MATERIALS LICENSE

Amendment No. 19

Pursuant to the Atomic Energy Act of 1954, as amended, the Energy Reorganization Act of 1974 (Public Law 93-438), and Title 10, Code of Federal Regulations, Chapter I, Parts 30, 31, 32, 33, 34, 35, 36, 39, 40, and 70, and in reliance on statements and representations heretofore made by the licensee, a license is hereby issued authorizing the licensee to receive, acquire, possess, and transfer byproduct, source, and special nuclear material designated below; to use such material for the purpose(s) and at the place(s) designated below; to deliver or transfer such material to persons authorized to receive it in accordance with the regulations of the applicable Part(s). This license shall be deemed to contain the conditions specified in Section 183 of the Atomic Energy Act of 1954, as amended, and is subject to all applicable rules, regulations, and orders of the Nuclear Regulatory Commission now or hereafter in effect and to any conditions specified below.

301972

Licensee	
1. Mallinckrodt Medical, Inc. 2. 2703 Wagner Place Maryland Heights, MO 63043	In accordance with letter dated October 21, 1996 3. License Number 24-04206-05MD is amended in its entirety to read as follows: 4. Expiration Date December 31, 2000 5. Docket or Reference No. 030-10801

6. Byproduct, Source, and/or Special Nuclear Material	7. Chemical and/or Physical Form	8. Maximum Amount that Licensee May Possess at Any One Time Under This License
A. Chromium-51	A. Sodium Chromate (NDA 16-708)	A. Not Applicable
B. Xenon-133	B. Gas (NDA 18-327)	B. Not Applicable
C. Iodine-125	C. Radioiodinated Human Serum Albumin (NDA 17-844)	C. Not Applicable
D. Iodine-131	D. Sodium Iodohippurate (NDA 16-666)	D. Not Applicable
E. Iodine-131	E. Sodium Iodide Capsules (NDA 16-517)	E. Not Applicable
F. Iodine-131	F. Sodium Iodide Solution (NDA 16-515)	F. Not Applicable
G. Phosphorus-32	G. Chromic Phosphate NDA 17-084)	G. Not Applicable
H. Phosphorus-32	H. Sodium Phosphate (NDA 11-777)	H. Not Applicable
I. Molybdenum-99	I. Molybdenum-99/ Technetium-99m generators (Mallinckrodt, Inc. Ultra-Technekow FM Generators NDA 17-243)	I. Not Applicable

d1

280096

2 30 SD

MATERIALS LICENSE
SUPPLEMENTARY SHEET

License Number
24-04206-05MD

Docket or Reference Number
030-10801

Amendment No. 19

6. Byproduct, source, and/or special nuclear material	7. Chemical and/or physical form	8. Maximum amount that licensee may possess at any one time under this license
J. Molybdenum-99	J. Molybdenum-99/ Technetium-99m generators (Mallinckrodt, Inc. Ultra-Technekow FM, NDA No. 17-243)	J. No single generator to exceed 12 curies on day of shipment
K. Molybdenum-99	K. Molybdenum-99/ Technetium-99m generators (Mallinckrodt, Inc. Ultra-Technekow FM, generators modified to use Medi-Physics depleted uranium (DU) shields, NDA No. 17-243)	K. No single generator to exceed 12 curies on day of shipment
L. Rhenium-186	L. Sodium Perrhenate or Rhenium-186 Etidronate (IND 34,326)	L. Not Applicable
M. Molybdenum-99	M. Molybdenum-99/ Technetium-99 generators (Mallinckrodt, Inc. Ultra-Technekow FM Dry Top Eluting Generators NDA No. 17-243/S-012)	M. No single generator to exceed 19 curies on day of shipment

9. Authorized Use:

Pursuant to Section 32.72 and 32.74 of 10 CFR Part 32, the licensee is authorized to distribute the byproduct material described in Items 6 and 7 of this license to persons licensed pursuant to Sections 35.14 and 35.100 of 10 CFR Part 35 (superseded) or Sections 35.100, 35.200 and 35.300 of 10 CFR Part 35 (effective April 1, 1987), or under equivalent licenses of Agreement Stations, for the Groups or Sections indicated below:

MATERIALS LICENSE
SUPPLEMENTARY SHEET

License Number: 24-04206-05MD

Docket or Reference Number: 030-10801

Amendment No. 19

A. Group I (superseded) or Section 35.100 (effective April 1, 1987).

B. Section 35.200 (effective April 1, 1987).

C. Group I (superseded) or Section 35.100 (effective April 1, 1987).

D. Group I and Group II (superseded) or Section 35.100 (effective April 1, 1987).

E. Group I, Group II, Group IV, and Group V (superseded) or Sections 35.100 or 35.300 (effective April 1, 1987).

F. Group IV and Group V (superseded) or Section 35.300 (effective April 1, 1987).

G. Group IV (superseded) or Section 35.300 (effective April 1, 1987).

H. Group IV (superseded) or Section 35.300 (effective April 1, 1987).

I. Group III (superseded) or Section 35.200 (effective April 1, 1987).

J. For distribution to Mallinckrodt, Inc. nuclear pharmacy licenses and other commercial nuclear pharmacies as described in letter dated March 14, 1994 with attachments and in accordance with statements, representations, and procedures listed in letters dated November 15, 1985 and October 3, 1986.

K. For distribution to nuclear pharmacy and hospital licenses, who are customers of Medi-physics, in accordance with statements, representations, and procedures listed in letters dated May 14, 1993 and May 25, 1993.

L. Group II (superseded) or Section 35.200 (effective April 1, 1987).

M. For distribution to Mallinckrodt, Inc. nuclear pharmacy licenses and other commercial nuclear pharmacies as described in letters dated 10/10/95, 8/14/95, 9/26/96 and 10/10/96, in accordance with statements, representations, and procedures listed in letters dated 11/15/95, 10/3/86, 10/21/96, 01/23/97 and 03/04/97.

