DRAX IMAGE

by Courier,

Mr Seung J. Lee,
Materials Safety and Inspection Branch,
Division of Industrial and Medical Nuclear Safety,
Office of Nuclear Material Safety and Safeguards,
United States Nuclear Regulatory Commission,
Washington,
DC 20555-0001

09 May 2000

Dear Mr. Seung,

In response to your letter of April 12th, 2000 concerning the DRAXIMAGE LS-1 Brachytherapy implant we are pleased to provide the attached responses.

If you need additional information we would be pleased to answer any questions that you might have.

Sincerely,

Richard J. Flanagan Ph.D.
Executive Vice President.

NRC-01.doc

DRAXIMAGE Inc. • 16751 Autoroute TransCanada Highway • Kirkland • Québec • Canada H9H 4J4
• Tél. 888-633-5343 • 514-630-7043 • Fax. 514-694-9295 • Web Site www.draximage.com

RESPONSES TO NUCLEAR REGULATORY COMMISSION QUESTIONS CONCERNING DRAXIMAGE LS-1 BRACHYTHERAPY IMPLANT

Question 1

Because the NRC has no jurisdiction over the foreign entity, the NRC has followed the regulation of 10 CFR Part 110.53 requiring for a foreign vendor to establish an address in the United States to which the NRC can correspond and serve papers as necessary to accomplish its mission. Please provide an US office address.

Answer

DRAXIMAGE Inc., has an official agent in the United States for all regulatory matters. Our agent is as follows;

AAC Consulting Group Inc.,
7475 Wisconsin Avenue,
Suite 850,
Bethesda,
Maryland 20814,
USA.

Attn Dr Gayle R. Dolecek

Question 2

The NRC does not review the draft documents in the application. Please provide the complete and final documents for those which are marked as draft in the application (e.g., indications for use on Page 3 of Section 2, shipping pot label, primary container label, warning insert in Section 4, promotional material in Appendix 2).

Answer

Indications for Use:

BrachySeeds with air kerma strengths up to 1.25U (approx. 1mCi apparent activity) are indicated for permanent interstitial implantation in the treatment ofselected localized tumors such as tumours of the head, neck, lung, pancreas, breast, uterus, and prostate. They can be used either as primary treatment or for residual disease after excision of the primary tumour or for recurring tumours. They may also be used at completion of external beam radiation.

BrachySeeds with strengths greater than 1.25U (approx. 1mCi)are indicated for temporary implantation or surface application to treat localized tumors.

See attached package insert and promotional leaflet.

Shipping and storage pot label:

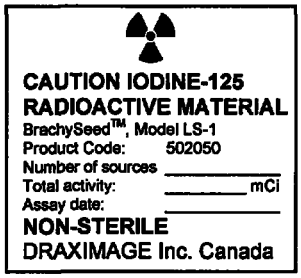
CAUTION - RADIOACTIVE MATERIAL
Sealed sources - handle with care and store in this container or similar. See the handling, storage and leak testing instructions in the WARNINGS AND PRECAUTIONS section of the package insert.

BrachySeed™, Model LS-1, Iodine-125 brachytherapy sources
Product code: 502050 Customer order no. _____
Total apparent activity: _____ (mCi) of iodine-125
Apparent activity per source: _____ (mCi)
Number of sources: _____
Avg. air-kerma strength _____ U
Assay date: _____
Lot number: _____

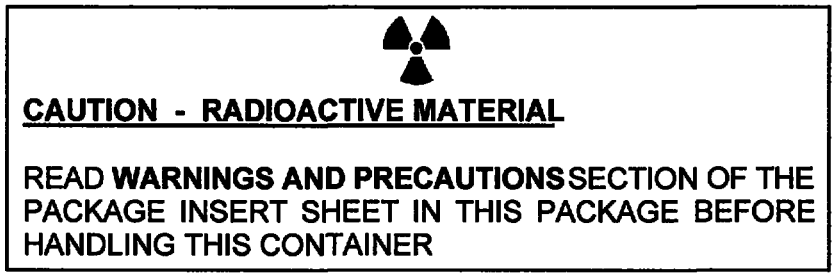
The U.S. Nuclear Regulatory Commission has approved distribution of the LS-1 to the persons licensed to use byproduct material identified in 35.57, 35.400, or 35.500 of 10 CFR, as appropriate, and to persons who hold an equivalent licence issued by an Agreement State.

WARNING: NON-STERILE
DRAXIMAGE Inc., Kirkland QC, Canada H9H 4J4

Primary container label:



Warning insert



A revised package insert is attached.

BrachySeed™

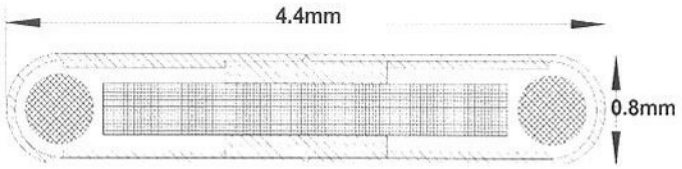
(DRAXIMAGE Inc. iodine-125 brachytherapy source, model LS-1)

DESCRIPTION

Source Design and Construction:

BrachySeed is an innovative iodine-125 brachytherapy source offering a dose distribution in tissue close to isotropic in the therapeutically critical region 0.5 - 2 cm out from the center of the source.

Each BrachySeed encapsulates I-l25 contained in two ceramic beads positioned one at each end. Between the beads lies a platinum/iridium alloy rod whose high density and high atomic number provide for radiographic detection. These components are enclosed in a biocompatible titanium capsule. The capsule is hermetically sealed around the central seam by a laser weld. The design allows little room for movement of the internal parts with consequent predictability of radiation output pattern. The integrity of the structure has been tested according to the standards ISO 2919:1999(E) and ANSI/HPS N43.6-1997.



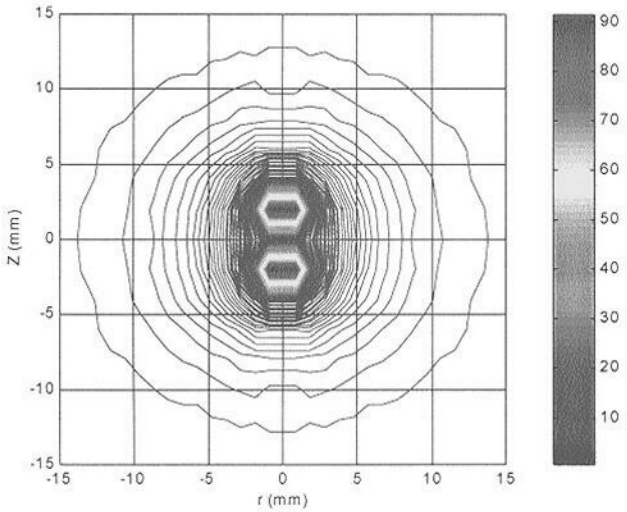
I-125 in ceramic bead, nominal φ = 0 .5 mm	Titanium wall 0.05 mm	Pt/Ir rod 0.37 x 3 mm

Radiation Emissions:

I-125 decays by electron capture with the emission of characteristic photons. The very low energy electrons emitted are absorbed within the source. The principal photon emissions are 27.4 and 31.0 keV X-rays and a 35.5 keV gamma-ray. Also emitted are 22.2 and 25.5 keV silver X-rays produced by fluorescence of the silver dopant in the ceramic bead radioisotope carriers. The radiation intensity along the axis ofBrachySeed at 1 cm from the center is over 80% of that along atrans-axis at 1cm. This fluence ratio promotes isotropic dose distribution.

Radiation Dose Distribution:

Iso-dose contours for BrachySeed calculated by a Monte Carlo method [1] are given below. The contours shown are plots of the raw unsmoothed Monte Carlo results. The patterns have been confirmed by experimental measurements [1].



Iodine-125 Decay Factors:

To correct for decay after the assay date of a source, apply one of the following decay factors (DF) based on the I-125 half-life of 59.43 days as used by NIST:

Days	DF	Days	DF	Days	DF
1	0.988	21	0.783	41	0620
2	0.977	22	0.774	42	0613
3	0.966	23	0.765	43	0606
4	0.954	24	0.756	44	0599
5	0.943	25	0.747	45	0592
6	0.932	26	0.738	46	0585
7	0.922	27	0.730	47	0578
8	0.911	28	0.721	48	0571
9	0.900	29	0.713	49	0565
10	0.890	30	0.705	50	0558
11	0.880	31	0.697	51	0552
12	0.869	32	0.689	52	0545
13	0.859	33	0.681	53	0539
14	0.849	34	0.673	54	0533
15	0.839	35	0.665	55	0527
16	0.830	36	0.657	56	0520
17	0.820	37	0.650	57	0514
18	0.811	38	0.642	58	0508
19	0.801	39	0.635	59	0503
20	0.792	40	0.627	60	0497

ACTIONS

The clinical efficacy of BrachySeeds depends only upon the interaction of the emitted ionizing radiation with the tissue being treated.

INDICATIONS

BrachySeeds with air kerma strengths up to 1.25U (approx. 1mCi) are indicated for permanent interstitial implantation in the treatment of selected localized tumors such as tumors of the head, neck, lung, pancreas, breast, uterus and prostate. They can be used either as primary treatment or for residual disease after excision of the primary tumor or for recurring tumors. They may also be used at completion of external beam radiation.

BrachySeeds with strengths greater than 1.25U (approx. 1mCi) are indicated for temporary implantation or surface application to treat localized tumors.

CONTRAINDICATIONS

The application of BrachySeed to tumors in generally poor condition (e.g. ulcerated) which would allow substantial source migration is not recommended.

ADVERSE REACTIONS

Exposure to radiation:

Since BrachySeed achieves its therapeutic effect through the delivery of radiation to target tissue, any adverse event associated with tissue radiation damage may theoretically be associated with its use. With implantation of I-125 sources in the prostate, impotence may arise in about 25% of cases and urinary incontinence and prostatitis have been reported in about 1% of cases. After prostate implants, transientdysuria and increased urinary frequency have been reported in about 15% of patients.

Biocompatibility:

BrachySeeds are hermetically sealed titanium capsules. Experience has shown that when titanium is used to completely encapsulate a radioactive source for implant, the danger of adverse tissue reaction is not significant and there have been no adverse reactions reported.

WARNINGS AND PRECAUTIONS

Source Manipulations:

A damaged source may release I-125 into the environment or into body fluids should the source be medically applied. If a source has been visibly damaged , seal it in a container and discard it immediately to radioactive waste and check the area for contamination. Under no circumstances should damaged sources be implanted.

Do not force BrachySeeds into (or from) any piece of equipment. Doing so may damage a source. With respect to sources used for temporary implant and reuse, when loading or removing sourcesfrom after-loading catheters, it is advisable to use a vented chemical hood which has adequate air flow. If a sharp tool is used to remove sources from after-loading catheters, use extra care.

