1	each	11.0 Ci	N892**	
Generator, Mo99 (DU)*	1	each	14.0 Ci	N893**	
Generator, Mo99 (DU)*	1	each	16.0 Ci	N894**	
Generator, Mo99 (DU)*	1	each	19.0 Ci	N895**	
Generator, Mo99 (L)*	1	each	1.5 Ci	N884**	
Generator, Mo99 (L)*	1	each	1.0 Ci	N883**	
Generator, Mo99 (L)*	1	each	2.0 Ci	N885**	
Generator, Mo99 (L)*	1	each	2.5 Ci	N886**	
Generator, Mo99 (L)*	1	each	3.0 Ci	N887**	
Generator, Mo99 (L)*	1	each	3.5 Ci	N888**	
Generator, Mo99 (L/T)*	1	each	7.5 Ci	N891**	

Generator, Mo99 (L/T)*	1	each	5.0 Ci	N889**
Generator, Mo99 (L/T)*	1	each	6.0 Ci	N890**

Features and Benefits

Features	Benefits
Efficiency	Our four-day generator production schedule and extensive delivery infrastructure provides customers excellent flexibility- helping to ensure generators with the required activity are delivered on the days you need them most.
Radiation Protection	As a result of our investment in Depleted Uranium (DU), tungsten, and robust auxiliary shielding, we provide a complete radiation protection system that is designed to minimize occupational exposure.

Frequently Asked Questions

Question	Answer
How many days a week are generators manufactured?	We manufacture generators four days a week: Sunday, Monday, Wednesday and Friday.
How do I place an order for a generator?	Generators can be ordered through your local Nuclear Medicine Specialist, or our Customer Service Department at 888-744-1414. A two-week order processing time has been established to allow adequate time to verify RAM licensing and to secure the required raw materials.
How do I go about making changes to a current standing order?	All standing order changes or cancellations are handled by the Customer Service Department at 888-744-1414. A two-week processing time on standing order changes or cancellations is required.
Who do I contact for additional safety or usage questions?	Call Imaging Solutions Product Monitoring at (800) 778-7898.

How Supplied

Distribution	Direct/Distributor
Calibration Day	Sunday, Monday, Wednesday and Friday each week
Expiration	14 days post manufacture
Storage Conditions	Controlled room temperature 20-25°C (68°F-77°F)

Indications for Use

Sodium pertechnetate Tc 99m is used IN ADULTS as an agent for: Brain imaging (including cerebral radionuclide angiography); thyroid imaging; salivary gland imaging; placenta localization; blood pool imaging (including radionuclide angiography); urinary bladder imaging (direct isotopic cystography) for detection of vesico-ureteral reflux; nasolacrimal drainage system imaging (dacryoscintigraphy)

Sodium pertechnetate Tc 99m is used IN PEDIATRIC PATIENTS as an agent for: Brain imaging (including cerebral radionuclide angiography); thyroid imaging; blood pool imaging (including radionuclide angiography); urinary bladder imaging (direct isotopic cystography) for the detection of vesico-ureteral reflux

Contraindications

None known.

Warnings

Radiation risks associated with the use of sodium pertechnetate Tc 99m are greater in pediatric patients than in adults and, in general, the younger the patient the greater the risk owing to greater absorbed radiation doses and longer life expectancy. These greater risks should be taken firmly into account in all benefit risk assessments involving pediatric patients. Only use generator eluant specified for use with the Ultra-Technekow DTE generator. Do not use any other generator eluant or saline from any other source.

**Ultra-TechneKow® DTE
(Technetium Tc-99m Generator)**

Rx Only

For the Production of
Sodium Pertechnetate Tc-99m Injection

DESCRIPTION

The Ultra-TechneKow® DTE Generator is prepared with fission-produced molybdenum Mo-99 adsorbed onto alumina in a lead shielded column. This generator provides a closed system for the production of sterile metastable technetium Tc-99m, which is produced by the decay of molybdenum Mo-99. Sterile, non-pyrogenic isotonic solutions of Sodium Pertechnetate Tc-99m can be obtained conveniently by periodic aseptic elution of the generator. These solutions should be clear, colorless, and free from any particulate matter.

The carrier-free solution may be used as is, or diluted to the proper concentration. Over the life of the generator, an elution will contain an amount of technetium Tc-99m in direct proportion to the quantity of Mo-99 decay since the previous elution of the generator. The exact quantity of Tc-99m in the eluate is determined by column elution efficiency, quantity of Mo-99 on the column, and the elapsed time between elutions.