CONDITIONS

10. This license does not authorize possession or use of licensed material.

11. The licensee shall notify the U.S. Nuclear Regulatory Commission within thirty (30) days of the termination of a "Notice of Claimed Investigational Exemption for a New Drug (IND) for licensed material described in Items 6 and 7.

MATERIALS LICENSE
SUPPLEMENTARY SHEET

License Number
24-04206-05MD

Docket or Reference Number
030-10801

Amendment No. 19

12. The licensee may transport licensed material in accordance with the provisions of 10 CFR Part 71, "Packaging and Transportation of Radioactive Material."

13. Any proposed changes in packaging, shielding, labeling or the package insert shall be submitted for review to the Material Licensing Section, U.S. Nuclear Regulatory Commission, 801 Warrenville Road, Lisle, Illinois 60532-4351.

14. The distribution of the Mallinckrodt Ultra-TechneKow FM (UTK-FM) Molybdenum-99/Technetium-99m Generators which contain Medi-Physics depleted uranium (DU) shields authorized in License Items 6.K. and 7.K. of this license does not relieve Mallinckrodt Medical, Inc. from compliance with applicable Food and Drug Administration (FDA) requirements before distribution begins.

15. Except as specifically provided otherwise by this license, the licensee shall manufacture, package, label and distribute licensed material described in Items 6. and 7. of this license in accordance with the statements, representations, and procedures contained in:

    A. Application dated July 31, 1990; and

    B. Letters dated November 15, 1985, October 3, 1986, May 14, 1993, May 25, 1993, March 14, 1994 (with attachments) and October 10, 1995, August 14, 1996, September 26, 1996, October 10, 1996, October 21, 1996, January 23, 1997, March 5, 1997, and March 7, 1997.

FOR THE U.S. NUCLEAR REGULATORY COMMISSION

Date March 13, 1997

By Cynthia D. Pederson
Nuclear Materials Licensing Branch, Region III

BETWEEN:

License Fee Management Branch, ARM
and
Regional Licensing Sections

(FOR LFMS USE)
INFORMATION FROM LTS

Program Code: 02511
Status Code: O
Fee Category: 3D
Exp. Date: 20001231
Fee Comments:
Decom Fin Assur Reqd: N

LICENSE FEE TRANSMITTAL

A. REGION

1. APPLICATION ATTACHED
   Applicant/Licensee: MALLINCKRODT MEDICAL INCORPORATED
   Received Date: 961022
   Docket No: 3010801
   Control No.: 301972
   License No.: 24-04206-05MD
   Action Type: Amendment

2. FEE ATTACHED
   Amount: 500
   Check No.: 312208

3. COMMENTS

Signed D. Hersey
Date 10-27-96

1996 OCT 28 AM 11:33

B. LICENSE FEE MANAGEMENT BRANCH (Check when milestone 03 is entered /)

1. Fee Category and Amount: 3D #430

2. Correct Fee Paid. Application may be processed for:
   Amendment ✓
   Renewal
   License

3. OTHER

Signed SC
Date 10/28/96

NOV 06 1996

Log OCT 12 III
Remitter
Check No. 312208
Amount $500 #430 Refund #70
Fee Category 3D
Type of Fee AMD
Date Check Rec'd 10/28/96
Date Completed
By SC

MALLINCKRODT
Nuclear Medicine

October 21, 1996

Mallinckrodt Medical, Inc.
2703 Wagner Place
Maryland Heights, MO 63043
Telephone (314) 770-7800

Cassandra F. Frazier
Nuclear Materials Licensing Section
U.S. Nuclear Regulatory Commission,
Region III
801 Warrenville Road
Lisle, Illinois 60532-4351

RE: License No. 24-04206-05MD

Dear Ms. Frazier,

Mallinckrodt Medical, Inc. (MMI) hearby applies for an amendment of the above referenced license for the distribution of Dry Top Eluting Mo-99/Tc99m Generators (DTE Generator) ranging in sizes from 9.7 Ci to 15.4 Ci. Currently, MMI has a license to distribute Ultra-TechnaKow (UTK) generators ranging from 0.25 Ci to 12.0 Ci sizes. MMI also has a pending license amendment application for the distribution of DTE generators ranging from 0.50 Ci to 12.0 Ci sizes. On the week of October 15, 1996, you indicated that you intended to sign the approval letter for the license amendment application which would allow MMI to distribute the 0.50 Ci to 12.0 Ci DTE generators.

Enclosed in Attachment I are technical data tables regarding the maximum precalibration activity amounts and radiation levels for the unpackaged generator. Surface and TI radiation levels for all the proposed packaged generator sizes are included in Attachment II.

The DTE generator labeling and drawings of the DTE DU shielding safes have been submitted in the license amendment application dated October 10, 1995, final approval letter dated August 14, 1996, and the second DU shielding safe drawing letter dated September 26, 1996

Please expedite this license amendment application. On the week of September 30, 1996 we had a telephone discussion regarding this license application and I mentioned that MMI was very eager to have this license amendment application reviewed and processed by the NRC at their earliest convenience. You recommended that MMI include a request

NOV 06 1996

RECEIVED
OCT 22 1996
REGION III

Pm; 10-21-96

301972

for the NRC to expedite the license application within the text of the license amendment application. We appreciate your agreement for an expedient review of this license amendment application.

We believe that we have included and reference all of the information you will need for your assessment of the application for additional larger size DTE generators. NRC Form 313 and a $500 check for the license amendment fee is attached.

We very much appreciate your prompt attention to this amendment request. Please contact me at (314) 779-7981 if you have any questions or require additional information.