To assure that sources have not been damaged following removal from equipment, a contamination survey should be conducted using a radiation monitor capable of detecting 27keV photons. This survey should include wipe (or leak) tests of sources and an overall area survey.

Source vibration, shock and elevated temperatures:

Do not expose BrachySeeds to undue vibration or shock, temperatures above 150°C for any period, or temperatures above 100°C for more than 2 hours.

Source corrosion:

The BrachySeedcapsule has excellent corrosion resistance. However,

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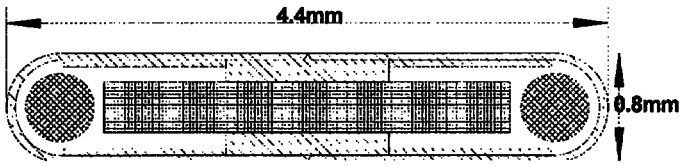

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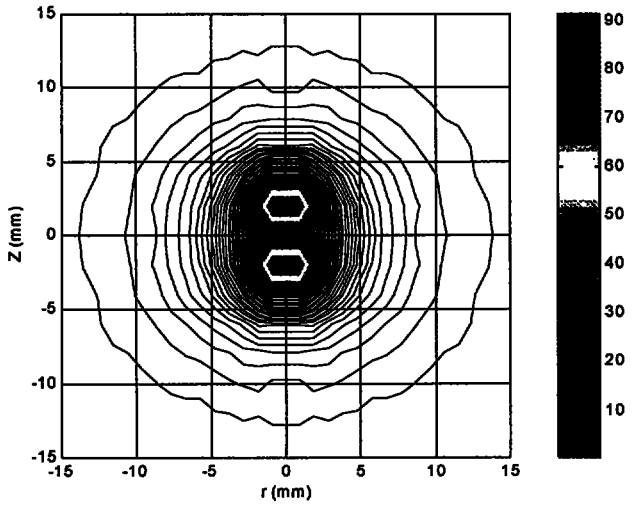

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6	0.932	26	0.738	46	0.585
7	0.922	27	0.730	47	0.578
8	0.911	28	0.721	48	0.571
9	0.900	29	0.713	49	0.565
10	0.890	30	0.705	50	0.558
11	0.880	31	0.697	51	0.552
12	0.869	32	0.689	52	0.545
13	0.859	33	0.681	53	0.539
14	0.849	34	0.673	54	0.533
15	0.839	35	0.665	55	0.527
16	0.830	36	0.657	56	0.520
17	0.820	37	0.650	57	0.514
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19	0.801	39	0.635	59	0.503
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Do not force BrachySeeds into (or from) any piece of equipment. Doing so may damage a source. With respect to sources used for temporary implant and reuse, when loading or removing sources from after-loading catheters, it is advisable to use a vented chemical hood which has adequate air flow. If a sharp tool is used to remove sources from after-loading catheters, use extra care.

To assure that sources have not been damaged following removal from equipment, a contamination survey should be conducted using a radiation monitor capable of detecting 27keV photons. This survey should include wipe (or leak) tests of sources and an overall area survey.

Source vibration, shock and elevated temperatures:

Do not expose BrachySeeds to undue vibration or shock, temperatures above 150°C for any period, or temperatures above 100°C for more than 2 hours.

Source corrosion:

The BrachySeed capsule has excellent corrosion resistance. However,

do not expose a source to acid or alkaline solutions exceeding one molar. The sources are not affected by common solvents such as acetone and alcohol or by mild detergents.

Personnel monitoring:

BrachySeeds are radioactive and appropriate precautions must be taken when handling them. All steps of the implantation procedure should be planned in advance to minimize radiation exposure to personnel Personnel monitoring is required. Typically a film or TLD dosimeter worn on the body and a ring dosimeter (during source handling) is adequate.

Shipping container:

BrachySeeds are shipped in a screw-capped vial inside a lead container which shields >99.9% of the radiation from 1-125. The lead container may be used for storage and transport of seeds within the hospital.

Source handling and storage:

BrachySeeds should be handled behind shielding of adequate thickness. A sheet of lead of thickness 0.25mm will reduce the exposure by >99%. Forceps should be used to maintain operator to source distance. Only gentle pressure should be applied so that sources are not damaged. BrachySeeds should not be picked up with the fingers. When in doubt about the fit of BrachySeeds into various source containers, tubes, cartridges, and applicators, load the containers first with non-radioactive sources to determine their compatibility with the sources. Packages of non-radioactive BrachySeeds are available from DRAXIMAGE Inc. (see contact details at end of this sheet).

BrachySeeds should be stored in the shipping vial and lead pot in a secure area according to the user's Federal or State licence.

Accidental source damage:

Although BrachySeeds have a high structural integrity, it is possible through rough handling to rupture a source causing it to release 1-125. If this happens, the area of the accident should be closed off; the sources should be sealed in a container; personnel movement should be controlled to avoid spread of any radioactive contamination; and the area and personnel should be decontaminated according to established procedures. Personnel working in or near the accident should also undergo a thyroid scan to determine if I-125 has accumulated in this organ through contact, ingestion or inhalation.

Source sterilization:

BrachySeeds are not sterile when shipped. Before implantation, they must be sterilized in an adequately shielded container using steam or ethylene oxide (EtO). Do not use dry heat or chemical sterilization.

Steam Sterilization (autoclave): Use the normal cycle (121°C at 15 psi for 15 to 30 minutes) or the flash cycle (132°C at 30 psi for 3 minutes). Autoclaves should be equipped with traps or other means to prevent seed loss through the drain hole.

Ethylene Oxide (EtO) Sterilization: Use cycle and aeration times recommended by the manufacturer of the sterilizer or use those determined at the hospital.

BrachySeeds may be loaded into various sorts of cartridges designed to be used with various sorts of applicators Use ethylene oxide to sterilize sources loaded into plastic tubes or cartridges; steam heat may warp the tubes and prevent source recovery.

Application to Patient:

BrachySeeds should be used only by individuals 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. Radiation detection equipment capable of detecting 27keV photons should be available whenever the sources are being handled.

All practical physical protection should be provided during the implantation procedure. Frequently, however, protective barriers are not practical in the surgery. In this circumstance, operators must rely upon distance and speed to minimize radiation exposure [2, 3].

Treatment of Patient:

All patients should be informed of the nature of BrachySeeds implants and the expected period of time during which radiation precautions will be necessary. Patients, their close associates and associated medical personnel should be instructed in the necessary radiation safety procedures required for someone who has received a BrachySeeds implant. Guidelines for necessary precautions have been established [4].

All patients should be advised of the possibility that one or more BrachySeeds might become detached as a tumor regresses. Under these circumstances, any bandages or linens which come into contact with the site of the implant should be scrutinized for small metallic tubes about 1/4 inch long and 1/32 inch thick. Patients should be advised that whenever sources are found, they should be picked up with a spoon and placed in a jar or other container, and placed in an inaccessible area in the home. The institution where the implant procedure was done should be notified of such an event as soon as possible after its occurrence.

Accountability/Disposal:

Iodine-125 is an accountable radioactive material. BrachySeeds must be strictly controlled and stored in a locked safe. If any significant amount of material cannot be accounted for, the loss must be reported to the appropriate licensing agency.

When disposal is indicated, BrachySeeds should be transferred to an authorized radioactive waste disposal agency, and not disposed of in normal waste.

Leak Testing:

Each BrachySeed has been leak tested prior to shipment and has shown <0.005 microCuries of removable 1-125. This value is printed on the Certification form that accompanies each shipment. Each BrachySeed must be leak-tested at intervals not exceeding six months until disposed of.

DOSAGE AND ADMINISTRATION

Established practice [5, 6, 7, 8, 9] should be followed for the calculation of the total activity to be implanted, the proper placement of the sources within the tissue, and the evaluation of the radiation dose distribution achieved. Dose distribution around each individual source is close to, but not perfectly, isotropic and the degree of anisotropy should be allowed for in patient dose calculations. The dose rate constant for BrachySeed is 1.04 cGy/h/U.

DIRECTIONS FOR USE

BrachySeeds are supplied non-sterile and must be sterilized before use (See above for sterilization guidance). During the treatment procedure, the patient must be appropriately anaesthetized . A qualified practitioner is to place the BrachySeeds on or throughout the tumor volume according to a treatment plan. Commercially available applicators and needles may be used.

HOW SUPPLIED

BrachySeed air-kerma strengths are traceable to the 1999 NIST standard. They are available in strengths from 0.1 to 50 U (microGray meter squared per hour, uGy-m^2/h), i.e. apparent activities approximately 0.08 to 40 milliCuries. The sources are packaged in a screw-capped vial containing labeling information on air-kerma strength and apparent activity per seed, total air-kerma strength and apparent activity, reference date, number of sources, and an order identity number. The vial is secured in a lead container similarly labeled. Any discrepancies in labeling or against the order paperwork noted upon receipt of the product must be reported immediately to DRAXIMAGE Inc. (see contact details at end of this sheet). BrachySeeds are not sterile when shipped.

LICENSING

The Atomic Energy Control Board of Canada has approved BrachySeeds for distribution to persons properly licensed for its use in Canada. Provincial law restricts this device to sale by or on the order of a physician. The US-Nuclear Regulatory Commission has approved BrachySeeds for distribution to persons properly licensed for its use in the United States. US Federal law restricts this device to sale by or on the order of a physician.

REFERENCES

1. Data on file at DRAXIMAGE Inc., W.Prestwich and G. Chan, McMaster University, Literature reference to be supplied.
2. "Protection Against Radiation From Brachytherapy Sources", NCRP Report No. 40, Washington D.C. (1972).
3. "Radiation Protection for Medical and Allied Health Personnel", NCRP Report No. 48, Washington D.C. (1976).
4. "Precautions in the Management at Patients Who Have Received Therapeutic Amounts of Radionuclides", NCRP Report No. 37, Washington D.C. (1970).
5. R. Nath, L.L. Anderson, G. Luxton, K.A. Weaver, J.F. Williamson, and A.S. Meigooni, "Dosimetry of interstitial brachytherapy sources: Recommendations ot the AAPM Radiation Therapy Committee Task Group No. 43", Med. Phys. 22, 209-234 (1995).
6. W.S. Rice, B.R. Prestlidge, J.J. Prete. and D.F Dubois, Clinical impact of implementing AAPM Task Group 43 on permanent prostate brachytherapy using I-125, Int. J Radiat. Oncol., Biol. Phys. 40, 1237-1241 (1998).
7. R. Nath, L.L. Anderson, J.A. Meti, A.J. Olch, J.A. Stitt, and J.F. Williamson, "Code of Practice for Brachytherapy Physics: Report of the AAPM Radiation Therapy Committee Task Group No. 56", Med. Phys. 24. 1557-1648 (1997).
8. H.D. Kubo, B.M. Coursey, WE Hanson, R.W. Kline, SM. Seltzer. RE. Shuping, and J,F. Williamson, "Report of the Ad Hoc Committee of the AAPM Radiation Therapy Committee on I-125 Sealed Source Dosimetry", Int. J. Radiat. Oncol., Biol., Phys. 40, 697-702 (1998).
9. "Interstitial Brachytherapy - Physical, Biological and Clinical Considerations", Interstitial Collaborative Working Group, Raven Press, New York (1990).