Each eluate of the generator should not contain more than the USP limit of 0.15 kilobecquerel molybdenum Mo-99 per megabecquerel technetium Tc-99m (0.15 microcurie Mo-99 per millicurie Tc-99m) per administered dose at the time of administration and an aluminum ion concentration of not more than 10 micrograms per milliliter of the generator eluate, both of which must be determined by the user before administration.

Since the eluate does not contain an antimicrobial agent, it should not be used after 12 hours from the time of generator elution.

Physical Characteristics

Technetium Tc-99m decays by isomeric transition with a physical half-life of 6.02 hours. The principal photon that is useful for detection and imaging studies is listed in Table 1.

Table 1. Principal Radiation Emission Data

Radiation	Mean Percent Per Disintegration	Energy (keV)
Gamma-2	89.07	140.5

External Radiation

The specific gamma ray constant for technetium Tc-99m is 0.78 R/hr-mCi at 1 cm. The first half-value layer is 0.017 cm of lead (Pb). A range of values for the relative attenuation of the radiation emitted by this radionuclide that results from interposition of various thicknesses of Pb is shown in Table 2. For example, the use of 0.25 cm thickness of Pb will attenuate the radiation emitted by a factor of about 1000.

Table 2. Radiation Attenuation by Lead Shielding

Shield Thickness (Pb) cm	Coefficient of Attenuation
0.017	0.5
0.08	10 ¹
0.16	10 ²
0.25	10 ³
0.33	10 ⁴

Molybdenum Mo-99 decays to technetium Tc-99m with a molybdenum Mo-99 half-life of 2.75 days. The physical decay characteristics of molybdenum Mo-99 are such that only 88.6% of the decaying molybdenum Mo-99 atoms form technetium Tc-99m. Generator elutions may be made at any time, but the amount of technetium Tc-99m available will depend on the interval measured from the last elution. Approximately 47% of the maximum available technetium Tc-99m is reached after 6 hours and 95% after 23 hours. To correct for physical decay of technetium Tc-99m, the fractions that remain at selected intervals of time are shown in Table 3.

Table 3. Physical Decay Chart; Technetium Tc-99m, Half-Life 6.02 Hours

Hours	Fraction Remaining	Hours	Fraction Remaining
0*	1.000	7	0.447
1	0.891	8	0.398
2	0.794	9	0.355
3	0.708	10	0.316
4	0.631	11	0.282
5	0.562	12	0.251
6	0.501		

* Calibration Time

* Koehler, David C. "Radioactive Decay Data Tables", DOE/TIC-11026, 138 (1981).

CLINICAL PHARMACOLOGY

The pertechnetate ion distributes in the body similarly to the iodide ion but is not organified when trapped in the thyroid gland. Pertechnetate tends to accumulate in intracranial lesions with excessive neovascularity or an altered blood-brain barrier. It also concentrates in the thyroid gland, salivary glands, stomach and choroid plexus. After intravenous administration it remains in the circulatory system for sufficient time to permit blood pool, organ perfusion, and major vessel studies. It gradually equilibrates with the extracellular space. A fraction is promptly excreted via the kidneys.

Following the administration of Sodium Pertechnetate Tc-99m as an eye drop, the drug mixes with tears within the conjunctival space. Within seconds to minutes it leaves the conjunctival space and escapes into the inferior meatus of the nose through the nasolacrimal drainage system. During this process the pertechnetate ion passes through the canaliculi, the lacrimal sac and the nasolacrimal duct. In the event of any anatomical or functional blockage of the drainage system there will be a backflow resulting in tearing (epiphora). Thus the pertechnetate escapes the conjunctival space in the tears.

While the major part of the pertechnetate escapes within a few minutes of normal drainage and tearing, it has been documented that there is some degree of transconjunctival absorption with turnover of 1.5% per minute in normal individuals, 2.1% per minute in patients without any sac and 2.7% per minute in patients with inflamed conjunctiva due to chronic dacryocystitis. Individual values may vary but these rates are probably representative and indicate that the maximum possible pertechnetate absorbed will remain below one thousandth of that used in other routine diagnostic procedures.