Sincerely,

Daniel Riemer
Radiation Safety Officer
Mallinckrodt Medical
Maryland Heights, MO

Attachments
NRC Form 313
Amendment Check Fee

The DTE Generator

Product Catalog No.; Size, Precalibration, Overlabeled Size, Surface Radiation Level and NDA Number

Catalog Number	Product (Day of Shipment)	Size (Ci)	b Number of Days Precalibration	Multiplier Factors For Over Labeled Size	d Shield Size	c mR/hr at Shield Surface @ Pre-Cal	NDA Number
N881A3	DTE - Mon	0.5 (13.2)[a]	13	26.4	L332	142	17-243
N882A2	DTE - Mon	0.75 (15.4)[a]	12	20.5	L332	166	17-243
N882B1	DTE - Fri	0.75 (12)[a]	11	16.0	L332	130	17-243
N882B2	DTE - Fri	0.75 (15.4)[a]	12	20.5	L332	166	17-243
N883A9	DTE - Mon	1.0 (9.7)[a]	9	9.7	L332	105	17-243
N883A1	DTE - Mon	1.0 (12.4)[a]	9	12.4	L332	134	17-243
N883B9	DTE - Fri	1.0 (12.4)[a]	10	12.4	L332	134	17-243
N884A9	DTE - Mon	1.5 (14.5)[a]	9	9.7	L332	156	17-243
N884B8	DTE - Fri	1.5 (11.3)[a]	8	7.5	L332	122	17-243
N886A6	DTE - Mon	2.5 (11.3)[a]	6	4.5	L332	122	17-243
N886B6	DTE - Fri	2.5 (11.3)[a]	6	4.5	L332	122	17-243
N886B7	DTE - Fri	2.5 (14.6)[a]	7	5.8	L332	157	17-243
N887A5	DTE - Mon	3.0 (10.6)[a]	5	3.5	L332	114	17-243
N887B6	DTE - Fri	3.0 (13.6)[a]	6	4.5	L332	147	17-243

a. Size on day of shipment.
b. These values may be less than or equal to the maximum days of precalibration.
c. These radiation levels may be less than or equal to the maximum mR/hr.
d. DU safe.

Attachment II

Radiation Levels
for
Packaged DU DTE Generators
(mR/hr)

Size (Ci)	Surface	TI
9.7	15.0	0.65
10.6	17.0	0.70
11.3	17.5	0.75
12.0	18.0	0.80
12.4	19.0	0.85
13.2	20.0	0.90
13.6	21.0	0.95
14.5	22.5	1.00
14.6	23.0	1.30
15.4	24.0	1.50

Note: The radioactivity amounts may be in excess of the above amounts at the time of shipment under special circumstances (i.e. holidays, long weekends and special customer requests). However, the maximum activity at the time of shipment will not exceed 19 curies under these conditions.

NRC FORM 313
(9-88)
10 CFR 30, 32, 33, 34, 35 and 40

APPLICATION FOR MATERIAL LICENSE

U.S. NUCLEAR REGULATORY COMMISSION
APPROVED BY OMB
3150-0120
Expires: 5-31-87

INSTRUCTIONS: SEE THE APPROPRIATE LICENSE APPLICATION GUIDE FOR DETAILED INSTRUCTIONS FOR COMPLETING APPLICATION. SEND TWO COPIES OF THE ENTIRE COMPLETED APPLICATION TO THE NRC OFFICE SPECIFIED BELOW.

APPLICATIONS FOR DISTRIBUTION OF EXEMPT PRODUCTS FILE APPLICATIONS WITH:

U.S. NUCLEAR REGULATORY COMMISSION
DIVISION OF FUEL CYCLE AND MATERIAL SAFETY, NMSS
WASHINGTON, DC 20555

ALL OTHER PERSONS FILE APPLICATIONS AS FOLLOWS. IF YOU ARE LOCATED IN:

CONNECTICUT, DELAWARE, DISTRICT OF COLUMBIA, MAINE, MARYLAND, MASSACHUSETTS, NEW HAMPSHIRE, NEW JERSEY, NEW YORK, PENNSYLVANIA, RHODE ISLAND, OR VERMONT, SEND APPLICATIONS TO:

U.S. NUCLEAR REGULATORY COMMISSION, REGION I
NUCLEAR MATERIALS SAFETY SECTION B
631 PARK AVENUE
KING OF PRUSSIA, PA 19406

ALABAMA, FLORIDA, GEORGIA, KENTUCKY, MISSISSIPPI, NORTH CAROLINA, PUERTO RICO, SOUTH CAROLINA, TENNESSEE, VIRGINIA, VIRGIN ISLANDS, OR WEST VIRGINIA, SEND APPLICATIONS TO:

U.S. NUCLEAR REGULATORY COMMISSION, REGION II
NUCEAR MATERIALS SAFETY SECTION
101 MARIETTA STREET, SUITE 2900
ATLANTA, GA 30323

IF YOU ARE LOCATED IN:

ILLINOIS, INDIANA, IOWA, MICHIGAN, MINNESOTA, MISSOURI, OHIO, OR WISCONSIN, SEND APPLICATIONS TO:

U.S. NUCLEAR REGULATORY COMMISSION, REGION III
MATERIALS LICENSING SECTION
799 ROOSEVELT ROAD
GLEN ELLYN, IL 60137

ARKANSAS, COLORADO, IDAHO, KANSAS, LOUISIANA, MONTANA, NEBRASKA, NEW MEXICO, NORTH DAKOTA, OKLAHOMA, SOUTH DAKOTA, TEXAS, UTAH, OR WYOMING, SEND APPLICATIONS TO:

U.S. NUCLEAR REGULATORY COMMISSION, REGION IV
MATERIAL RADIATION PROTECTION SECTION
611 RYAN PLAZA DRIVE, SUITE 1000
ARLINGTON, TX 76011

ALASKA, ARIZONA, CALIFORNIA, HAWAII, NEVADA, OREGON, WASHINGTON, AND U.S. TERRITORIES AND POSSESSIONS IN THE PACIFIC, SEND APPLICATIONS TO:

U.S. NUCLEAR REGULATORY COMMISSION, REGION V
NUCLEAR MATERIALS SAFETY SECTION
1450 MARIA LANE, SUITE 210
WALNUT CREEK, CA 94596

PERSONS LOCATED IN AGREEMENT STATES SEND APPLICATIONS TO THE U.S. NUCLEAR REGULATORY COMMISSION ONLY IF THEY WISH TO POSSESS AND USE LICENSED MATERIAL IN STATES SUBJECT TO U.S. NUCLEAR REGULATORY COMMISSION JURISDICTION.

