



KENNETH C. SCHTZLE
Director

The University of Michigan

OCCUPATIONAL SAFETY AND ENVIRONMENTAL HEALTH
1077 NORTH UNIVERSITY BUILDING

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ANN ARBOR, MI 48109-1057
(313) 764-8310

30-1988

November 6, 1992

Kevin G. Null
Materials Licensing Section
U.S. Nuclear Regulatory Commission, Region III
799 Roosevelt Road
Glen Ellyn, Illinois 60137

RE: Additional Information for Amendments to NRC License Number
21-00215-04 [Control Number 93714]

Dear Mr. Null:

Per your correspondence dated October 27, 1992, please find below the responses to the items for which additional information or clarification were requested.

1.0 Animal Studies to be Performed at 2615 Gale Road

Please be advised that this particular location request will be withdrawn from this license amendment request. The researcher no longer desires to use radioactive material at the 2615 Gale Road location.

2.0 Californium-252 Sealed Source Maintenance

Please be advised that this particular request to lengthen the frequency for checking the integrity of the storage tank water will be withdrawn from this license amendment request. The researcher has decided that the current frequency is satisfactory and analyses data will continue to be documented to demonstrate water quality trends.

3.0 Blood Bank Irradiator - University of Michigan Hospital

The minor revisions to the supporting information as submitted in Attachment 1.4 of the University of Michigan's July 16, 1992 amendment request are as follows:

3.1 Page 1 / 1st Paragraph: the wording in parentheses "(as loaded on October 3, 1984)" was added.

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- 3.2 Page 1 / 2nd Paragraph: the wording "a minimum dose of 1,500 rads in less than five minutes" has been added.

In addition, this paragraph now indicates that the blood bank irradiator will be used by "research personnel" in addition to blood bank technical personnel and that the irradiator will be used "to irradiate blood for use in research projects."

- 3.3 Page 1 / Section 1.0: previous submittal regarding this irradiator indicated the architectural room number; the actual University Hospital room number is now listed as "2F225".

- 3.4 Page 1 / Section 2.0: the wording "(currently known as Nordion International, Inc.)" has been added.

- 3.5 Page 1 / Section 3.0: same wording as Section 3.4 above.

- 3.6 Page 2 / Section 4.0: the radiation instrumentation has been replaced with a "Victoreen Model 425 SN C492 with Victoreen Model 493-50 SN 3372 Probe" and denotes that it is capable of "detecting gamma radiation."

- 3.7 Page 3 / Section 7.1: notes the actual University Hospital Room to be "2F225".

- 3.8 Page 3 / Section 8.1(E): should be revised to read: "At the end of the exposure time, the chamber will automatically return to the loading position. The key will be switched to the OFF position."

The previous submittal noted that the key would be removed from the switch and returned to the storage hook location; this is no longer the case because the irradiator is under constant surveillance during normal working hours or the room is secured when the source is left unattended afterhours.

- 3.9 Page 3 / Section 8.1(B): the wording "...by turning the keyswitch to RESET, and release it" was added.

- 3.10 Page 4 / Section 8.2(A): the wording in Section 8.2(A) was revised slightly.

- 3.11 Page 4 / Section 8.3: the Irradiator Coordinator emergency phone # has been revised to 936-6861.

3.12 Page 7 / Section 10.0: training session may include a "one hour hands-on or videotape/hands-on practice session which will allow the learner to operate the blood bank irradiator and review previous material. This session includes, but is not limited to: ...".

4.0 J.L. Shepherd Irradiator - Model 6810 Source

Please note that the July 16, 1992 amendment request indicating that the source model was "J.L. Shepherd Model 25" was incorrect. Further investigation revealed that the source Model Number is 6810, while the actual mounting irradiator is Model Number 25. License 21-00215-04 / Section 7 (Subitem CC) is currently correct indicating Source Model No. 6810.

5.0 Personnel Monitoring for Irradiator Workers

Please note that the July 16, 1992 amendment was not requesting that radiation monitoring dosimeters not be worn by irradiator operators; that request had been authorized by the NRC (William Adam, Ph.D.) during the 1990 License renewal process. Rather, the amendment request was a rather simple revision to the previous wording "The film badges will be evaluated monthly by the Radiation Detection Corporation and...".

The intended amendment request was to revise the wording to: "The dosimeters will be evaluated monthly by a NVLAP-accredited dosimeter processing service and the ...". The U-M did not want to commit to a specific dosimeter processor such as "Radiation Detection Corporation".

Hopefully, justification for the workers not to be required to wear dosimeters is no longer needed by your office because it had been approved previously. However, should you require further clarification with respect to this issue we will be happy to forward area monitoring results.