INDICATIONS AND USAGE

Sodium Pertechnetate Tc-99m is used **IN ADULTS** as an agent for:

- Brain Imaging (including cerebral radionuclide angiography)
- Thyroid Imaging
- Salivary Gland Imaging
- Placenta Localization
- Blood Pool Imaging (including radionuclide angiography)
- Urinary Bladder Imaging (direct isotopic cystography for detection of vesico-ureteral reflux)
- Nasolacrimal Drainage System Imaging (dacryoscintigraphy)

Sodium Pertechnetate Tc-99m is used **IN PEDIATRIC PATIENTS** as an agent for:

- Brain Imaging (including cerebral radionuclide angiography)
- Thyroid Imaging
- Blood Pool Imaging (including radionuclide angiography)
- Urinary Bladder Imaging (direct isotopic cystography for the detection of vesico-ureteral reflux)

CONTRAINDICATIONS

None known.

WARNINGS

Radiation risks associated with the use of Sodium Pertechnetate Tc-99m are greater in pediatric patients than in adults and, in general, the younger the patient the greater the risk owing to greater absorbed radiation doses and longer life expectancy. These greater risks should be taken firmly into account in all benefit risk assessments involving pediatric patients.

Only use generator eluant specified for use with the Ultra-TechneKow® DTE Generator. Do not use any other generator eluant or saline from any other source.

PRECAUTIONS

As in the use of any radioactive material, care should be taken to minimize radiation exposure to the patient consistent with proper patient management and to insure minimum radiation exposure to occupational workers.

Radiopharmaceuticals should be used only by physicians who are qualified by training and experience in the safe use and handling of radionuclides and whose experience and training have been approved by the appropriate government agency authorized to license the use of radionuclides.

After the termination of the nasolacrimal imaging procedure, blowing the nose and washing the eyes with sterile distilled water or an isotonic sodium chloride solution will further minimize the radiation dose.

Since the eluate does not contain an antimicrobial agent, it should not be used after 12 hours from time of generator elution.

Carcinogenesis, Mutagenesis, Impairment of Fertility

No long-term animal studies have been performed to evaluate carcinogenic or mutagenic potential or whether Sodium Pertechnetate Tc-99m may affect fertility in males or females.

Pregnancy Category C

Animal reproductive studies have not been conducted with Sodium Pertechnetate Tc-99m. It is also not known whether Sodium Pertechnetate Tc-99m can cause fetal harm when administered to a pregnant woman or can

affect reproductive capacity. Sodium Pertechnetate Tc-99m should be given to pregnant women only if the expected benefits to be gained clearly outweigh the potential hazards.

Ideally, examinations using radiopharmaceutical drug products - especially those elective in nature - of women of childbearing capability should be performed during the first ten days following the onset of menses.

Nursing Mothers

Technetium Tc-99m is excreted in human milk during lactation, therefore, formula-feedings should be substituted for breast-feedings.

Pediatric Use

See **INDICATIONS AND USAGE** and **DOSAGE AND ADMINISTRATION** sections. Also see the description of additional risk under **WARNINGS**.

ADVERSE REACTIONS

Allergic reactions including anaphylaxis have been reported infrequently following the administration of Sodium Pertechnetate Tc-99m.

DOSAGE AND ADMINISTRATION

Sodium Pertechnetate Tc-99m is usually administered by intravenous injection, but can be given orally. When imaging the nasolacrimal drainage system, instill the Sodium Pertechnetate Tc-99m by the use of a device such as a micropipette or similar method which will ensure the accuracy of the dose.

For imaging the urinary bladder and ureters (direct isotopic cystography), the Sodium Pertechnetate Tc-99m is administered by direct instillation aseptically into the bladder via a urethral catheter, following which the catheter is flushed with approximately 200 mL of sterile saline directly into the bladder.

The dosage employed varies with each diagnostic procedure. If the oral route is elected, the patient should fast for at least six (6) hours before and two (2) hours after administration.

The suggested dose ranges employed for various diagnostic indications in the average ADULT PATIENT (70 kg) are as follows:

- Vesico-ureteral imaging: 18.5 to 37 MBq (0.5 to 1 mCi)
- Brain imaging: 370 to 740 MBq (10 to 20 mCi)
- Thyroid gland imaging: 37 to 370 MBq (1 to 10 mCi)
- Salivary gland imaging: 37 to 185 MBq (1 to 5 mCi)
- Placenta localization: 37 to 111 MBq (1 to 3 mCi)
- Blood pool imaging: 370 to 1110 MBq (10 to 30 mCi)
- Nasolacrimal drainage system: Maximum dose of 3.7 MBq (100 µCi)

The recommended dosages in PEDIATRIC PATIENTS are:

- Vesico-ureteral imaging: 18.5 to 37 MBq (0.5 to 1 mCi)
- Brain imaging: 5.18 to 10.36 MBq (140 to 280 µCi) per kg body weight
- Thyroid gland imaging: 2.22 to 2.96 MBq (60 to 80 µCi) per kg body weight
- Blood pool imaging: 5.18 to 10.36 MBq (140 to 280 µCi) per kg body weight

Minimum dose of 111 to 185 MBq (3 to 5 mCi) should be employed if radionuclide angiography is performed as part of the brain imaging or blood pool imaging procedures.