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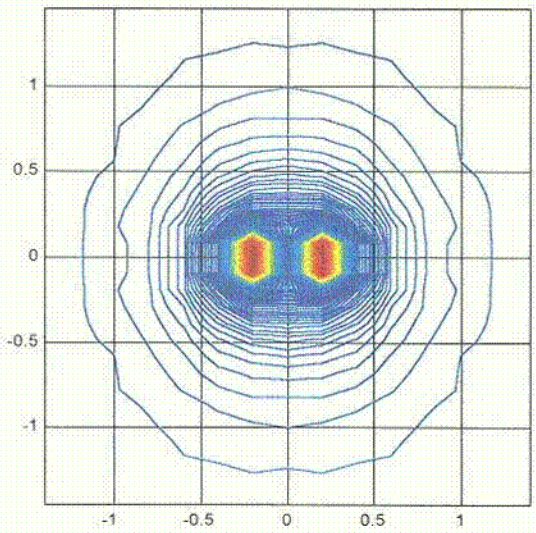
Kirkland QC, Canada H9H 4J4

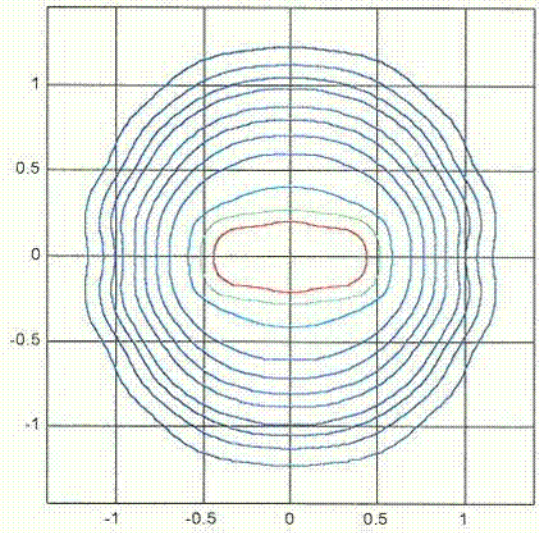
Tel. 1-888-633-5343
or (514) 630-7043
Fax (514) 694-9295

DRAXIMAGE Inc.'s
Interstitial I-125 Brachytherapy Seed

BrachySeed™



Raw MC data
(scales in cm)



Smoothed MC data
(scales in cm)

Monte Carlo (MC) calculated iso-dose contours
(confirmed by laboratory experiment)

Laser welded titanium capsule ● Iodine-125 in ceramic matrix

Dimensions compatible with current protocols

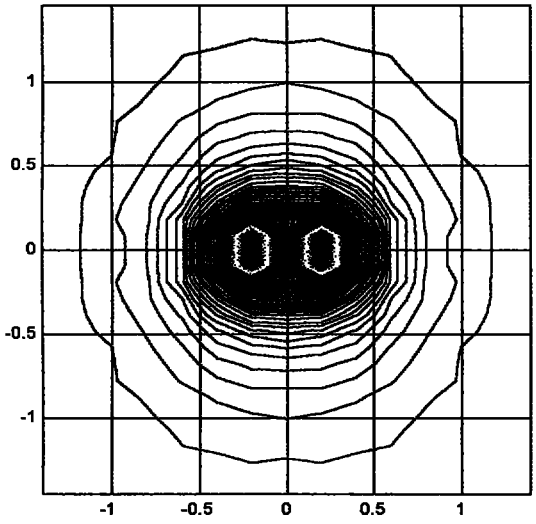
High density Pt/Ir marker for radiographic detection

Output strength traceable to 1999 NIST air kerma standard

C-2

DRAXIMAGE Inc.'s
Interstitial I-125 Brachytherapy Seed

BrachySeed™



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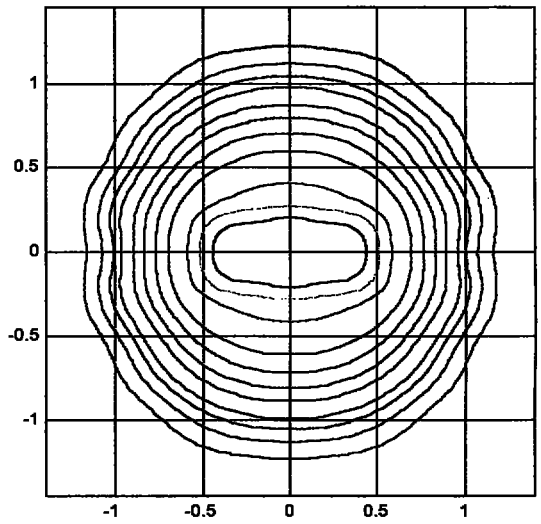

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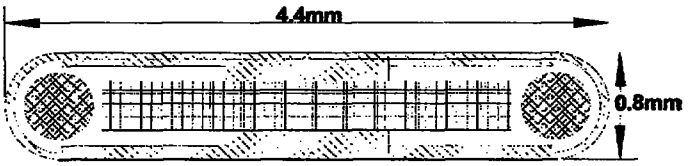


Source output values:

Approximate apparent activities are given in millicuries (mCi) and the NIST traceable air kerma strengths are given in U (uGy-m²/h). (Note that the dose rate constant for BrachySeed is 1.04 cGy/h/U).

Activity (mCi)	Air kerma units (U)	Activity (mCi)	Air kerma units (U)
0.24	0.31	0.36	0.46
0.25	0.32	0.37	0.47
0.26	0.33	0.38	0.48
0.27	0.34	0.39	0.49
0.28	0.35	0.39	0.50
0.28	0.36	0.40	0.51
0.29	0.37	0.41	0.52
0.30	0.38	0.42	0.53
0.31	0.39	0.43	0.54
0.31	0.40	0.43	0.55
0.32	0.41	0.44	0.56
0.33	0.42	0.45	0.57
0.34	0.43	0.46	0.58
0.35	0.44	0.46	0.59
0.35	0.45	0.47	0.60

On your order, please specify desired seed strength from the Air Kerma Strength (U) columns above. Please call if you need different source strengths than these.

To order, call DRAXIMAGE toll free at 1-888 633-5343

DRAXIMAGE Inc.
16751 Trans Canada Highway
Kirkland, QC
Canada H9H 4J4

Tel. (514) 630-7043
Fax (514) 694-9295

Question 3

In Section 2, please provide the estimated or surveyed annual radiation exposures for hospital personnel preparing for and performing the implant procedure and people near the patient after the implant with the sources having maximum activity of 75 mCi.

Answer

Sources with strengths greater than 1 mCi are indicatedfor temporary implants only and would be used in small numbers per implant. Seeds of 75 mCi(Apparent activity approx. 50 mCi) would normally be used singly or perhaps in pairs for smaller tumours. Inoperable brain tumour would be a typical application. The activity summed over the seeds used in such an application would not be greatly different to that in more mainstream brachytherapy applications, perhaps higher by a factor of two. Given similar technique, the radiation doses incurred by practitioners would also be similar on implant, although an approximate further doubling could be expected because of the source removal procedure associated with temporary implants. Overall, a factor of four increase in radiation dose per procedure to hospital personnel relative to mainstream applications might be reasonably expected, although this could be offset by the fewer number of seeds involved and thus a reduction in overall exposure time.

People outside the hospital would not be affected because the implant is temporary within the hospital.

Question 4

In Section 3.3, there is a discrepancy regarding the tolerances between the end cap and the annulus. You indicated that these components will be "pressure fitted." However, when the values of the tolerances are considered, a 0.0002" clearance could exist between the inner and the outer diameters. Please clarify the issue of pressure fit. Please also consider if the X-ray marker can slide against the annulus, how can you prevent that the X-ray marker will not damage the isotope carrier bead?

Answer

Please note that the component specifications given in Section 3.3 are ordering specifications. The manufacturers have to be given reasonable tolerances. However, seed assembly constraint specifications are also given in Section 3.3 and these are used to match, accept or reject component batches as part of the quality control of incoming materials. In particular, the annulus assembly constraint will be used to ensure that all annuluses are oversize relative to end tubes and that a firm press fit will result.

In answer to the second part of this question, the marker does slide against the annulus, but the masses are so small (a seed weighs 12 mg) and the beads are so hard that no significant erosion can be expected. We have subjected two LS-1 seeds to a test. These seeds are two of the five used for NIST air kerma output calibration. Their history is as follows. They were manufactured at DRAXIMAGE on 11/30/99. They were measured and shipped to NIST on 12/01/99. They were then examined and measured by NIST and shipped sequentially to the three ADCL labs around the US for further measurements. In January of this year they were shipped back to DRAXIMAGE where they were again measured. On 04/26/00 to 04/27/00, they were subjected to a vigorous tumbling test. After output measurements, they were attached to the rim of an 8" wheel and rotated at 60 rpm. Seed #1 was fixed inside a tissue pad inside a3 mL polyethylene vial. Seed #2 was loose inside a similar vial. Both vials were inverted 120 times per minute for 10 hours and then their output was measured again. The results of all of the output measurements in air kerma units are recorded below. Any significant erosion of the isotope carriers caused by seed movements would have been reflected in a significant output change caused by shifting of the radioactivity and thus differential source self-shielding. The data below show no divergences in gross output. Any slight differences recorded are well within measurement errors.

	Seed #1 (U)*		Seed #2 (U)*	
Post manufacturing, 12/01/99, 10:45:	2.74	(2.39)	2.97	(2.60)
NIST measurement: 12/13/99, 00:00:01	2.39	(2.39)	2.55	(2.55)
Post return from ADCL=s, 03/20/00, 11:00	0.761	(2.40)	0.799	(2.52)
Pre tumbling test, 04/26/00, 22:20	0.481	(2.35)	0.505	(2.47)
Post tumbling test, 04/27/00, 12:45	0.482	(2.37)	0.508	(2.50)

* Values in brackets are decay corrected to time of NIST measurements using a half-life of 59.43d

Question 5

In Section 3.5.1, the molecular sieve zeolite beads are screened to have diameters between 0.710 and 0.600 mm. However, the maximum space would permit insertion of an object with a diameter of 0.59 mm into the end tube. Please clarify the beads can be dispensed into each end tube.

Answer

Upon fusion, the bead diameter is reduced to 77% of the starting diameter. A bead of 0.71 mm is thus reduced to about 0.55 mm. Please see the description of the fusion process for the seed in the original submission on pages 5 & 8.