6.0 I-125 & I-131 Meta-iodo-benzylguanidine (MIBG)

6.1 Justification for I-131 (MIBG) Increase

The University of Michigan is requesting an increase from the previously licensed 500 millicuries to 2.0 curies for iodine-131 (MIBG) because the demand for this investigational new drug has increased significantly in the United States and the University of Michigan is the sole source of MIBG in North America.

Over 800 samples of MIBG have been shipped to 127 hospitals worldwide in 1991. This increase in demand for diagnostic and therapeutic MIBG has made it difficult to remain below the license limit of 500 mCi without inefficient ordering and production practices.

Currently, MIBG has shown clinical utility in the diagnosis and treatment of metastatic pheochromocytoma, neuroblastoma, and myocardial and adrenomedullary abnormalities. In addition, research continues to indicate other possible uses of MIBG.

6.2 Justification for I-131 (NP-59) Increase

As noted above for MIBG, the University of Michigan is the sole source of this investigational drug in North America and the demand is extremely high for NP-59 because of its value in the diagnosis of various endocrine diseases. For instance, the uptake of NP-59 is directly related to its ability to mimic cholesterol and as such is an excellent adrenal imaging agent. Like MIBG, medical research efforts continue to identify additional uses for NP-59.

Over 225 samples of NP-59 had been shipped to 53 hospitals within the past year. Higher activity iodinations may actually result in less handling of the radioactive material because fewer iodinations will be necessary to meet the demand for the radiopharmaceutical.

6.3 Purpose & Use of I-125 (MIBG)

Like I-131 (MIBG), iodine-125 (MIBG) is an investigational new drug which can be expected to show clinical utility in the diagnosis and therapeutic treatment of neuroblastoma. Because I-125 emits very low energy gamma rays, the energy is nearly totally absorbed within a few microns of their emission point, thereby imparting lethal radiation to the nuclei of the cancerous cells in which they reside.

Therefore, even individual neuroblastoma cells can be irradiated by I-125 MIBG. Current therapy doses of 400 - 600 millicuries are anticipated; however, levels may need to be increased to 1.0 curie as the study progresses.

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6.4 Description of Facilities Used to Process MIBG

Please refer to Attachment 1.0 for diagrams of each laboratory where MIBG will be processed. Note that all MIBG syntheses will be performed at the Phoenix Memorial Laboratory (PML) on the North Campus of the University of Michigan.

Currently, Room 3060 of the PML facility is used for the syntheses of iodine-125 MIBG and Room 3064 of the PML is used for the syntheses of iodine-131 MIBG and NP-59. The dispensing of the diagnostic quantities of the labeled radioiodinated pharmaceutical is performed in Room 3031 of the PML facility.

Note that Attachment 2.0 lists all the radiation monitoring equipment currently available for use within the PML facility and specifically within Rooms 3031, 3060, and 3064 of the facility.

6.5 Criteria Used By RSC to Evaluate Adequacy of Laboratories

The PML facility is staffed with a full-time Health Physicist and a full-time Radiation Safety Technician from Radiation Safety Service. These individuals are responsible for the day-to-day radiological safety at the facility.

The Health Physicist is specifically responsible for evaluating the radiological safety features of the MIBG and NP-59 radioiodination facilities. These features include, but are not limited to, shielding requirements, ventilation systems, air sampling, etc.

The researchers performing MIBG and NP-59 radioiodinations receive approval from the U-M Radiation Policy Committee (RPC) based on the recommendations of the facility Health Physicist. Authorization applications are completed by the responsible Authorized User, reviewed by the facility Health Physicist, and evaluated by the RPC every two years. In addition, amendments to the authorization are reviewed and approved by the Health Physicist and RPC.

Therefore, in summary, the facility Health Physicist is primarily responsible for assuring radiological safety features are adequate at the facility and he briefs the Radiation Safety Officer and RPC as needed.

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6.6 Description of Typical Labeling Frequencies

Although tentative at this particular time, the proposed labeling frequency is as follows:

- (1) I-131 MIBG Diagnostic Production - approx. 180 mCi twice monthly
- (2) I-131 MIBG Therapy Production - approx. 1.0 curie twice monthly
- (3) I-125 MIBG Therapy Production - approx. 6 at 1.0 curie per year
- (4) I-131 NP-59 Diagnostic Production - approx. 100 mCi twice monthly

6.7 Air Sampling Program for General Area & Breathing Zones

Please note that all exhaust stacks associated with the PML facility are monitored continuously for radionuclide emissions using activated charcoal cartridges and particulate filters. In addition, a breathing zone monitor has been in use in the I-131 radioiodination facility located in Room 3064 for many years.