NOTE: Up to 1 gram of pharmaceutical grade potassium perchlorate in a suitable base or capsule may be given orally prior to administration of Sodium Pertechnetate Tc-99m for brain imaging, placenta localization and blood pool imaging. When Sodium Pertechnetate Tc-99m is used in pediatric patients for brain or blood pool imaging, administration of potassium perchlorate is especially important to minimize the absorbed radiation dose to the thyroid gland.

The patient dose should be measured by a suitable radioactivity calibration system immediately prior to administration.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit. The solution to be administered as the patient dose should be clear, colorless, and contain no particulate matter.

Radiation Dosimetry

The estimated absorbed radiation doses* to an average ADULT patient (70 kg) from an intravenous injection of a maximum dose of 1110 megabecquerels (30 millicuries) of Sodium Pertechnetate Tc-99m distributed uniformly in the total body of subjects not pretreated with blocking agents, such as pharmaceutical grade potassium perchlorate, are shown in Table 4. For placental localization studies, when a maximum dose of 111 megabecquerels (3 millicuries) is used, it is assumed to be uniformly equilibrated between maternal and fetal tissues.

* Modified from: Summary of Current Radiation Dose Estimates to Normal Humans from Tc-99m as Sodium Pertechnetate, MIRD Dose Estimate Report No. 8, J. Nucl. Med., 17 (1):74-7, 1976.

A88010 R112706

ULTRA-
TECHNEKOW® DTE
(TECHNETIUM Tc-99m
GENERATOR)

883/895

Ultra-TechneKow® DTE
(Technetium Tc-99m Generator)

Table 4. Absorbed Radiation Doses from Intravenous Injection (ADULTS)

Tissue	1110 MBq (30 mCi) Dose				111 MBq (3 mCi) Dose	
	Resting Population		Active Population		mGy	rads
	mGy	rads	mGy	rads		
Bladder Wall	15.9	1.59	25.5	2.55		
Gastrointestinal Tract:						
Stomach wall	75.0	7.50	15.3	1.53		
Upper large intestine wall	20.4	2.04	36.0	3.60		
Lower large intestine wall	18.3	1.83	33.0	3.30		
Red Marrow	5.7	0.57	5.1	0.51		
Testes	2.7	0.27	2.7	0.27		
Ovaries	6.6	0.66	9.0	0.90		
Thyroid	39.0	3.90	39.0	3.90		
Brain	4.2	0.42	3.6	0.36		
Total Body	4.2	0.42	3.3	0.33		
Placenta					0.5	0.05
Fetus					0.5	0.05

The estimated absorbed radiation doses to an ADULT patient from the nasolacrimal imaging procedure using a maximum dose of 3.7 megabecquerels (100 microcuries) of Sodium Pertechnetate Tc-99m are shown in Table 5.

Table 5. Absorbed Radiation Doses from Dacryoscintigraphy

Tissue	3.7 MBq (100 µCi) Dose of Sodium Pertechnetate Tc-99m	
	mGys	rads
Eye Lens:		
If lacrimal fluid turnover is 16%/min	0.140	0.014
If lacrimal fluid turnover is 100%/min	0.022	0.002
If drainage system is blocked	4.020	0.402
Total Body*	0.011	0.001
Ovaries*	0.030	0.003
Testes*	0.009	0.001
Thyroid*	0.130	0.013

* Assuming no blockage of draining system. MIRD Dose Estimate Report No. 8. J. Nucl. Med. 17:74-77, 1976.

In PEDIATRIC patients, the maximum radiation doses when a dose of 185 megabecquerels (5 millicuries) Sodium Pertechnetate Tc-99m is administered to a neonate (3.5 kg) for brain or blood pool imaging with radionuclide angiography are shown in Table 6.