Question 6

In Section 4, please revise the trefoil symbol in accordance with 10 CFR 20.1901 on the shipping pot label, primary container label, and warning insert.

Answer

Please see question 2

Question 7

In Section 4, please add the following statement to the label in accordance with 10 CFR 32.74(a)(3): "The U.S. Nuclear Regulatory Commission has approved distribution of the LS-1 to the persons licensed to use byproduct material identified in 35.57, 35.400, or 35.500 of 10 CFR, as appropriate, and to persons who hold an equivalent license issued by an Agreement State."

Answer

Please see question 2

Question 8

In Section 4, per 10 CFR 32.74(a)(2)(viii), please provide the radiation safety instructions for handling and storing the source. These instructions are to be included on a durable label attached to a permanent storage container for the source. If these instructions are lengthy for such label, they may be summarized on the label and printed in detail on a brochure which is referenced on the label.

Answer

Please see question 2

Question 9

In Section 5, please provide the information on the well-type sodium iodide detector.

Answer

The NaI detector described in Section 5 is a Bicron Model 2MW2/2 2 in. x 2 in. crystal with a central 5/8 in. diameter x 1 3/8 in. deep well. The detector is attached to a Canberra Packard Model 2007 tube base preamplifier. The preamplified data signal feeds into a Wilkinson-type Analog to Digital Converter in a Canberra Series 35+ Multichannel Analyzer. Data is stored in Pulse Height Analysis mode into 1024 channels of memory.

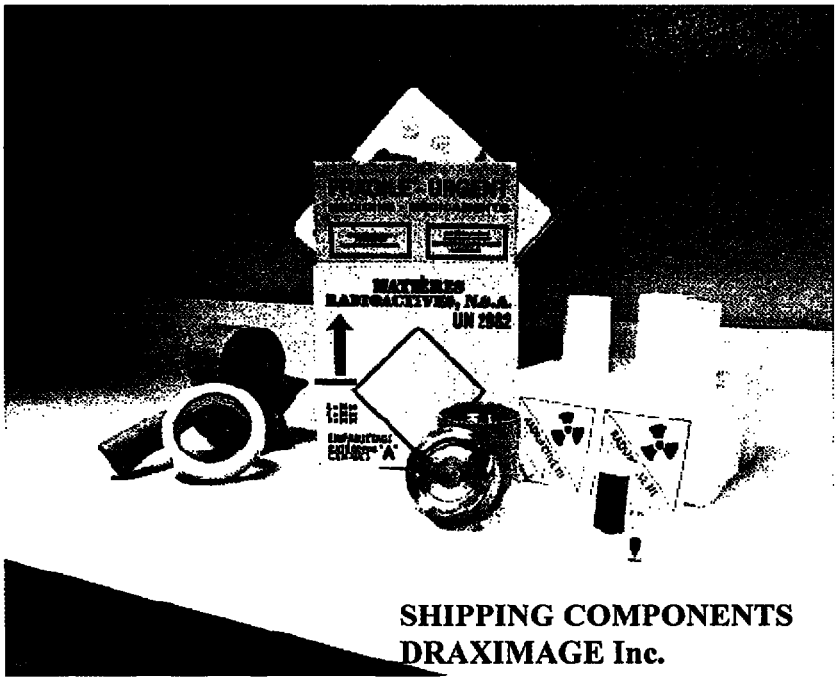
The Series 35+ MCA/NaI counting system is calibrated directly with a ^{125}I NIST Standard Reference Material once per year. The standard is used to calculate efficiency and for energy calibration. Daily checks of the system stability and energy calibration are performed with a ^{137}Cs standard. Detector resolution is verified on a monthly basis at 662 keV.

Question 10

In Section 5, please provide integrity test results for the transportation/storage package. Your application has addressed the prototype testing of the individual beads. However, the integrity of the package, containing the beads, must also be addressed. Please provide information on package integrity. When addressing likely accident conditions for the package, please address such scenarios as dropping the package from the table top height to a concrete floor, or somebody placing a heavy object on the package.

Answer

DRAXIMAGE Type A Package



The DRAXIMAGE Type A package system is a specially designed and tested shipping container for the transport of radioactive materials. Type A packages are capable of withstanding normal and accidental conditions of "ground" and "air" transport

The DRAXIMAGE packaging system meets all the tests required for shipping radioactive materials that are specified by the International Atomic Energy Agency (IAEA), the International Air Transport Association (IATA) and the Canadian Nuclear Safety Commission (CNSC).

The physical tests described in above regulations are intended to simulate conditions such as falling from vehicles, being dropped, being struck by a sharp object, being exposed to heavy rain, or having heavy cargo stacked on the package.

The Type A packaging system has been officially tested and a copy of the test report is attached in Appendix 1.

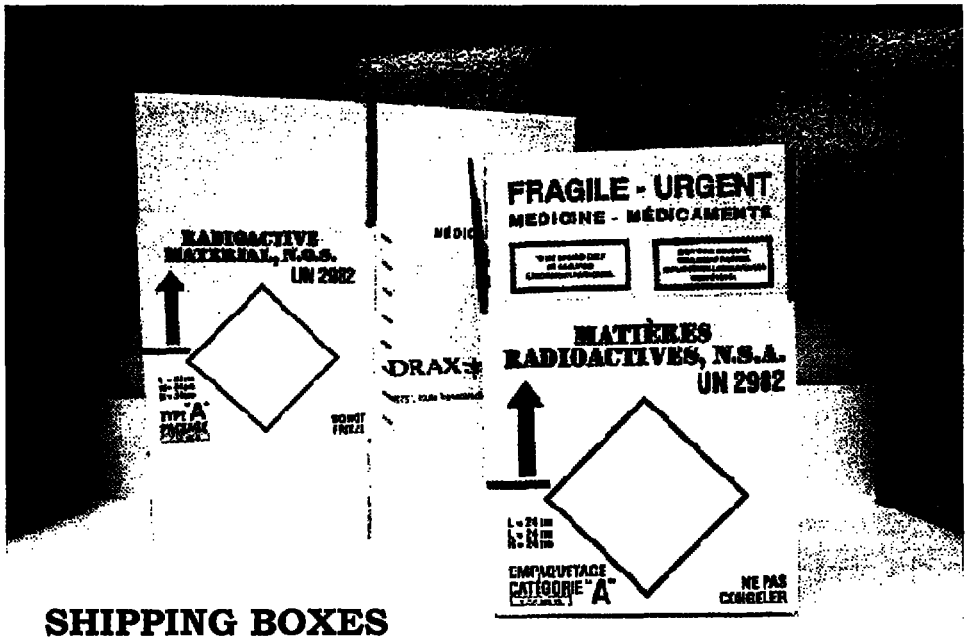
Summary of packaging system

1. Packing Sequence

A glass vial containing the seeds is cushioned with a Kimberly Clarke Low Lint Wiper and placed inside a lead pot. The pot is sealed with yellow adhesive tape, wrapped with sponge foam packing material and placed in a small fiber drum. The fiber drum is then placed in the styrofoam packer inside a Type A cardboard box.

2. Cardboard Box

Made by: Smurfit-MBI
1035 Hodge St
St-Laurent, Quebec
Canada, H4N 2B4
Tel: 514-855-4420



SHIPPING BOXES
DRAXIMAGE Inc.

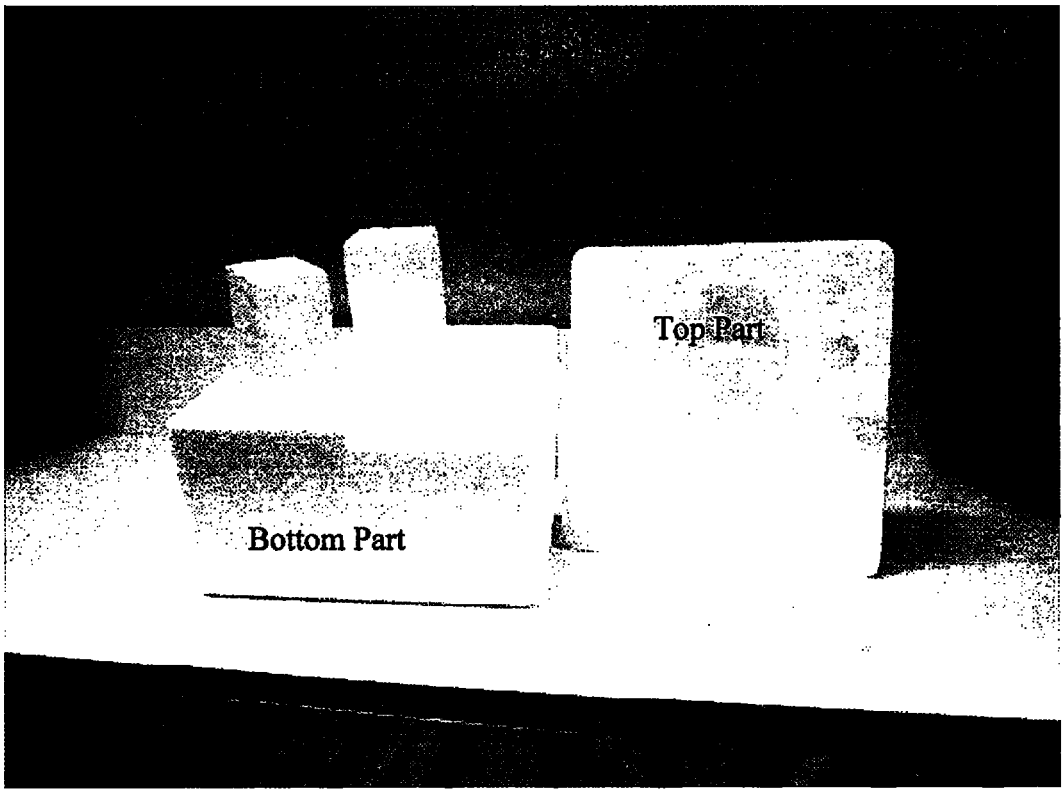
The exterior of the package is made of heavy cardboard designed to meet N.S.A. UN2982 . The package is designed in relation to the weight, volume and shape of the lead pot containing the radioactive material.

The box has a cubic shape, measuring 24 x 24 x 24 cm. It can hold safely 200 pounds. Together with it's content, the package meets the requirements for shipping, set by IAEA, IATA and CNSC tests for Air and Ground Transport of Radioactive goods.

3. Styrofoam Packing Material

The foam components are made and supplied by Domfoam Internationals Co.

Address: 8785 Langelier Boul.
St-Leonard, Quebec
Canada, H1P 2C9
Tel: 514-325-8120



The styrofoam packer consist of five molded components; a top, a bottom and three support inserts to hold the lead pot. The styrofoam contains no chlorofluocarbons (CFC), and has a density of 15.2 to 16.8 Kg/m^3 and can withstand extreme temperatures.