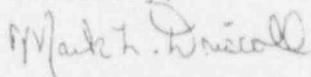
In addition to the continuous effluent and breathing zone air monitoring, the University of Michigan has a dedicated thyroid bioassay program established to monitor radioiodinators for iodine-125 and iodine-131 uptakes. The equipment used to monitor thyroids is state-of-the-art, sensitive, and very effective in determining nanocurie levels of various radioiodines in a person's thyroid.

Therefore, the U-M has the capability of measuring actual uptakes by individuals and not merely airborne concentrations as measured with breathing zone air samplers.

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Thank you for your time, effort, and consideration in this amendment request. Please do not hesitate to contact me at Radiation Safety Service [(313) 764-4420] should you have any additional questions, comments, or concerns regarding this amendment request. Please contact Health Physicist Alan Jackson [(313) 936-1587] regarding the radioiodination section of this correspondence.

Sincerely,



Mark L. Driscoll
Director/Radiation Safety Officer
Radiation Safety Service

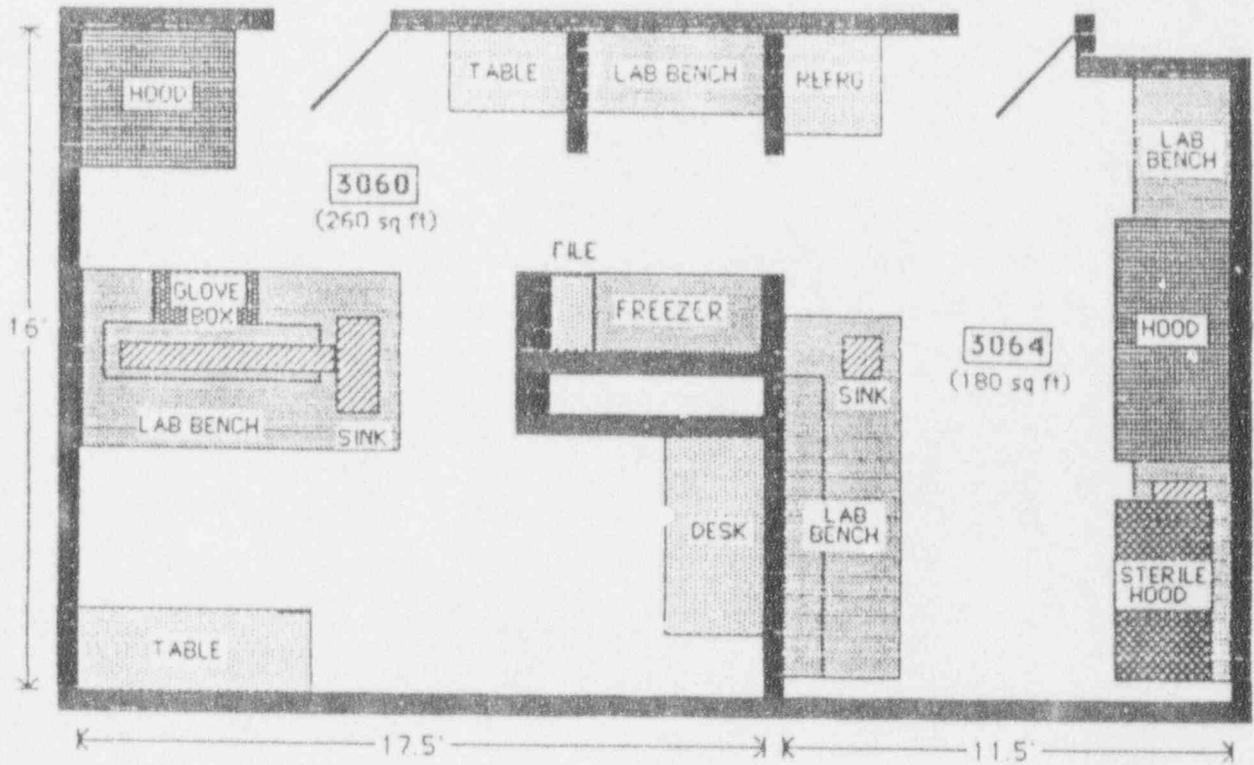
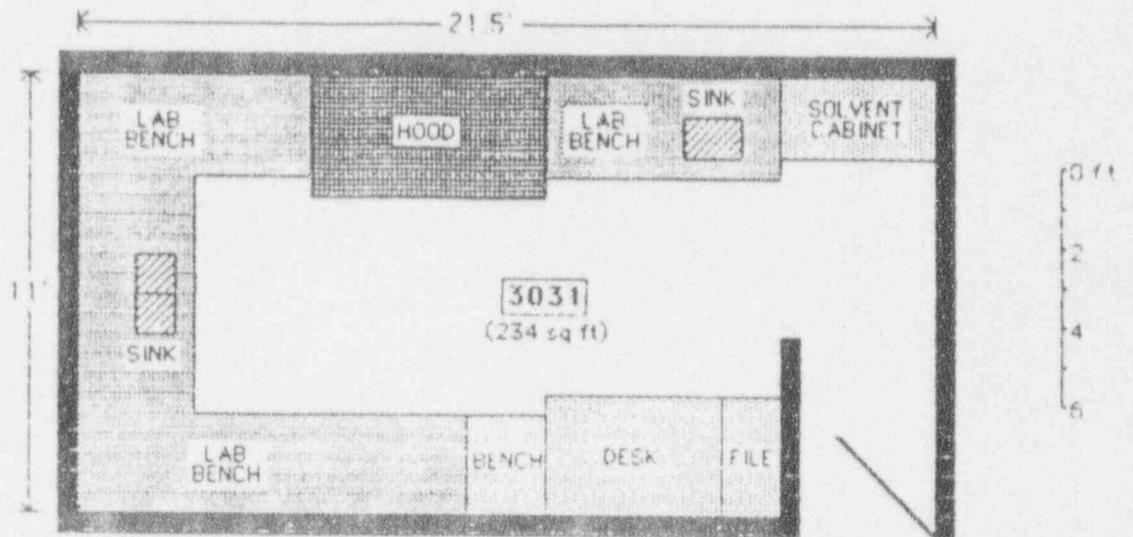
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Enclosures