In pediatric patients, an average 30 minute exposure to 37 megabecquerels (1 millicurie) of Sodium Pertechnetate Tc-99m following instillation for direct cystography, results in an estimated absorbed radiation dose of approximately 300 micrograys (30 millirads) to the bladder wall and 40 to 50 micrograys (4 to 5 millirads) to the gonads.*

Table 6. Absorbed Radiation Doses from Intravenous Injection (PEDIATRIC)

Tissue	37 MBq (1 mCi) Dose		185 MBq (5 mCi) Dose	
	mGys	rads	mGys	rads
Thyroid (without perchlorate)	46.0	4.60	230.0	23.0
Thyroid (with perchlorate)	9.7	0.97	48.5	4.85
Large Bowel (with perchlorate)	19.0	1.90	95.5	9.55
Testes	1.0	0.10	5.1	0.51
Ovaries	2.2	0.22	11.0	1.10
Total Body	1.5	0.15	7.6	0.76

* Conway, J.J., et al., Direct and indirect radionuclide cystography. J. Urol. 113:689-693, May 1975.

HOW SUPPLIED

The Ultra-TechneKow® DTE (Technetium Tc-99m) Generators contain the following amount of molybdenum Mo-99 at the date and time of calibration stated on the label.

Catalog No.	Activity	(Curie)
883	37 gigabecquerels	(1.0 curie)
NDC 0019-9883-03		
884	55.5 gigabecquerels	(1.5 curies)
NDC 0019-9884-04		
885	74 gigabecquerels	(2.0 curies)
NDC 0019-9885-05		
886	92.5 gigabecquerels	(2.5 curies)
NDC 0019-9886-06		
887	111 gigabecquerels	(3.0 curies)
NDC 0019-9887-07		
888	129.5 gigabecquerels	(3.5 curies)
NDC 0019-9888-08		
889	185 gigabecquerels	(5.0 curies)
NDC 0019-9889-09		
890	222 gigabecquerels	(6.0 curies)
NDC 0019-9890-10		
891	277.5 gigabecquerels	(7.5 curies)
NDC 0019-9891-11		
892	407 gigabecquerels	(11.0 curies)
NDC 0019-9892-12		
893	518 gigabecquerels	(14.0 curies)
NDC 0019-9893-13		
894	592 gigabecquerels	(16.0 curies)
NDC 0019-9894-14		
895	703 gigabecquerels	(19.0 curies)
NDC 0019-9895-15		

Each generator is supplied with the following components for the elution of the generator:

- 7 - Evacuated Collecting Vials, 10 mL, Sterile, Non-Pyrogenic
- or
- 5 - Evacuated Collecting Vials, 20 mL, Sterile, Non-Pyrogenic
- 7 - 70% (v/v) Isopropyl Alcohol Wipes
- 7 - Pressure-sensitive "Caution - Radioactive Material" collecting vial labels
- 7 - Pressure-sensitive radioassay data labels for lead elution shield
- 1 - Generator Eluant Vial, 135 mL, Sterile, Non-Pyrogenic
- or
- 2 - Generator Eluant Vials, 135 mL, Sterile, Non-Pyrogenic
- 1 - TechneStat™ Vial, 5 mL, containing 0.5 mL of 1.5 mg/mL methylparaben and 0.2 mg/mL propylparaben
- 1 - Package Insert

The sterile, non-pyrogenic solution used to elute the generator column contains 0.9% sodium chloride. The eluant does not contain an antimicrobial agent.

EVAQUATED COLLECTING VIALS. Collecting vials are available on request in 10 and 20 milliliter sizes.

Storage

Store generator and Sodium Pertechnetate Tc-99m solution at controlled room temperature 20° to 25°C (68° to 77°F) [see USP Controlled Room Temperature].

Expiration Date

The generator should not be used after the expiration date stated on the label.

The expiration time of the Sodium Pertechnetate Tc-99m solution is not later than 12 hours after time of elution. If the eluate is used to reconstitute a kit, the radiolabeled kit should not be used after 12 hours from the time of

generator elution or after the expiration time stated on the labeling for the prepared drug, whichever is earlier.

Directions for Use of the Technetium Tc-99m Generator

NOTE 1: Immediately upon delivery, the generator should be placed within a minimum of one-inch of lead shielding in such a manner so as to minimize radiation exposure to attending personnel.

NOTE 2: Wear waterproof gloves during the elution procedure and during subsequent reconstitution of kits with the eluate.