1. THIS IS AN APPLICATION FOR (Check appropriate item)

- [ ] A. NEW LICENSE
- [X] B. AMENDMENT TO LICENSE NUMBER 24-04206-05MD
- [ ] C. RENEWAL OF LICENSE NUMBER _____

2. NAME AND MAILING ADDRESS OF APPLICANT (Include Zip Code)

Mallinckrodt Medical
2703 Wagner Place
Maryland Heights, MO 63043

3. ADDRESS(ES) WHERE LICENSED MATERIAL WILL BE USED OR POSSESSED.

2703 Wagner Place
Maryland Heights, MO 63043

4. NAME OF PERSON TO BE CONTACTED ABOUT THIS APPLICATION

Daniel Riemer

TELEPHONE NUMBER: 314-770-7981

SUBMIT ITEMS 5 THROUGH 11 ON 8½ x 11" PAPER. THE TYPE AND SCOPE OF INFORMATION TO BE PROVIDED IS DESCRIBED IN THE LICENSE APPLICATION GUIDE.

5. RADIOACTIVE MATERIAL
a. Element and mass number, b. chemical and/or physical form, and c. maximum amount which will be possessed at any one time.

6. PURPOSE(S) FOR WHICH LICENSED MATERIAL WILL BE USED.

7. INDIVIDUAL(S) RESPONSIBLE FOR RADIATION SAFETY PROGRAM AND THEIR TRAINING AND EXPERIENCE.

8. TRAINING FOR INDIVIDUALS WORKING IN OR FREQUENTING RESTRICTED AREAS.

9. FACILITIES AND EQUIPMENT.

10. RADIATION SAFETY PROGRAM.

11. WASTE MANAGEMENT.

12. LICENSEE FEES (See 10 CFR 170 and Section 170.31)
FEE CATEGORY: 3C
AMOUNT ENCLOSED: $ 500.00

13. CERTIFICATION. (Must be completed by applicant) THE APPLICANT UNDERSTANDS THAT ALL STATEMENTS AND REPRESENTATIONS MADE IN THIS APPLICATION ARE BINDING UPON THE APPLICANT.

THE APPLICANT AND ANY OFFICIAL EXECUTING THIS CERTIFICATION ON BEHALF OF THE APPLICANT, NAMED IN ITEM 2, CERTIFY THAT THIS APPLICATION IS PREPARED IN CONFORMITY WITH TITLE 10, CODE OF FEDERAL REGULATIONS, PARTS 30, 32, 33, 34, 35, AND 40 AND THAT ALL INFORMATION CONTAINED HEREIN, IS TRUE AND CORRECT TO THE BEST OF THEIR KNOWLEDGE AND BELIEF.

WARNING: 18 U.S.C. SECTION 1001 ACT OF JUNE 25, 1948, 62 STAT. 749 MAKES IT A CRIMINAL OFFENSE TO MAKE A WILLFULLY FALSE STATEMENT OR REPRESENTATION TO ANY DEPARTMENT OR AGENCY OF THE UNITED STATES AS TO ANY MATTER WITHIN ITS JURISDICTION.

SIGNATURE—CERTIFYING OFFICER	TYPED/PRINTED NAME	TITLE	DATE
[signature]	Les Sabo	D.R., U.S. Nuc. Med Ops.	14 Oct 96

14. VOLUNTARY ECONOMIC DATA

a. ANNUAL RECEIPTS

- [ ] <$250K
- [ ] $250K–500K
- [ ] $500K–750K
- [ ] $750K–1M
- [ ] $1M–3.5M
- [ ] $3.5M–7M
- [ ] $7M–10M
- [ ] >$10M

b. NUMBER OF EMPLOYEES (Total for entire facility excluding outside contractors)

c. NUMBER OF BEDS

d. WOULD YOU BE WILLING TO FURNISH COST INFORMATION (Dollar and/or staff hours) ON THE ECONOMIC IMPACT OF CURRENT NRC REGULATIONS OR ANY FUTURE PROPOSED NRC REGULATIONS THAT MAY AFFECT YOU? (NRC regulations permit it to protect confidential commercial or financial—proprietary—information furnished to the agency in confidence)

- [ ] YES
- [ ] NO

FOR NRC USE ONLY

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OCT 22 1996
REGION III

TYPE OF FEE	FEE LOG	FEE CATEGORY	COMMENTS	APPROVED BY
AMOUNT RECEIVED	CHECK NUMBER			DATE

DIVISION OF ACCOUNTING AND FINANCE
REQUEST FOR REFUND TO EMPLOYEE/VENDOR

THE EMPLOYEE/VENDOR IDENTIFIED BELOW HAS OVERPAID THE NUCLEAR REGULATORY COMMISSION FOR GOODS AND/OR SERVICES PROVIDED AND IS DUE A REFUND

EMPLOYEE/VENDOR/PAYEE CODE: _____

NAME: Mallinckrodt Medical, Inc.