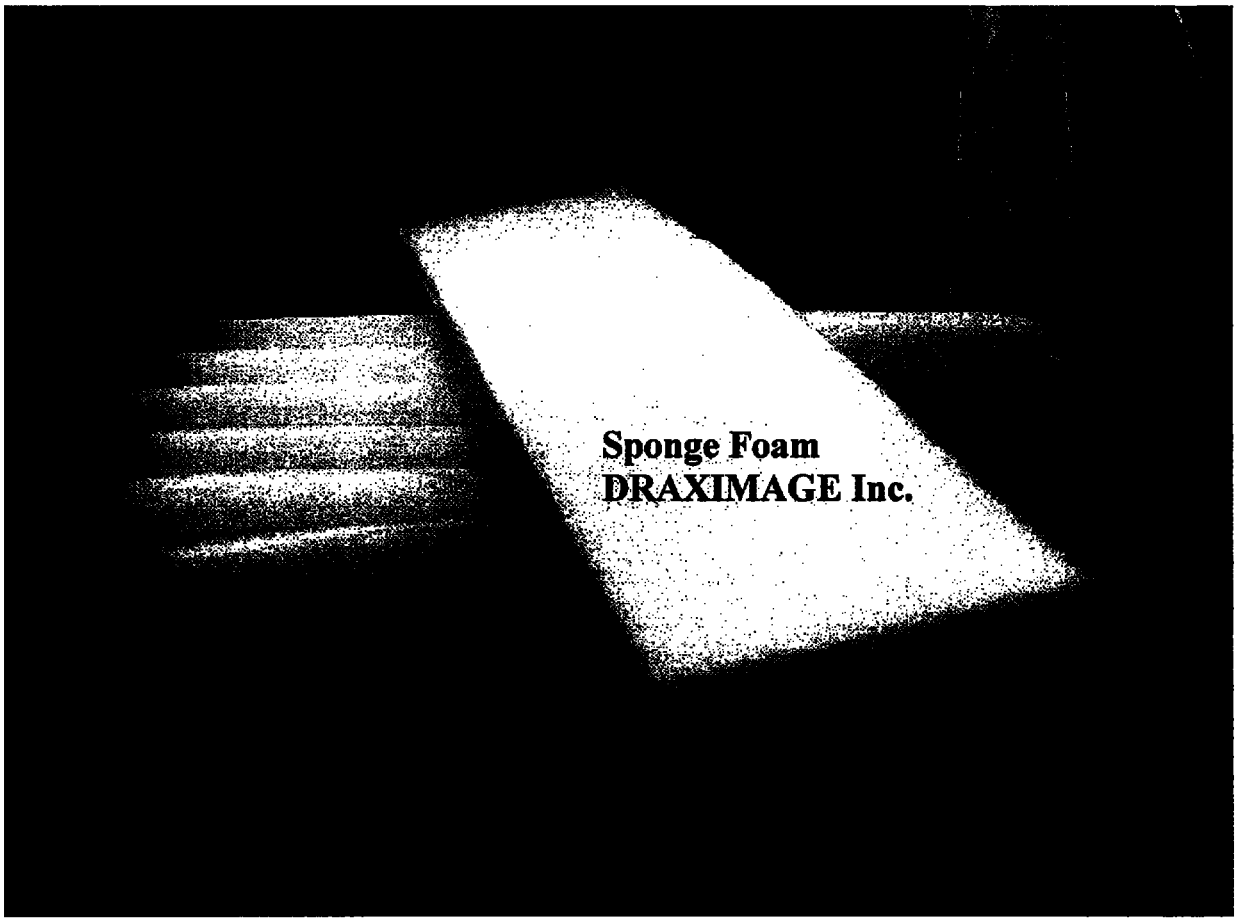
4. Miscellaneous

(A) Yellow Tapes: ¾" and 1" "Thick "Models. Catalog Numbers are UT18333Y (3/4") and UT2433Y (1"). They are used to wrap the lead pot containing the radioactive vial. Three turns around the lid and pot are made, and two bands to securevertically the lid to the lower part.

(B) Clear Tape: 3" wide "thick" Model, Catalog No. PVC 7266
(see picture) . Used to seal and secure the exterior of the carboard box (top and bottom).

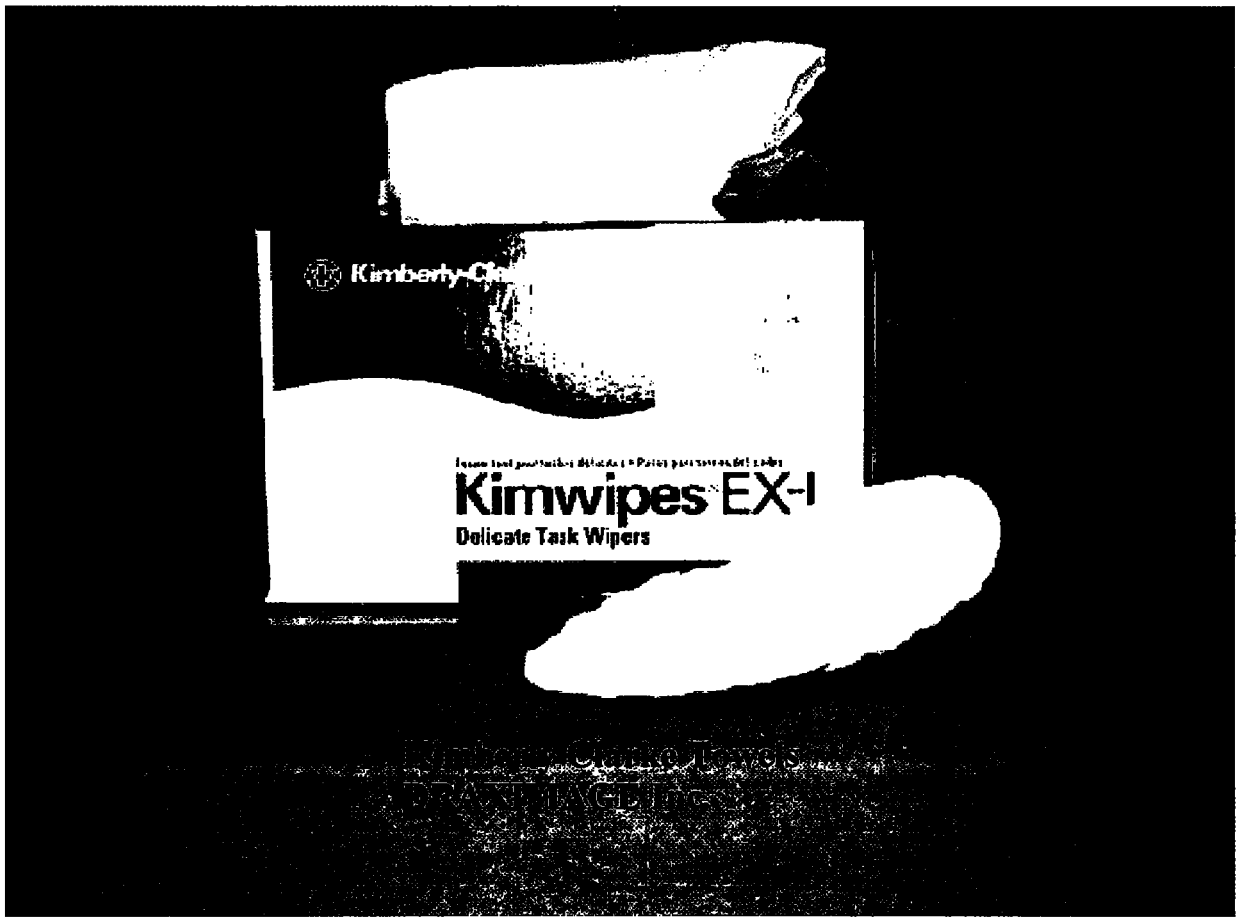
The distributor is Emballages Circo Packaging Inc.
1812 Onesime-Gagnon
Lachine,
Quebec,
Canada H8T 3M6
Tel: 514-633-8120

(C) Sponge Foam P.C.S.: 4" x 12" x ½" "Thick" Model.(see picture)
Distributed by Emballages Circo PackagingInc.
1812 Onesime-Gagnon
Lachine, Quebec,
Canada H8T 3M6
Tel: 514-633-8120



(D) Kimberly Clarke: Low Lint Wipers, EX-L (see attached Specificationsand picture). Size 4.5" x 4.5"

Distributed by Fisher Scientific Ltd.
112 Colonnade Road
Nepean,
Ontario,
Canada K2Y 7L6
Tel: 1-800-234-7437



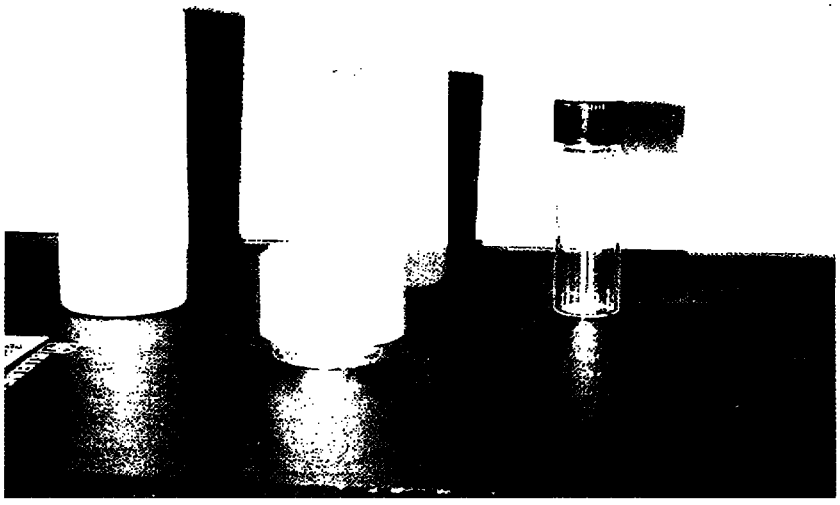
5. Lead Pots and Glass Vial

Lead Pots are supplied by two manufacturers:

Address: Gauthier Non-ferrous Products,
3525 Robert Provencher,
Montreal,
Quebec,
Canada, H1A 3R7,
Tel: 514-630-8226

Canada Metal,
8271 Lafrenaie,
St-Leonard,
Quebec,
Canada, H1P 2B1,
Tel: 514-327-7810

Lead Pot 1/8"
DRAXIMAGE Inc.



The lead pot has a 1/8" wall around, and will contain some Antimony (2-3%).Up to 4 pots per fiber drum can be shipped per Type A package.

The glass vial is a standard USP Type 1 borosilicate, 4 mL, clear, 15 x 48 mm, screw cap vial manufactured by Wheaton Glass products (cat no 224722).