NOTE 3: Use a shielded syringe to withdraw patient dose or to transfer Sodium Pertechnetate Tc-99m into mixing vials during kit reconstitution.

NOTE 4: The needles in the generator are sterile beneath their covers, and the generator has been cleaned underneath the top cover. Additional disinfection of these areas with agents containing alcohol may unfavorably influence the Tc-99m yield.

Eluting the generator every 24 hours will provide optimal amounts of Sodium Pertechnetate Tc-99m. However, the generator may be eluted whenever sufficient amounts of technetium Tc-99m have accumulated within the column.

For Example

Time After First Elution (hrs.)	Approximate Yield (% of First Elution)
1	10
2	19
3	27
4	35
5	41
6	47

Preparation

NOTE: The following instructions are applicable for operation of the Ultra-TechneKow® DTE Generator with or without the utilization of the alignment adaptor.

1. Rotate the top cover 30° counterclockwise and lift up to remove.
2. Lift the generator by its handle and position it inside the auxiliary shield, aligning the notch in the elution station with the front of the auxiliary shield. Move the handle so that it is not covering the generator top by pushing it off to the side in between the generator and the auxiliary shield.
3. Remove the flip-top cap of the eluant vial; disinfect the stopper, allowing the stopper to dry before use. Remove and store the needle cover from the eluant needles; invert the eluant vial and push down into place on the eluant needles.
4. Place the alignment adaptor onto the top of the generator with the raised portion of the adaptor located over the elution station.
5. Remove the flip-top cap of the TechneStat™ vial; disinfect the stopper, allowing the stopper to dry before use. Secure the TechneStat™ vial into the TechneStat™ vial shield.
6. Remove and store the needle cover from the elution needle. Place the auxiliary shield lid onto the top auxiliary shield ring ensuring alignment of the key-hole with the elution needle.
7. Carefully lower the TechneStat™ vial shield containing the TechneStat™ vial through the key-hole, inserting the shielded TechneStat™ vial onto the elution needle.

Elution

1. Remove the flip-top cap of the appropriate evacuated vial; disinfect the stopper, allowing the stopper to dry before use. Place the evacuated vial into the elution shield utilizing the spacer if required.
2. Remove the shielded TechneStat™ vial by carefully lifting the TechneStat™ vial shield from the elution needle. Position the shielded evacuated vial by carefully lowering the elution shield into the elution station. Piercing the septum of the evacuated vial with the elution needle will begin the elution process.
3. Wait until the evacuated vial has completely filled itself. Depending on the size of the evacuated vial, this may take a few minutes. **Never interrupt the elution by lifting the elution shield! NOTE: Do not use generator eluate if its appearance is discolored.**
4. Carefully remove the elution shield and replace with the shielded TechneStat™ vial (see Step 6 of the Preparation section).
5. Determine the technetium Tc-99m concentration and molybdenum Mo-99 content for dispensing purposes. **NOTE: Molybdenum Mo-99 Breakthrough Limit** - The acceptable limit is 0.15 kilobecquerel molybdenum Mo-99 per megabecquerel technetium Tc-99m (0.15 microcurie Mo-99 per millicurie Tc-99m) per administered dose in the injection, at the time of administration (see USP, Sodium Pertechnetate Tc-99m Injection).
6. Determine the aluminum ion concentration of the eluate. **NOTE: Aluminum Ion Breakthrough Limit** - The acceptable limit is not more than 10 micrograms per milliliter of eluate (see USP, Sodium Pertechnetate Tc-99m Injection).

ULTRA-TECHNEKOW® DTE (TECHNETIUM Tc-99m GENERATOR)

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Subsequent Elutions

Repeat steps 1 through 6 of the Elution procedure above.

Vacuum Loss

If the vacuum in the collecting vial is lost, do not attempt to re-evacuate the vial, but discard and use a new collecting vial.

Expired Generator Disposal

1. Following the life of the generator, remove and dispose of the used TechneStat™ vial and the eluant vial.
2. If appropriate, remove and store the Alignment Adaptor for use with replacement generator.
3. Cover the elution and eluant needles with the stored needle covers.
4. Close the generator system with its top cover by rotating with downward pressure.
5. The intact generator assembly should be either returned to Mallinckrodt Inc. or disposed of in accordance with applicable regulations.

This generator is approved for use by persons licensed by the U.S. Nuclear Regulatory Commission to use by-product material identified in Section 35.200 or under equivalent licenses of Agreement States.