ADDRESS: Attn: Mr. Daniel Riemer, RSO

ADDRESS: 2703 Wagner Place

CITY: Maryland Hts. STATE: MO ZIP: 63043

TRANS CODE: PX

TRANS TYPE: FE	FUND: X5280	JOB CODE: _____	AMOUNT: $70"
TRANS TYPE: IR	FUND: R1435	JOB CODE: INTR	AMOUNT: _____
TRANS TYPE: IR	FUND: R1099	JOB CODE: ADCH	AMOUNT: _____
TRANS TYPE: IR	FUND: R1099	JOB CODE: FINE	AMOUNT: _____

TOTAL REFUND AMOUNT: $70"

COMMENTS: Lic 24-04206-05MD/ck 312208/Rfnd 10/21/96 Reg.

(Limit comments to 40 characters, including spaces)

PREPARED BY: Shirley Crutchfield DATE: Oct. 28, 1996

AUTHORIZED BY: Sandra Kimberly DATE: 10/29/96

ORIGINAL INV. NO: _____ DATE PAID: _____ AMOUNT: _____

REFUND ENTERED INTO COLLECT BY: _____

REFUND DETERMINED BY: _____ DATE: _____

Oct 12 III
Amd 3D $430
Ck 312208 PLEASE ATTACH APPROPRIATE SUPPORTING DOCUMENTATION
Ltd 10/16/96 $500
201972

MAR 1 4 1997

Daniel Riemer
Radiation Safety Officer
Mallinckrodt Medical, Inc.
2703 Wagner Place
Maryland Heights, MO 63043

Dear Mr. Riemer:

Enclosed is Amendment No. 19 to your NRC Material License No. 24-04206-05MD in accordance with your request.

Please review the enclosed document carefully and be sure that you understand all conditions. If there are any errors or questions, please notify the U.S. Nuclear Regulatory Commission, Region III office so that we can provide appropriate corrections and answers.

Please be advised that your license expires at the end of the day, in the month, and year stated in the license. Unless your license has been terminated, you must conduct your program involving byproduct materials in accordance with the conditions of your NRC license, representations made in your license application, and NRC regulations. In particular, note that you must:

1. Operate in accordance with NRC regulations 10 CFR Part 19, "Notices, Instructions and Reports to Workers; Inspections," 10 CFR Part 20, "Standards for Protection Against Radiation," and other applicable regulations.

2. Not possess and use materials authorized in Items 6, 7, and 8, on the license until:

   a. You have constructed the facilities and obtained the equipment described in the license application and supporting documentation; and

   b. You have notified the U. S. Nuclear Regulatory Commission, Region III, ATTN: Chief, Nuclear Materials Safety Branch, in writing, that activities authorized by the license will be initiated.

3. Notify NRC, in writing, within 30 days:

   a. When an authorized user or Radiation Safety Officer permanently discontinues performance of duties under the license or has a name change; or

301972

b. When the licensee's mailing address changes (no fee is required if the location of byproduct material remains the same).

4. In accordance with 10 CFR 30.36(b) and/or license condition, notify NRC, promptly, in writing, and request termination of the license:

a. When you decide to terminate all activities involving materials authorized under the license; or

b. If you decide not to complete the facility, acquire equipment, or possess and use authorized material.

5. Request and obtain a license amendment before you:

a. Receive or use byproduct material for a clinical procedure permitted under Part 35 but not permitted by your license issued pursuant to this Part;

b. Permit anyone, except a visiting authorized user described in 10 CFR 35.27, to work as an authorized user under the license;

c. Change Radiation Safety Officers;

d. Order byproduct material in excess of the amount, or radionuclide, or form different than authorized on the license;

e. Add or change the areas of use or address or addresses of use identified in the license application or on the license; or

f. Change ownership of your organization.

6. Submit a complete renewal application with proper fee or termination request at least 30 days before the expiration date of your license. You will receive a reminder notice approximately 90 days before the expiration date. Possession of byproduct material after your license expires is a violation of NRC regulations. A license will not normally be renewed, except on a case-by-case basis, in instances where licensed material has never been possessed or used.

In addition, please note that NRC Form 313 requires the applicant, by his/her signature, to verify that the applicant understands that all statements contained in the application are true and correct to the best of the applicant's knowledge. The signatory for the application should be the licensee or certifying official rather than a consultant.

You will be periodically inspected by NRC. Failure to conduct your program in accordance with NRC regulations, license conditions, and representations made in your license application and supplemental correspondence with NRC will result in enforcement action against you. This could include issuance of a notice of violation, or imposition of a civil penalty, or an order suspending, modifying or revoking your license as specified in the General Policy and Procedures for NRC Enforcement Actions, 10 CFR Part 2, Appendix C. Since serious consequences to employees and the public can result from failure to comply with NRC requirements, prompt and vigorous enforcement action will be taken when dealing with licensees who do not achieve the necessary meticulous attention to detail and the high standard of compliance which NRC expects of its licensees.

Sincerely,

Original Signed By
Cassandra Frazier
Nuclear Materials Licensing Branch

License No. 24-04206-05MD
Docket No. 030-10801

Enclosure: Amendment No. 19

DOCUMENT NAME: M:\03010801.CL7
To receive a copy of this document, indicate in the box: "**C**" = Copy without attachment/enclosure "**E**" = Copy with attachment/enclosure "**N**" = No copy

OFFICE	DNMS/RIII									
NAME	CFFrazier:brt									
DATE	03/ /97									

OFFICIAL RECORD COPY

MALLINCKRODT MEDICAL

Health Physics Department
Maryland Heights, MO

Facsimile Communication

Daniel Riemer
Radiation Safety Officer

Mallinckrodt Medical, Inc.
675 McDonnell Boulevard
PO Box 5840
St. Louis, MO 63134

Telephone (314) 770-7981
Facsimile (314) 770-7998

To: Ms. Cassandra Frazier
Company: Nuclear Materials Licensing Section
U.S. Nuclear Regulatory Commission
Region III
Fax Number: (630) 515-1078
Date: 03/10/97

Number of Pages *(including cover sheet)*: 9

- ☐ For your information
- ☐ Please respond
- ☐ Urgent
- ☐ Confidential

Comments:

Re: Correspondence between Mallinckrodt and FDA regarding larger size generators in NDA 17-243 supplement S-012.