cc: James E. Carey, Chairman
Radiation Policy Committee

Kenneth C. Schatzle, Director
Occupational Safety & Environmental Health

PHOENIX MEMORIAL LABORATORY



RADIATION DETECTION INSTRUMENT INVENTORY
August 25, 1992

<u>TYPE</u>	<u>MANUFACTURER</u>	<u>MODEL</u>	<u>SERIAL #</u>	<u>LOCATION</u>	<u>LAST CHECKED OR CALIBRATED</u>
G-M	Johnson Assoc	GSM-5	1657	Room 1069	08-04-92
G-M	Johnson Assoc	GSM-5	1963	Emerg. Closet	08-05-92
G-M	Johnson Assoc	GSM-5	2239	Co-60 Well	07-22-92
G-M	Eberline (non-mobile)	RM-14	1508	Room 3031-A	08-04-92
G-M	Eberline (non-mobile)	RM-14	3394	Room 3045	08-03-92
G-M	Eberline (non-mobile)	RM-14	3608	Room 3064	08-04-92
G-M	Eberline (non-mobile)	RM-14	4744	Room 3060	08-04-92
G-M	Nucleus	Mod-L	----	Room 1066	08-04-92

Ion Chamber	Victoreen	450B	686	Pool Floor	07-22-92
Ion Chamber	Eberline	RO-2A	183	P-Tube	07-13-92
Ion Chamber	Eberline	RO-2A	187	Bromine	07-22-92
Ion Chamber	Eberline	RO-2A	188	Emerg. Closet	07-13-92
Ion Chamber	Eberline	RO-2A	189	Emerg. Closet	07-22-92
Ion Chamber	Eberline	RO-2	358	Pool Floor	@ Eberline
Ion Chamber	Eberline	RO-2	413	Room 3064	07-22-92
Ion Chamber	Eberline	RO-2A	1101	Pool Floor	@ Eberline
Ion Chamber	Eberline	RO-2A	2399	Basement Entry	07-22-92
Ion Chamber	Eberline	RO-2	4526	Beamhole Floor	07-13-92

Neutron Ball	Ludlum	Mod-3	5050	Beamport Floor	08-20-92
Neutron Ball	Ludlum	Mod-12	UM138597	Room 1034-A	08-20-92