Question 11

In Section 6, the radiation dose measurements were shown using the 2.88 mCi. However, the maximum activity you request is up to 75 mCi, please provide the radiation field using the maximum activity of 75 mCi.

Answer

In the table below, the values in the second part of the table in Section 6.3 have been scaled to reflect a source containing 75 mCi (apparent activity 50 mCi). Also, the units have been changed from dose units (rem) to field units (R). (See the answer to Q12 below).

Source-detector distance	Calculated field (mR/h)	Measured field (mR/h)
100 cm	7.5	7.5
30 cm	81	73
5 cm	2900	2500
Contact	-	22000

Question 12

In Section 6.3, please clarify the values for the radiation dose constant for iodine-125: 0.7 rem-cm^2/mCi/hr is specified in "Engineering Compendium on Radiation Shielding," Vol. 1, pp. 21-30, while a value of 1.45 is shown in your application.

Answer

In comparison with our stated value, the NRC has also stateda dose rate constant 0.7 rem-cm^2/mCi/h. However, we should have been using the exposure rate constant. A value of 1.45 R-cm^2/mCi/h for the exposure rate constant for iodine-125 seeds is given in the book "Interstitial Brachytherapy", Raven Press 1990. This value also appears in literature from the Wisconsin ADCL dated 01/29/99. Single page copies of these references are attached. We acknowledge having made an error in applying this exposure rate constant bystating rem units instead of R units. In Section 6.3 of our document, all of the mrem dose units must be replaced by mR field units, including the readout units for the Ludlum survey meter. This difference in units explains the numerical discrepancy you state. However, after applying the correction in units, we stand by the data in Section 6.3.

Question 13

In Section 7, please provide the quality assurance manual. Please clarify the statement "leak testing by a method approved by NRC" (p. 18); if the method is in accordance with NRC requirements, please state it in such terms

Answer

A copy of the DRAXIMAGE Quality Manual is attached in Appendix 2.

The leak testing described on page 18 of the submission is being submitted for NRC approval.

Question 14

Please describe how the test results provided in Appendix 3, in accordance with ISO and ANSI integrity tests, apply to the Model LS-1 with the maximum activity of 75 mCi.

Answer

All of the sources tested were about 2 mCi at the time of the tests.

In the ISO tests, none of the sources showed leakage exceeding 0.01nCi after their tests. Scaling up, this indicates that the use of 75 mCi sources would have resulted in leakages of less than 0.4 nCi which is a factor of 12.5 less than the test failure criterion of 5 nCi.

In the ANSI drop tests, neither of the sources showed leakage exceeding 0.05nCi after their tests. Scaling up, this indicates that the use of 75 mCi sources would have resulted inleakages of less than 2 nCi, which is considerably less than the test failure criterion of 5 nCi.

Question 15

Table 2.4 in Appendix 3, the detection limit was determined to be 0.05nCi and was calculated as 4 times the square root of the background. Whereas, in Table 3.1, the detection limit was determined to be 0.01 nCi and was calculated as 4 times the square root of the background. Please clarify this discrepancy (0.05 nCi vs 0.01 nCi).

Answer

For the ANSI drop test seeds, where the immersion with boiling leakage test was applied, a 1 mL sample from a total leak test solution volume of 5 mL (including washes) was taken for counting. In the ISO tests, the whole leak test solution volume of 1 mL was counted. This explains the factor of five difference in detection limits for the two different series of tests.

Question 16

In Appendix 3, the Table 3.2 shows that the activity after the test is higher than before the test. Pl~ase explain why it happens.

Answer

From the data presented in Table 3.2, an average of 1.831 mCi is calculated for these seeds both before and after the tests. Differences in the measurements pre-test vs. post-test are well within experimental measurement error bounds. With respect to Note 2, the discrepancy between the two measurements for Impact Source #2 can be explained by impact induced rearrangement of the radioactivity within the source.

Question 17

Please confirm that in Figure 1, page 5, the "well region" displays the tapering correctly. If incorrect, please provide a revised drawing.

Answer

The weld area shown in Figure 1, page 5 shows the tapering correctly. This is a component assembly drawing. The tapering disappears upon welding.

Appendix 1

Test Results for the DRAXIMAGE Type A Package

Research & Technical Services
1035 rue Hodge
St. Laurent, Quebec
H4N 2B4
TEL: (514) 744-6461
FAX: (514) 744-9089

IATA COMPLIANCE TESTING

FOR THE

TRANSPORTATION OF RADIOACTIVE MATERIAL BY AIR

Testing Performed for

FROSST RADIOPHARMACEUTICALS
Type A Package for Liquids
(Sample A)

Technical Service Report No. 96-34M

January 12, 1996

Maria Lopez Pietravalle,
Senior Research Associate

Distribution List

V. del Gaudio (2)

J. Kee

J. Vandercraats

OBJECTIVE

To perform the Compliance tests on the Packagings submitted as per the I.A.T.A. Dangerous Goods Regulations for Radioactive Materials in Type A Packages designed for liquids.

Note: The section numbers referred to in the following report are those indicated in the I.A.T.A. regulations.

PACKAGE DESCRIPTION:

Outer Corrugated Container
Styrofoam Insert
Fibre Drum with Cover
Sponge Foam
Lead Container
Glass Vial
Absorbent Cotton Pads

See Photo No. 1

PRODUCT INFORMATION:

Name:	Radioactive Material, N.O.S.
UN Number:	UN2982
Hazard Classification:	7
Gross Weight:	3 kg

TESTS REQUIRED: Section 10.6.2.4 & 10.6.2.5
Water Spray Test
Free Drop Test
Stacking Test
Penetration Test

TEST METHODS & EQUIPMENT

The three performance tests, i.e. Free Drop Test, Stacking Test and Penetration Test, each preceded by the Water Spray Test, were performed on three different packages. The packages were filled with dummy material, assembled and closed as per shipment by Frosst.

i) Water Spray Test

Equipment:

- Garden hose
- Adjustable brass nozzle
- 45 gallon fish tank
- Plastic meshed platform to keep boxes out of the water
- Support stand
- Adjustable clamp

Procedure:

All packages were subjected to a water spray, simulating a rainfall for 1 to 1 1/2 hours. The packages were rotated every 15 minutes to expose all sides. The performance tests were conducted immediately following the water spray test.

Observations:

At the end of the test period, the excess moisture was removed and it was observed that the vertical edges were a little soft, however, overall the package still felt rigid and strong.

See Photo #2

ii) Free Drop Test

Drop Height: 9 3/4 metres

After the water spray test, the package was placed in a plastic bag and brought to the roof of the building overlooking the parking lot. At this location the height is 32 ft. (9 3/4 m). The package was dropped onto the asphalt surface. The package impacted on one of it's vertical edges then came to rest on its side.

Observations:

The package remained sealed and intact. Only the impacted edge was pushed in.

On opening, it was noted that the styrofoam insert was not damaged. Inside, the fibre drum, the lead container and its contents were also undamaged. No leakage of the red dye was observed.

Results: Pass

See Photos # 3 & 4

iii) Stacking Test:

Equipment: Instron Universal Testing Instrument, floor model (II) *(see diagram & certificate of calibration attached).*

Procedure:

After the water spray test, the package was subjected to a compressive load equal to the value calculated by method (b) for at least 24 hours.

Compressive Load Calculation

a) 5 x (mass of package)
5 x 3.5 kg = 17.5 kg.

b) 13 Kpa x (vertically projected area)
or
2 lb/in² x (Vertically projected area)
2 lb/in² x (9 1/4 in x 9 1/4 in)
2 x 85.6 = 171 lb or 78 kg.

Observations:

At the end of the 24 hour period the package was in excellent condition. There was no visible bulging or distortion of the package.

Results: Pass

See photo #5

iv) Penetration Test (10.6.2.5(b)

Equipment: Steel Bar
Dimensions: 975 mm x 32 mm
Weight: 6 kg

Drop Height: 1.7 m from the end of the bar to the top of the package.

Procedure:

After the water spray test, the package was placed on the floor in front of a table. One technician stood on the table and held the bar over the centre of the box. Another technician measured the 1.7 m distance from the top of the box to the bottom of the steel bar. The bar was released.

Observations

The bar penetrated the top of the box a little off centre. The bar was removed. A hole of approximately 5 cm in diameter was observed. Inside, the top of the styrofoam insert had been pierced and the fibre drum was damaged. The lead container was not damaged and there was no leakage.

Results: Pass

See Photos # 6, 7 & 8

CONCLUSION

The three Sample A packages passed all the tests with minimal damage. In all cases there was no leakage.

Maria Lopez Pietravalle mm

ML/mm Maria Lopez Pietravalle.