MALLINCKRODT
Nuclear Medicine

March 7, 1997

Mallinckrodt Medical, Inc.
2703 Wagner Place
Maryland Heights, MO 63043
Telephone (314) 770-7800

Ms. Cassandra Frazier
Nuclear Materials Licensing Section
U.S. Nuclear Regulatory Commission
Region III
801 Warrenville Road
Lisle, Illinois 60532-4351

RE: NRC Question Related to the Pending Second License Amendment for the Distribution of 9.7 Curie (Ci) to 15.4 Ci Ultra-TechnaKow, Dry Top Eluting (DTE) Mo-99/Tc-99m Generators.

Dear Ms. Frazier:

Earlier today we had a telephone discussion regarding the correspondence between Mallinckrodt and the Food and Drug Administration (FDA) regarding 19 Ci size DTE generators. You noted that the New Drug Application (NDA) supplement in the March 5, 1997 response, regarding Mallinckrodt's application for a NRC amendment to distribute larger size generators, referenced a supplement number of "S-013" and that the FDA approvable letter which Mallinckrodt sent to you in an August 14, 1997 response referenced a supplement number of "S-012". We agreed that to resolve this issue, I would need to provide clarification regarding the identity of the two different supplements and also provide a correspondence from Mallinckrodt to the FDA which referenced both the S-012 supplement and larger size generators. The issue regarding the different supplement numbers was discussed with Mr. Ron Bartnick, Manager of Quality/Regulatory Compliance. He stated that the S-012 NDA supplement was for the manufacture and distribution of DTE generators and the S-013 was a supplement to utilize Mo-99 from an additional vendor.

Enclosed as Attachment I, for your review, are portions of the July 1992, Mallinckrodt supplement S-012 for NDA 17-243. In the attachment you will see that S-012 is referenced in the cover letter and the larger size DTE generators, 25 Ci, is referenced in the protocol tests and the test data table. Please also note that the "DTE" generator was previously nicknamed the "Hybrid Generator".

We believe that these documents satisfy the issues which you and I discussed earlier today.

Please contact me at (314) 770-7981 if you have any additional questions or if I may be of assistance in any other way.

Sincerely,

Daniel Riemer
Radiation Safety Officer
Mallinckrodt, Inc.
Maryland Heights Facility

Attachment

Attachment I
1 of 6

MALLINCKRODT MEDICAL

July 31, 1992

Mallinckrodt Medical, Inc.
675 McDonnell Boulevard
PO Box 5840
St. Louis, MO 63134
Telephone 314 895 2000

Food and Drug Administration
Center for Drug Evaluation & Research
Office of Drug Evaluation I
Division of Medical Imaging, Surgical
and Dental Drug Products, HFD #160
ATTN: Document Control Room 18B-03
5600 Fishers Lane
Rockville, Maryland 20857

RE: NDA 17-243
Ultra-TechneKow(R) FM
Supplement S-012

Dear Sir/Madam:

Please refer to Mallinckrodt Medical's approved NDA 17-243 for Ultra-TechneKow FM (Technetium Tc 99m Generator).

On November 15, 1990, representatives from Mallinckrodt Medical met with FDA officials to review a program for modifying our present generator. At the meeting it was understood that FDA would require an NDA supplement that would include a full description of the generator, methods of manufacture and control, stability data, and revised labeling.

On July 1, 1991 Mallinckrodt Medical sent to FDA a draft stability protocol for the modified (Hybrid) generator. Based on FDA comments received on July 31, 1991, we revised the stability protocol.

Mallinckrodt Medical, hereby, supplements NDA 17-243 with information that provides for the manufacture and distribution of the modified generator.

Sincerely,

Robert S. Lake

Robert S. Lake
Sr. Regulatory Affairs Associate

cc: S. Lange

NDA 17-243J U L Y 1992

TRADE SECRET

Attachment I
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Ultra-TechneKow(R) FM
(Technetium Tc 99m Generator)

NDA 17-243
Supplement

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TRADE SECRET

Mallinckrodt Medical, Inc.
St. Louis, Missouri

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PHARMACEUTICAL R & D
PHARMACEUTICS SECTION
STABILITY PROTOCOL
PAGE 1 OF 3

Product: Code 100/107H Hybrid Mo-99/Tc99m Generators — Date: 5-May-91

LOT NO.: — Original 26-May-92

PURPOSE: Comparison of Hybrid and M/H Generator Performance & Pharmaceutical Quality of Sodium Pertechnetate Tc-99m Injection.

FORMULATION: As per Code 100/107C Code 100/107H D225 & D228 Batch Sheets

CONTAINER: Code 100/107H Generator System as Shown in Exploded Drawing on Page 1.005 of Volume 1.

CLOSURE: Code L378 Stopper 13 mm Column, Punched
Code L325 Stopper, Connector Fitting
Code K230 & L376 Closure, Aluminum

DATE MANUFACTURED: DATE STUDY INITIATED:

GENERATOR/Tc-99m QUALITY TEST	LIMITS	ELUTION/TEST SCHEDULE[2] Elution No.	TEST INTERVAL
Tc-99m Yield	>70% of available Tc-99m	1 thru 10	Initial
Radionuclidic Purity:			
Mo-99	<0.15 uCi Mo-99 per mCi of Tc-99m	1 thru 10	Init & 12 Hr
I-131	<0.05 uCi of I-131 per mCi of Tc-99m	1st & 10th	Init & 12 Hr
Ru-103	<0.05 uCi of Ru-103 per mCi of Tc-99m	1st & 10th	Init & 12 Hr
Sr-89	<0.0006 uCi Sr-89 per mCi of Tc-99m	1st & 10th	Init & 12 Hr
Sr-90	<0.00006 uCi Sr-90 per mCi of Tc-99m	1st & 10th	Init & 12 Hr
Other Beta & Gamma	<0.1 uCi Other Beta & Gamma/mCi Tc-99m	1st & 10th	Init & 12 Hr
Gross Alpha	<0.000001 uCi Alpha per mCi Tc-99m	1st & 10th	Init & 12 Hr