Ultra-TechneKow® and TechneStat™ are trademarks of Mallinckrodt Inc.

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Mallinckrodt Inc.
St. Louis, MO 63134

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Rev 112706 rra4



MATERIAL SAFETY DATA SHEET

Ultra-TechneKow® DTE (Technetium Tc 99m Generator)

SECTION 1. CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

Product Name: Ultra-TechneKow® DTE
(Technetium Tc 99m Generator)
Synonyms: UTK-DTE Generator; Technetium
Tc-99m Generator; Mo-99; Tc-99m.
Manufacturer: Mallinckrodt Inc.
2703 Wagner Place
Maryland Heights, MO 63043

Revision Date: January 1, 2003
Information Telephone Number: (888) 744-1414
Emergency Telephone Number: (314) 654-7860
CHEMTREC: 1-800-424-9300
CANUTEC: 613-996-6666

SECTION 2. COMPOSITION, INFORMATION ON INGREDIENTS

Chemical Ingredients:

<u>Component</u>	<u>CAS #</u>	<u>Wt %</u>
Sodium Molybdate Mo-99	38848-45-2	< 1%
Sodium Pertechnetate Tc-99m	23288-60-0	<1%
Sodium Chloride	7647-14-5	0.9%
Water	7732-18-5	~99%

SECTION 3. HAZARDS IDENTIFICATION

EMERGENCY OVERVIEW

CAUTION! RADIOACTIVE MATERIAL. Read Package Insert prior to use. Promptly remove any contamination from the skin, eyes, or clothing. Radioactive drugs must be handled by qualified personnel in conformity with regulations appropriate to the government agency authorized to license the use of this radionuclide. The Technetium Tc-99m Generator should be kept within its container or within heavier shielding. Avoid contact with the radioactive contents which would cause unnecessary exposure to radiation.

POTENTIAL HEALTH EFFECTS

Inhalation:

Sodium Molybdate Mo-99 and Sodium Pertechnetate Tc-99m do not easily become airborne. Not expected to be a health hazard via inhalation.

Ingestion:

May cause asymptomatic physiological uptake by specific target organs or tissues.

Skin Contact:

Not expected to produce any acute adverse health effects.

Eye Contact:

No adverse effect expected, but may cause mechanical irritation.

Chronic Exposure:

The health risks associated with chronic radiation exposure (cancer, leukemia, genetic and teratogenic effects) are believed to involve levels of radiation exposure which are much higher than those permitted occupationally.

Aggravation of Pre-existing Conditions:

No information found.

Ultra-TechneKow® DTE (Technetium Tc 99m Generator)

SECTION 4. FIRST AID MEASURES

Inhalation:

Notify radiation safety personnel immediately. The amount of material inhaled should be assessed and documented.

Ingestion:

Notify radiation safety personnel immediately. The amount of material ingested should be assessed and documented.

Skin Exposure:

If skin contact occurs, wash the affected area thoroughly with soap and water until no more radioactivity can be removed. Always blot dry. Do not abrade skin. Notify radiation safety personnel.

Eye Exposure:

If a splash occurs, wash eyes with water for at least 15 minutes or until no more radioactivity can be removed. Notify radiation safety personnel.

SECTION 5. FIRE FIGHTING MEASURES

Fire: Not considered to be a fire hazard.

Explosion: Not considered to be an explosion hazard.

Fire Extinguishing Media: Use any means suitable for extinguishing surrounding fire.

Special Instructions: In the event of a fire, wear full protective clothing and NIOSH-approved self-contained breathing apparatus with full facepiece operated in the pressure demand or other positive pressure mode.

SECTION 6. ACCIDENTAL RELEASE MEASURES

If the product is received in a leaking condition or any loss or release of the radioactive contents occurs, notify your Radiation Safety Department and Mallinckrodt at (314) 654-7860. All cleanup operations should be performed according to the Standard Operating Procedures (SOPs) established for your facility and by the NRC or other applicable local, state or federal regulations.

SECTION 7. HANDLING AND STORAGE

Store at 15°C to 30°C. Handling time should be kept to a minimum and appropriate shielding should be used. Storage and disposal of product should be controlled in a manner which is in compliance with the appropriate regulations of the federal or state government agency authorized to license the use of these radionuclides.

SECTION 8. EXPOSURE CONTROLS, PERSONAL PROTECTION

Airborne Exposure Limits:

–NRC Occupational concentration limits:

For Mo-99: 1×10^{-6} $\mu\text{Ci/mL}$ of air.