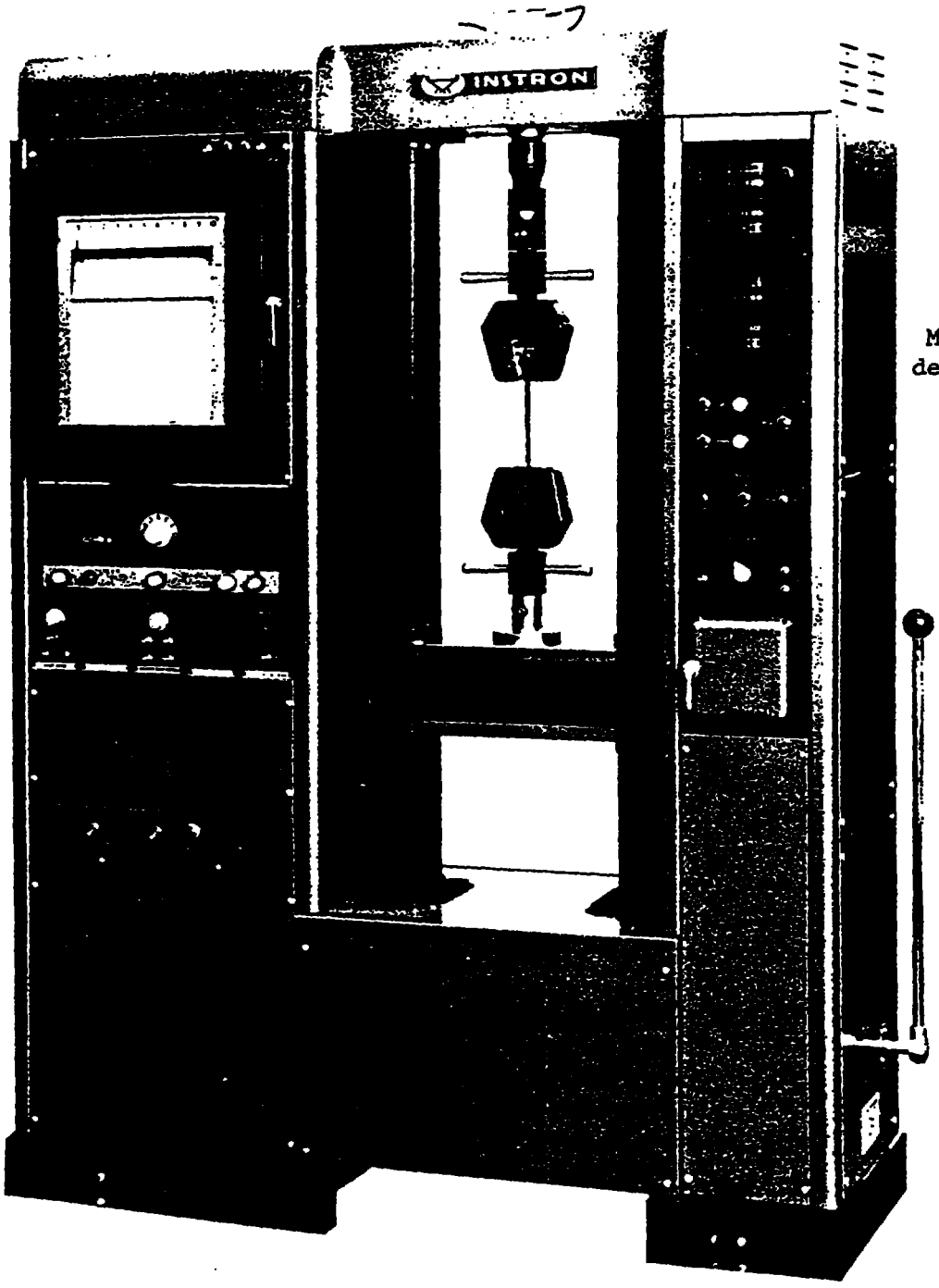


FIGURE 1 – Instron Universal Testing Instrument, floor-model (TT)

For the stacking test the Instron is fitted with plattens and the load cell is placed on the bottom.

ASTM E4-89 CERTIFICATE OF FORCE CALIBRATION

REPORT# 05019504

CUSTOMER: MACMILLAN BATHURST INC.
LOCATION: 1035 HODGE ST.
ST. LAURENT, QUE.

VERIFICATION DATE: 05/01/95
AMBIENT TEMP. deg C: 23
REF STD TEMP. deg C: 23

MACHINE: INSTRON TTC, S/N 40488
SENSOR: 10 KLB LOADCELL, S/N UKFR108

DIRECTION: COMPRESSION

This document is to verify that the above described machine has been calibrated by "VACS Ltd." and the ASTM E4 certified loading range below to be within a tolerance of 1% of indicated load using Reference Standards having a minimum 4:1 accuracy ratio, unless otherwise noted.

MACHINE RANGE	E4-89 CERTIFIED LOADING RANGE	OTHER
10 KLB	200 LBS TO 5000 LBS	

AS FOUND IN CONDITION: WITHIN 1% TOLERANCE

LEFT IN CONDITION: WITHIN 1% TOLERANCE

General Statement:

NOTE: CUSTOMER HAS REQUESTED AND ACCEPTS THIS OLDER ASTM E4 STANDARD "E4-89".

1. *The reference standards used for this verification have been calibrated per A.S.T.M E74-91. unless otherwise noted.*
2. *The uncertainties are for a confidence level of not less than 95% for reference standards used.*
3. *The National Research Council of Canada (NRC) has assessed the measurement capability of this laboratory and its traceability to recognized National Standards and to the units of measurement realized at the corresponding National Standards Laboratory. This certificate or calibration report is issued in accordance with the conditions of accreditation granted by the Standards Council of Canada (SCC) and the conditions of certification granted by National Research Council (NRC). unless otherwise noted.*
4. *Copyright of this certificate is owned by VACS Ltd. and may not be reproduced other than in full except with prior written approval of VACS Ltd. and the client.*

Measurements performed by:

Derek Magee, C.E.T.

Approved by:

Derek Magee, Q.A. Manager

Dated: 05/08/95

Appendix 2

DRAXIMAGE Inc. Quality Manual

DRAX IMAGE

Quality Manual

March, 2000

Table of Contents

8.0 Final Product Release

- 8.1 Analytical Report
- 8.2 Batch Record Review
- 8.3 Final Product Release
- 8.4 Batch Dispensing Record

9.0 Returned Goods

10.0 Complaints

1.0 General Quality Policies

Draximage Inc. will meet or exceed all current industry and regulatory standards to assure that its products are manufactured and tested according to current Good Manufacturing Practices and Good Laboratory Practices, and that only safe and effective products are released for sale to the marketplace.

1.1 Quality Goal

Our goal is to provide the highest possible quality of products and services to our customers worldwide. This is accomplished by creating and maintaining a working culture that encourages all employees to share in the Company's commitment to Quality.

1.2 Quality Responsibilities

Quality Operations - It is the responsibility of the Quality Operations department to ensure that the quality objectives of the Company are achieved. QO provides support to the manufacturing department to ensure control of raw materials components and final products through the use of validated methods. QO receives and investigates customer complaints, supports any recall effort that may be necessary, provides manufacturing with GMP advice and guidance, and monitors the GMP compliance of manufacturing, suppliers, and contract analytical services through audit activities.

Manufacturing - It is the responsibility of the manufacturing department to employ Good Manufacturing Practices and trained employees in producing products in compliance with company and regulatory standards. Manufacturing is responsible for establishing standard operating procedures conforming to cGMP and regulatory requirements, reporting all deviations from the approved process, and maintaining all equipment and facilities in good operating order as established during documented qualification.

Research and Development - It is the responsibility of the Research and Development group to provide products and processes that conform to the current standards of quality, stability, process reproducibility, and regulatory requirements. R&D provides advice and technical guidance to the manufacturing and Quality Operations departments to assist in attaining their quality objectives.

Draximage Employees - The responsibility for product quality and customer service is the responsibility of all Draximage employees.

2.0 Organization and Personnel

2.1 Quality Management / Organization:

The Draximage Quality Operations Department is responsible for all Quality Control and Quality Assurance functions. The Director reports to the Executive Vice-President of Draximage. All quality decisions are taken independently of the production organization. It is the responsibility of the Director or his delegate to release product to the marketplace or to reject unsuitable product.

An organizational chart of the Quality Operations department is included in Appendix A.

2.2 Auditing:

The Quality Operations department is responsible for performing internal audits of the manufacturing and quality departments. Audits of suppliers and contract laboratories and manufacturers are performed as required.

2.3 Training:

All quality personnel are trained in specific analytical methods, and training records are retained in a training file maintained for each analyst. Training records also include any GMP training and off-site courses.

3.0 Buildings and Facilities

3.1 Design and Construction:

Draximage products are manufactured in a spacious facility conforming to current GMP standards for design, construction materials, and work flow. Separate areas are provided for receiving, quarantine, quality control, warehousing, manufacturing, dispensing of final product, and shipping. Adequate lighting both natural and artificial is provided in each area.

Floors, walls, and ceiling are finished in easily cleaned and resistant finishes.

Air supply to the manufacturing area is 100% fresh air, heated, cooled, and humidity controlled before passing through high efficiency particulate air filters maintained under positive pressure. A qualified building automation system monitors the proper operation of the environmental controls at all times.

Air exhaust is equipped with two redundant (one in use, one back-up) activated charcoal filter systems designed to trap volatile radioactive contaminants that may be released during manufacturing processes.

3.2 Sanitation:

A building sanitation program exists to assure the cleanliness of the building at all times.

3.3 Qualification:

The building construction and utilities have been validated for installation qualification and operational qualification. Performance qualification of building systems is ongoing.

4.0 Equipment

4.1 Equipment design and construction:

Most equipment used in the manufacture of radiopharmaceuticals fall into one of two types; commercially available pharmaceutical processing equipment for non-radioactive products, or custom, built-to-purpose equipment for radioactive manufacturing. Design and materials of construction are chosen to allow easy cleaning.

4.2 Equipment IQ/OQ/PQ:

New manufacturing and testing equipment undergoes installation qualification, operational qualification and performance qualification before it is approved for use. Draximage has developed a validation master plan for the validation of manufacturing and facilities equipment qualification.

5.0 Control of Raw Materials, Labels, and Packaging Components

5.1 Purchasing:

The issue of a purchase order initiates each shipment of raw material, label, or packaging component. These materials are ordered only from approved manufacturers and suppliers.

5.2 Receipt:

Upon receipt, a copy of the purchase order issued for the shipment accompanies each lot of goods. A written procedure describes the receipt, sampling, and storage of the component or material. A unique receiving number is applied to every shipment received. Each material purchased is assigned a unique identifier code. Different shipments of the same lot number of material receive separate receiving numbers.

The receiving record lists the name of the material, quantity received, including number of containers, supplier identity, lot number of the material, the supplier's expiry date, and the purchase order number.

Quarantine:

Upon receipt and until completion of testing, each lot of material is withheld from use in a quarantine area. Access to the quarantine area is strictly limited to Quality Operations personnel. Authority to release from quarantine rests only with the Quality group.

Storage:

Storage of raw materials, labels, and packaging components is in such a way as to prevent contamination, damage and mix-ups.

5.3 Testing:

Sampling of raw materials, labels, and packaging components is performed according to established sampling instructions.

After sampling all raw materials, labels, and packaging components are tested to established specifications upon receipt. All are withheld from use until successful completion of testing.

Raw materials are retested after storage for long periods, and returned to use only after successful completion of such tests.

5.4 Rejected raw materials, labels, and packaging components:

To prevent their use, rejected raw materials, labels, and packaging components are identified and withheld from the manufacturing area for return to the supplier or destruction, as appropriate.

6.0 Production and Process Control

6.1 Master Formula Cards:

Each Draximage product is manufactured under controlled conditions and using written procedures process controls and ingredients described in a batch manufacturing recipe or formula card. These formula cards are copies of master formula cards that have been reviewed and approved by both manufacturing and quality operations senior management.

The formula card that is followed during the actual manufacturing process, also documents the manufacturing process for that batch, and becomes the batch manufacturing record.

Only approved components that are within their predetermined useful shelf life are used in the manufacture of drug products.

6.2 In-process testing:

When appropriate, in-process testing will confirm the suitability of a batch of product still unfinished, and allow a decision to be made whether to continue, reprocess, or reject the batch.

6.3 Standard Operating Procedures:

Each Draximage department manufacturing, testing, or handling drug product components, intermediates or finished products has Standard Operating Procedures to describe those procedures which could impact directly or indirectly on the quality of the drug product or on customer service. These documents form the basis for the daily operation of the manufacturing facility.

A list of S.O.P.'s from each of the Production, Quality, Injectables, and Research and Development departments is found in appendix B

6.4 Atypical Investigations:

Deviations from established masters manufacturing instructions or established standard operating procedures are documented in atypical investigations. These investigations attempt to discover the cause of the deviation, to evaluate the implications to product and regulatory compliance, to render decision regarding batch disposition, and to prevent a recurrence of the deviation.