2 All generators to be eluted daily on Monday through Friday up to the expiry date of the generator.

2.297

JULY 1992

Mallinckrodt Medical, Inc. TRADE SECRET
St. Louis, Missouri

Attachment I
4 of 6

PHARMACEUTICAL R & D
PHARMACEUTICS SECTION
STABILITY PROTOCOL
PAGE 2 OF 3

PRODUCT: Code 100/107H Hybrid Mo-99/Tc99m Generators

Date: 5-May-91

Original 26-May-92

GENERATOR/TC-99M QUALITY TEST	LIMITS	ELUTION/TEST SCHEDULE Elution No.	Test Interval
Radionuclidic Identity	140 Kev gamma	1st & 10th	Init & 12 Hr
Radiochemical Purity	>95% as TcO_4^-	1, 5 & 10th	Init & 12 Hr
Appearance	Clear, Colorless, Free of Visible Particulates.	1, 5 & 10th	Init & 12 Hr
pH	4.5 to 7.5	1, 5 & 10th	Init & 12 Hr
Aluminum	<10 ug/ml	1, 5 & 10th	Init
NaCl	0.8 to 1.0%	1st & 10th	Init
Endotoxin	<175 Eu/elution	1st & 10th	Init
Sterility	Conforms	1st & 10th	Init & 12 Hr

2.208

TRADE SECRET

Mallinckrodt Medical, Inc.
St. Louis, Missouri

Attachment II
5 of 6

PHARMACEUTICAL R & D
PHARMACEUTICS SECTION
STABILITY PROTOCOL

PRODUCT: Code 100/107H Hybrid Mo-99/Tc99m Generators (Cont'd)

Date: 5-May-91

Original 26-May-92

Generator Allocation[3] Chart

Generator Type	Size	Storage Conditions[4] Refrig.	RT	50°C
M/H	0.25 Ci	X	X	X
Hybrid	0.25 Ci	X	X	X
M/H	1.5 Ci	X	X	X
Hybrid	1.5 Ci	X	X	X
M/H	3.0 Ci	X	X	X
Hybrid	3.0 Ci	X	X	X
M/H	25.0 Ci	X	X	X
Hybrid	25.0 Ci	X	X	X

Formulator _____

Supervisor _____

3. A minimum of 3 lots of generators will be manufactured and tested. Each lot will consist of an equal number of M/H (Control) generators and Hybrid Generators.

4. Generators are to placed at designated storage conditions after packaging into shipping cartons. The generators will be unpacked and transferred to room temperature storage just before the first elution.

2.209

Mallinckrodt Medical, St. Louis, Missouri

TABLE A-X2005-1. HYBRID Tc-99m GENERATOR, (Per Cent Yield of Tc-99m from Generator)

TEST CATEGORY			Technetium-99m Yield (% Elution Efficiency) (Limit = > 70%)									
Generator Lot No.			X2005									
Date Manufactured			03/13/92									
Date Testing Initiated			03/16/92									
Type Gen.	Gen. Size	Gen. No.	1 Mon.	2 Tues.	3 Wed.	4 Thur.	5 Fri.	6 Mon.	7 Tues.	8 Wed	9 Thur.	10 Fri.
2-8C:	(Cl)											
CONTROL	25.0	4	106.23	94.10	91.09	92.75	94.22	93.40	93.17	93.43	92.91	93.49
HYBRID	25.0	1	106.13	96.64	91.36	92.57	95.81	94.12	93.51	93.05	91.76	94.49
16-30C:												
CONTROL	25.0	5	104.09	93.55	91.46	92.37	93.72	92.90	93.17	92.54	92.86	93.35
HYBRID	25.0	2	107.64	97.03	94.87	95.99	98.02	97.32	97.12	96.12	96.11	96.59
50C:												
CONTROL	25.0	6	99.27	92.73	91.00	92.17	93.46	92.90	93.17	92.54	92.39	92.76
HYBRID	25.0	3	103.60	92.12	90.01	91.40	92.93	93.86	91.76	92.00	92.88	91.74

TRADE SECRET

c:\x2005\yldmostum.wk1 - Linked to X2005.wk1

MALLINCKRODT
Nuclear Medicine

March 5, 1997

Mallinckrodt Medical, Inc.
2703 Wagner Place
Maryland Heights, MO 63043
Telephone (314) 770-7800

Ms. Cassandra Frazier
Nuclear Materials Licensing Section
U.S. Nuclear Regulatory Commission
Region III
801 Warrenville Road
Lisle, Illinois 60532-4351

RE: NRC Question Related to the Pending Second License Amendment for the Distribution of 9.7 Curie (Ci) to 15.4 Ci Ultra-TechnaKow, Dry Top Eluting (DTE) Mo-99/Tc-99m Generators.

Dear Ms. Frazier:

On March 3, 1997 we had a telephone conversation regarding a January 23, 1997 Mallinckrodt response to NRC questions which were the result of your review of the Mallinckrodt Inc. October 21, 1996 24-04206-05MD license amendment application for the distribution of larger size DTE generators. You stated during this conversation that you required a Mallinckrodt document, which would have been sent to the Food and Drug Administration (FDA), which referenced 19 Ci DTE generators. You stated that a document containing this information would likely address the remaining NRC requirement for the Mallinckrodt license amendment application.

Enclosed as Attachment I, for your review, is a Mallinckrodt response to a April 30, 1996 FDA Approvable letter for New Drug Application (NDA) 17-243/S-013. We believe that this document satisfies your requirement.