Ratemeter (W/G-M)	Ludlum	28	5217	PoolFloor Map	06-08-92
Ratemeter (W/G-M)	Ludlum	28	5218	Beamport Map	06-08-92
Ratemeter (W/G-M)	Ludlum	28	5219	Stack Map	06-08-92
Ratemeter (W/G-M)	Ludlum	28	5220	Room 1069	08-04-92
Ratemeter (W/G-M)	Ludlum	28	5221	Room 1034	SPARE
Ratemeter (W/G-M)	Ludlum	28	5245	Room 1054	08-04-92
Ratemeter (W/G-M)	Ludlum	177-46	31321	Room 1034-A in co-60 well	08-20-92
G-M	Ludlum	Mod-3	30541	Room 1066	
Ratemeter (W/G-M)	Ludlum	177-44	52569	Dr. Griffin Room 3103	08-04-92 08-04-92
Ratemeter (W/G-M)	Ludlum (H&F)	40	23005	1st Floor	07-28-92
Ratemeter (W/G-M)	Ludlum (H&F)	32	35978	(Rm 1042)	
Ratemeter (W/G-M)	Ludlum (H&F)	40	23006	3rd Floor	07-28-92
		32	35979	(Rm 3072)	

RADIATION DETECTION INSTRUMENT INVENTORY
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Rateometer (W/G-M)	Ludlum (H&F)	40 32	23011 35977	2nd Floor (Rm 2068)	At Ludlum
Na I	Johnson Assoc	LS-4A	730415	Room 1042	03-02-92
HP Ge	Canberra	18020	8911264	Room 1042	08-21-92
GPC	Tennelec	LB 5120	345	Room 1042	06-19-92
Ion Chamber	Capintec	CRC- 12R	12347	Room 3064	07-16-92
Rateometer (W/G-M)	Ludlum	177- 44-9	52604	Pool Floor	08-04-92
Na I	Thyroid Spec Nuclear Data	880703	860027	Room 1042	04-28-92
Na I	Bicron	Landfill Monitor	AB08V	Loading Dock	08/04/92
Na I	Bicron	Analyst	A369E	Room 3031	08-04-92
Na I	Bicron	Analyst	A553Q	Room 1034	08-05-92
Na I	Bicron	Frisk Tech	B237A	Room 3045	08-04-92
G-M	Ludlum	177-67	UM241207	Room 2109 (FNR GAD)	07-23-92
G-M	Ludlum	177-67	UM241208	Room 3073 (Stack GAD)	07-16-92
G-M	Ludlum	177-67	Back-up	Elec Shop	SPARE
Pocket Dosimeter	Radiacmeter	00910	08789	Emerg. Closet	07-21-92
Pocket Dosimeter	Johnson	SEQ5- 0.2R	280710	Emerg. Closet	07-21-92
Pocket Dosimeter	Johnson	SEQ5- 0.2R	280780	Emerg. Closet	07-21-92
Pocket Dosimeter	Johnson	SEQ5- 0.2R	292709	Control Room	07-21-92
Pocket Dosimeter	Johnson	SEQ5- 0.2R	350329	Emerg. Closet	07-13-92
Pocket Dosimeter	Dosimeter	Fast neutron	B020047	Emerg. Closet	07-21-92
Pocket Dosimeter	Dosimeter	100r	604011	Emerg. Closet	07-21-92
Pocket Dosimeter	Dosimeter	100r	6040010	Emerg. Closet	07-21-92
Pocket Dosimeter	Dosimeter	638 200R	2060075	Emerg. Closet	07-21-02
Pocket Dosimeter	Dosimeter	638 200R	2060076	Emerg. Closet	07-21-92

RADIATION DETECTION INSTRUMENT INVENTORY
August 25, 1992

<u>TYPE</u>	<u>MANUFACTURER</u>	<u>MODEL</u>	<u>SERIAL #</u>	<u>LOCATION</u>	<u>LAST CHECKED OR CALIBRATED</u>
Pocket Dosimeter	Dosimeter	608 10R	2041657	Emerg. Closet	07-21-92
Pocket Dosimeter	Dosimeter	608 10R	2041658	Emerg. Closet	07-21-92
Pocket Dosimeter	Dosimeter	862	2023652	Lobby	07-21-92
Pocket Dosimeter	Dosimeter	862	2023653	Lobby	07-21-92
Pocket Dosimeter	Dosimeter	862	2023654	Lobby	07-13-92
Pocket Dosimeter	Dosimeter	862	2023655	Lobby	07-21-92
Pocket Dosimeter	Dosimeter	862	2023656	Lobby	07-13-92
Pocket Dosimeter	Dosimeter	862	2023657	Lobby	07-14-92
Pocket Dosimeter	Dosimeter	862	2023658	Lobby	07-21-92
Pocket Dosimeter	Dosimeter	862	2023659	Lobby	07-21-92
Pocket Dosimeter	Dosimeter	862	2023660	Lobby	07-13-92
Pocket Dosimeter	Dosimeter	862	9080012	Lobby	07-14-92
Pocket	Dosimeter	608 10R	2041656	Control Room	07-21-92
Chirper	Dosimeter	1888B	120-790	Control Room	02-12-92