For Tc-99m: 6×10^{-5} $\mu\text{Ci/mL}$ of air.

Engineering Controls:

Properly sealed containers are not expected to require any special ventilation.

Respiratory Protection:

Not expected to require personal respirator usage.

Skin Protection:

Disposable plastic, latex, or rubber gloves; labcoat.

Eye/Face Protection:

Safety glasses.

Precautions:

No smoking, eating, or drinking should be allowed in any area where radioactive materials are handled or stored.

Ultra-TechneKow® DTE (Technetium Tc 99m Generator)

SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance: Clear, colorless solution.

Odor: Odorless.

Solubility: Soluble in water.

Boiling Point: ca. 100°C (212°F).

Melting Point: ca. 0°C (32°F).

Radioactivity: 0.25 to 3.00 Ci of Mo-99/Tc-99m on the calibration date and time.

Concentration: 25 to 300 mCi/mL of Tc-99m on the calibration date and time when eluted with 10 mL evacuated vials.

Specific Activity: 480 mCi/μg of Mo., 5266 mCi/μg of Tc-99m on the calibration date and time.

Half-Life: Mo-99: 2.75 days; Tc-99m: 6.02 hours.

SECTION 10. STABILITY AND REACTIVITY

Stability: Stable under ordinary conditions of use and storage.

Hazardous Decomposition Products: May emit radioactive fumes containing Mo-99 and Tc-99m when heated to decomposition.

Hazardous Polymerization: Will not occur.

Incompatibilities: No information found.

SECTION 11. TOXICOLOGICAL INFORMATION

It is widely accepted by the scientific community that exposure to sufficient quantities of ionizing radiation can potentially cause harmful biological effects which include cancer, leukemia, and genetic and teratogenic effects. For detailed toxicological information on specific components, write to the address listed in Section 1 - Attn: Regulatory Compliance Department.

SECTION 12. ECOLOGICAL INFORMATION

Because this product is intended for use by hospital or clinic patients, it is expected to be treated by standard wastewater treatment facilities with no adverse environmental impacts.

SECTION 13. DISPOSAL CONSIDERATIONS

The Ultra-TechneKow® DTE (Technetium Tc 99m Generator) is Radioactive Waste until the activity has decayed to nondetectable levels. Radioactive waste must be handled in accordance with procedures established by your Radiation Safety Officer, NRC and other applicable regulations.

If medical waste is involved, such as blood, blood products, or sharps, the waste must be handled as a Biohazard and disposed of accordingly.

If not radioactive or a biohazard, a spent Ultra-TechneKow DTE (Technetium Tc 99m Generator) may still be considered special waste due to the lead shielding inside the unit. Consult local, state and federal regulations for proper disposal.

SECTION 14. TRANSPORT INFORMATION

DOT (Department of Transportation):

Proper Shipping Name: Radioactive Material, n.o.s.

Hazard Class: 7

Identification Number: UN2982

SECTION 15. REGULATORY INFORMATION

CERCLA Reportable Quantities:

Tc-99m = 100 Ci (3.7 E 12 Bq); Mo 99 = 100 Ci (3.7 E 12 Bq)

Releases to air, land or water of these hazardous substances which exceed the Reportable Quantity (RQ) must be reported to the National Response Center at 800-424-8802.

SARA Title III

302 Extremely Hazardous Substances: None

311/312 Hazard Categories: Chronic

313 Toxic substances subject to annual release reporting requirements: Chronic.

RCRA Hazardous Waste Status

Non-hazardous (See Section 13 for additional details.)

California Proposition 65 Warning

This product contains a substance known to the State of California to cause cancer.

Australian Hazchem Code: None allocated.

Australian Poison Schedule: None allocated.

WHMIS: This MSDS has been prepared according to the hazard criteria of the Controlled Products Regulations (CPR) and the MSDS contains all of the information required by the CPR.

SECTION 16. OTHER INFORMATION

MSDS Status: Revised in accordance with ANSI Guideline Z400.1-1998

NFPA Ratings: Health: 1 Flammability: 0 Reactivity: 0

Product Use: Diagnostic imaging agent

Revision Information: Sections 8, 9 updated.

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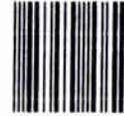
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Ms. Patricia Pelke
Materials Licensing Branch
U.S Nuclear Regulatory Commission, Region III
2443 Warrenville Road, Suite 210
Lisle, IL 60532-4352

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