Please contact me at (314) 770-7981 if you have any additional questions or if I may be of assistance in any other way.

Sincerely,

Daniel Riemer
Radiation Safety Officer
Mallinckrodt, Inc.
Maryland Heights Facility

Attachment

Attachment I

Mallinckrodt Medical, Inc.

UltraTechneKow-FM Generator
NDA 17-243/S-013
MMI Responses to Approvable Letter 4/30/96

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1. *The kit testing data submitted, is for the 12 Ci and 20 Ci generator sizes and does not include any generator size that will actually be marketed. Please provide the kit testing data from the generator sizes that will be marketed.*

MMI Response: In the teleconference on May 14, 1996 between FDA and MMI, FDA requested further explanation of the pre-calibration process to show that the test data submitted in the supplement does represent data from generator sizes that will be marketed.

Pre-calibration is a process whereby the generator columns are loaded with enough activity (but not to exceed 20 Ci) so that when the customer is ready to use the generator, the label amount of activity is available. Pre-calibration is a common, necessary practice that is employed by manufacturers of virtually all radioactive drug products, and which take into account the radiodecay properties of nuclides.

An example of day of manufacture, day of calibration and the decay scheme for generator columns loaded with approximately 20 Ci and approximately 12 Ci Mo-99 is provided below:

Item Code		Fri.	Sat.	Sun.	Mon.	Tues.	Wed.	Thu	Fri.	Sat.	Sun.
N104	Ci Mo 99 @8PM	19.5 (Date of Mfr.)	15.2	11.8	9.2	7.1	5.5	4.3	3.3	2.6	2.0 (Date of Calib.)
N105	Ci Mo 99 @8PM				11.3 (Date of Mfr.)	8.8	6.9	5.3	4.1	3.2	2.5 (Date of Calib.)

In the case of the N104, the column is loaded with approximately 19.5 Ci of Mo-99 on Friday with the intent of the customer using the generator at label of 2.0 Ci 9 days later. The N105 generator is loaded with approximately 11.3 Ci of Mo-99 on Monday so that the customer has the label amount of 2.5 Ci 6 days later.

The generators loaded with 12 and 20 Ci Mo-99 were specifically chosen for the kit testing to represent the highest amount of activity loaded on the generators. Use of the larger size generators presents a "worse case scenario" with the potential of introducing impurities in the Tc-99m solution derived from the generator, which could impact elution efficiency, Mo-99 breakthrough, Aluminum breakthrough or pH. We believe data previously provided for supplement S-013 have represented generator sizes that will be marketed.

Section II.D.5. (pages 1.078 - 1.082) from supplement S-012 in July of 1992 describes the pre-calibration procedure and is provided for your review.

MALLINCKRODT
Nuclear Medicine

January 23, 1997

Mallinckrodt Medical, Inc.
2703 Wagner Place
Maryland Heights, MO 63043
Telephone (314) 770-7800

Ms. Cassandra Frazier
Nuclear Materials Licensing Section
U.S. Nuclear Regulatory Commission
Region III
801 Warrenville Road
Lisle, Illinois 60532-4351

RE: NRC Questions Related to the Pending Second License Amendment for the Distribution of 9.7 Curie (Ci) to 15.4 Ci Dry Top Eluting (DTE) Mo99/Tc99m Generators

Dear Ms. Frazier

This letter is in references to our recent telephone conversations and telephone message correspondences, during the month of December and our telephone conversation today, regarding the two questions you had related to the Mallinckrodt Inc. October 21, 1996 24-04206-05MD license amendment application for the distribution of larger size Ultra-TechnaKow, Dry Top Eluting (DTE) generators (9.7 Ci to 15.4 Ci sizes). This application was an amendment to an existing license amendment for the distribution of DTE generators (0.5 Ci to 12 Ci sizes) which was approved by the NRC on October 16, 1996.

Your first question was related to radiation levels for a 19 Ci DTE Depleted Uranium (DU) generator. We discussed, on the telephone, that a DTE generator, pre-calibrated to larger sizes but not to exceed the 19 Ci Maryland Heights ceiling, was provided in the October 21,1996 amendment request. However, information related to the radiation levels for the 19 Ci ceiling were not included. You stated that information regarding radiation levels (i.e. unpackaged and packaged generator canister) would likely satisfy your remaining questions regarding this particular issue. Please refer to Attachment I.

Your second question was regarding the Food and Drug Administration (FDA) being aware that the DTE generator could contain amounts of radioactivity up to 19 Ci. This question was presented to Mr. Ron Bartnick, the Maryland Heights Manager of Quality/Regulatory Compliance. Mr. Bartnick is responsible for all FDA compliance issues related to Mallinckrodt, Maryland Heights products.

Mr. Bartnick indicated that the FDA is aware that, based upon precalibration date, the DTE generator could contain amounts of radioactivity up to 19 Ci. Also the New Drug Application (NDA) for DTE generators contains test data to support efficacy of generators which could contain radioactivity in excess of 19 Ci. The FDA approved the NDA supplement in July 16, 1996.

Please contact me at (314) 770-7981 if you have any further questions or comments related to the October 21, 1996 NRC license amendment application.

Sincerely,

Daniel Riemer
Radiation Safety Officer
Mallinckrodt Inc.
Maryland Heights Facility

Attachment

Attachment I

Radiation Levels for a 19.0 Ci DTE Generator

Generator Canister (Unpackaged)

Surface	205.0 mR/hr

Packaged Generator

Surface	29.6 mR/hr
TI	1.85 mR/hr

NOTE:

A given generator size may be pre-calibrated to larger amount of radioactivity but will not exceed 19 Ci at time of shipment. The generator would be manufactured with a DTE DU safe; code number L332.

The NDA supplement number is 17-243.