PUBLIC/PDR

MALLINCKRODT
Nuclear Medicine

24-04216-05MD
030-10801

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 II
2 of 6

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

NDA 17-243
Supplement

TABLE OF CONTENTS

Mallinckrodt Medical, Inc.
St. Louis, Missouri

Attachment I
3 of 6

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.

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

PHARMACEUTICAL R & D
PHARMACEUTICS SECTION
STABILITY PROTOCOL
Page 3 of 3

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.

Attachment I
6 of 6

Mallinckrodt Medical, St. Louis, Missouri

TABLE A-X2005-1. HYBRID To-99m GENERATOR, (Per Cent Yield of To-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	108.23	94.10	91.09	92.75	94.22	93.40	93.17	93.43	92.91	93.49
HYBRID	25.0	1	108.13	96.64	91.36	92.57	95.81	94.12	93.51	93.05	91.76	94.49
15-30C:												
CONTROL	25.0	5	104.09	93.55	91.40	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

JULY 1992

TRADE SECRET

2.293

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