7.0 Laboratory Controls

7.1 Good Laboratory Practices:

Draximage analytical laboratories maintain Good Laboratory Practices designed to assure sample integrity, and reliable test results according to established quality standards known as product specifications.

7.2 Specifications:

Established specification documents listing the quality attributes and analytical tests required to confirm those attributes exist for every raw material, intermediate, packaging component and final product. These master documents are reviewed and approved by senior Quality, Research and Development, Production, and Regulatory Affairs personnel. Each receiving lot or manufacturing lot is tested according to the methods described in the specification to confirm that it conforms before its release for use in manufacturing or for distribution.

7.3 Contract Laboratories:

Contract laboratories that are approved through a program of audits and inspections provide outside analytical services.

8.0 Final Product Release

8.1 Analytical Reports:

The results of testing performed on raw materials, intermediates, packaging components and finished products are listed on analytical reports. These reports are reviewed and approved by senior Quality personnel before authorizing the release of the material. The reports are filed on-site for a pre-determined period, and are readily available.

8.2 Batch Record Review:

The manufacture of every batch of product produces a permanent batch manufacturing record that documents all steps and control points during the manufacture of the batch. This batch record is reviewed by the Quality Department and must be found to be complete and satisfactory before the batch can be approved for release.

8.3 Final Product Release:

Final product release follows the successful completion of all required analytical testing, batch review, and product inspection. Only the Director, Quality Operations or his delegate is authorized to give final product release for distribution.

8.4 Batch Dispensing Record:

All released product lots are issued a product release and dispensing record from which document the lot distribution is recorded. Every shipment of product from the lot is recorded on this record. The record is retained on site for a pre-determined period and is readily available.

9.0 Returned Goods

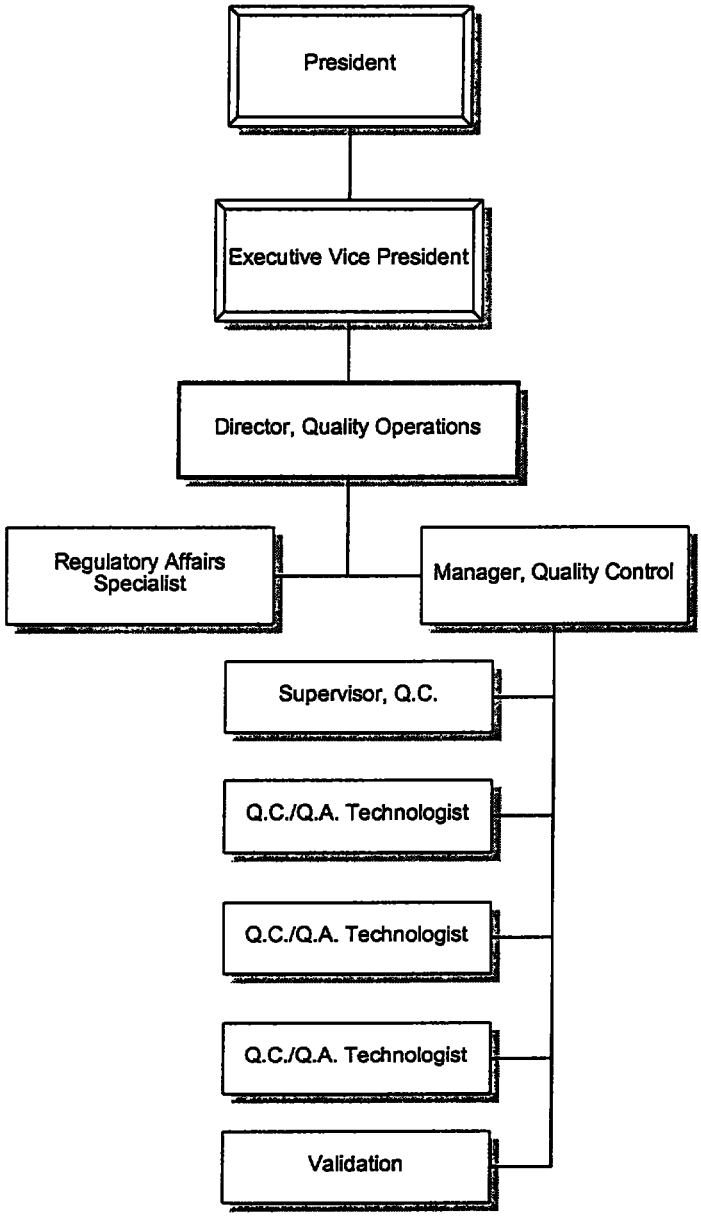
Goods are returned only with prior approval. In the case of radioactive products, the customer must be equipped to make radioactive shipments in order to return goods. The custom-filled nature of most Draximage radioactive products, the company maintains a policy of no return to inventory of radioactive goods. Draximage also maintains a policy of no return to inventory of non-radioactive goods.

10.0 Complaints

Complaints are received by the Quality Operations Department. A product complaint report is issued for every complaint received. Product complaints are investigated by Quality personnel, assisted as required by the Research and Development, Production and Customer Service departments. Each investigation into a product complaint attempts to establish the most probable cause of the complaint, (including product defect), the appropriate immediate action required, and the recommendation to prevent a recurrence.

All product complaints are reviewed by the Director, Quality Operations before close-out.

Draximage Inc.
Quality Operations Organization Chart



RADIOPHARMACEUTICAL QUALITY CONTROL
INDEX OF STANDARD OPERATING PROCEDURES

S.O.P. No.	Subject	Date
C.02.005.001	Stability/Linearity testing of Dose Calibrators	Dec. 20, 1995
C.02.005.002	Stability Testing of MCA/NaI Systems	Oct. 1, 1996
C.02.005.003	Operation of Genie PC MCA System	Nov. 21,1994
C.02.005.004	Operation and Calibration of pH Meter	Nov. 28, 1994
C.02.005.005	Calibration of Berthold TLC System	Oct. 20, 1998
C.02.005.006	Cleaning and Maintenance of Sterile Enclosures	Apr. 17,1995
C.02.005.008	Leak Testing of Sealed Radioactive 137Cs Sources	Jan 27, 1997
C.02.005.009	Surface Contamination Wipe Test	June 06, 1996
C.02.005.010	Operation of the Conductivity Meter	Aug. 26, 1997
C.02.005.011	Cleaning of Radioactive Glassware	May 27, 1997
C.02.009.001	Control of Reagents for Use in Q.C.	May 17,1995
C.02.009.002	Control of Preparations for Use in Q.C.	Sept. 30, 1994
C.02.009.003	Control of Non-Radioactive Raw Materials	Nov.28, 1994
C.02.011.001	Preparation and Maintenance of S.O.P's	Nov. 3, 1994
C.02.012.001	Investigation of Atypical Events in Radiopharmaceutical Production	Aug 18, 1999
C.02.012.010	Reporting of Irregularities in Radiopharm. Production	Oct.25,1994
C.02.013.001	Signature Documentation	June 5, 1996
C.02.014.001	Release of Bulk and Finished Radioactive Product Batches	Nov. 3,1994
C.02.014.002	Investigation of OOS and Atypical Test Results	Nov.23, 1994
C.02.014.003	Verification of Analytical Reports for Release of Kit Products	Dec. 7, 1995
C.02.018.001	Bacterial Endotoxin Test	July 8, 1998
C.02.018.002	Sterility Test	Apr. 3,1995
C.02.018.003	Inspection and Release of Kits	Jan. 1,1998
C.02.018.004	Inspection and Release of Customer Orders	Nov. 3, 1994
C.02.018.005	Returned Goods	Dec. 7, 1995
C.02.018.008	Radiopharm Safety Test on Mice & Guinea Pigs	March 24, 1998
C.02.018.021	Preparation of Sterility Sentinel Vials	April 17, 1995
C.02.028.001	Stability Testing of Radioactive Products	Feb. 11, 1999
C.02.028.002	Stability Testing of Kit Products	Feb. 18, 1999
C.02.029.001	Microbiological Monitoring of Sterile Enclosures	May 3,1994
C.03.202.001	Label Control – Radioactive Products	Oct. 1, 1997

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Appendix

SOP Number	SOP Description
RPH_R&D_026	Calibration Procedure for the Sartorium Analytical Balance (Type 2255S0008)
RPH_R&D_027	Use of the Sartorius Analytical Balance Type (2255S0008)
RPH_R&D_028	Calibration Procedure for the Sartorius Balance (Type 3862MP)
RPH_R&D_029	Use of the Sartorius Balance (Type 3862MP)
RPH_R&D_030	Linearity Verification of Camberra Multichannel Analyzer (Gamma Counter)
RPH_R&D_031	Procedure for MEDAC Controlled Temperature Shipments
RPH_R&D_032	Collection Method of Deionized Water
RPH_R&D_033	
RPH_R&D_034	
RPH_R&D_0035	Statistical Outlier Elimination for the EILISA & the Biological Testing
RPH_R&D_036	Equipment Cleaning Validation for Cytochalasin B
RPH_R&D_037	Calibration of Mechanical Burettes

Appendix

SOP Number	SOP Description
RPH_R&D_001	Preparation of SOP's
RPH_R&D_002	The Stability Program
RPH_R&D_003	The Release Program
RPH_R&D_004	Calibration of Equipment
RPH_R&D_005	Labelling of Standard Solutions
RPH_R&D_006	Care and Use of Animals
RPH_R&D_007	Recording and Storage of Experimental Data
RPH_R&D_008	Identification of Animals for Biodistribution Studies
RPH_R&D_009	Standardization of Volumetric Solutions
RPH_R&D_010	Relative Standard Deviation of Analytical Procedures
RPH_R&D_011	Use of the Canberra Multichannel Analyser (Series 30)
RPH_R&D_012	Use of Packard Cobra Automatic Gamma Counter
RPH_R&D_013	Use of the Capintech Dose Calibrator
RPH_R&D_014	Use of the Mettler Analytical Balance
RPH_R&D_015	Use of the Waters Capilliary Electrophoresis System
RPH_R&D_016	Use of the Berthold Thin Layer Radiochromatogram Analyser
RPH_R&D_017	Testing of Millipore Water System
RPH_R&D_018	Calibration of the Packard Cobra Automatic Gamma Counter
RPH_R&D_019	Calibration of the Capintech Dose Calibrator
RPH_R&D_020	Calibration of the Berthold Thin Layer Radiochromatogram Analyser
RPH_R&D_021	Controlled Temperature Shipments to Thomae
RPH_R&D_022	Use of the PH Meter
RPH_R&D_023	Calibration of Mettler Balance
RPH_R&D_024	Investigation of Out of Specification and Atypical Results
RPH_R&D_025	Calibration of the Spectronic Genesis 5 Spectrophotometer

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