Boehringer Mannheim Diagnostics, Inc.
Bio-Dynamics Boehringer Mannheim Diagnostics Boehringer Mannheim Biochemicals

25 July 1985

Mrs. Evelyn R. Matson
Materials Licensing Section
Nuclear Regulatory Commission
Region III
799 Roosevelt Road
Glen Ellyn, Illinois 60137

Re: Control Number 79281

Dear Mrs. Matson:

Pursuant to your letter dated July 18th, Boehringer Mannheim Diagnostics is hereby submitting the additional information you requested.

1.a. Ms. Patricia Jemison has attended an 8-10 hour Radiation Safety Course conducted by Mr. Bob Anger, RSO and Health Physicist at Indiana University Medical Center, Indianapolis, Indiana. The course consisted of approximately 2 hours of training in each of the four areas listed below with additional emphasis on safety aspects:

i) principles and practices of radiation protection.
ii) radiaoactivity measurements and monitoring techniques.
iii) mathematics basic to use and measurement of radioactivity.
iv) biological effects of radiation.

1.b. Ms. Jemison has experience with the following specific isotopes:

^{3}H-30mCi limit
^{125}I-5mCi limit
^{32}P-2mCi limit

^{3}H and ^{125}I were used to radiolabel bacterial proteins (^{125}I generally by the Bolten-Hunter chloramine T method, or lactoperoxidase method).

^{32}P was used to radiolabel DNA. Ms. Jemison's on the job training consists of 5 years experience including radiolabeling, all record keeping pertaining to receiving and disposal of radioactive material, and specific activity calculations for quantities needed.

Ms. Jemison has also gained over one year experience in the mathematics and measurement of radioactivity while selling commercially available RIA kits for Serono Diagnostics.

2. As discussed, Ms. Jemison will be the only person handling radioactive material. Boehringer Mannheim is in the process of setting up an Immunology Division, and as personnel are hired, their qualifications and training will be submitted as per Item 1 a and b.

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9115 Hague Road, P.O. Box 50100, Indianapolis, IN 46250 (317) 845-2000 FAX 317-845-2090 TELEX 27-6066

3. All personnel working with radiation will receive initial instruction through the Radiation Safety Officer. Following the basic outline (see attached) the following additional articles will be provided:

   A. Mettler, Fred, "Danger: Radiation Cannot Be Seen, Smelled, Tasted, Heard or Felt." Lab World, April 1981.

   B. U.S. Nuclear Regulatory Commission Appendix to Regulatory Guide 8.13 "Possible Health Risks to Children of Women Who are Exposed to radiation During Pregnancy."

   C. An article on the cellular effects of ionizing radiation by John Little, New England Journal of Medicine, 278:308, 1968.

   D. Other publications deemed pertinent.
   A seminar will be held on an annual basis to review all of the above along with any new information.

4. Ancillary personnel will be trained by the RSO using the general guidelines for instruction of radiation workers. This instruction will provide personnel with a general knowledge of radioactive material with special emphasis on safety aspects. All personnel will be taken through the restricted areas and shown specifically where everything pertinent is located. Personnel will be given specific instruction within the area and also who to contact in case of emergencies or questions. This instruction will be given both initially and annually thereafter.

5. Procedures for disposing of short-lived radioactive waste material:
   1) Solid radioactive waste will be separated as follows:
      a) ^{125}I bottles from commercially available kits.
      b) test tubes, pipette tips, absorbant paper, etc.

   Radioactive waste from 1.a. will be held for a minimum of 10 half-lives. Prior to disposal as normal waste, this material will be monitored using a Ludlum Model 3 G-M counter with a Model 44-3 detector to determine that it's radioactivity cannot be distinquished from background. All radiation labels will be removed or obliterated.

   Prior to disposal as normal wastes, radioactive waste from 1.b. will be held until it's radioactivity cannot be distinguished from background when monitored using a Ludlum Model 3 G-M counter with a Model 44-3 detector. All radiation labels will be removed or obliterated. Upon disposal of any radioactive waste, the date, the length of time material was held, individual, survey results and instrument identification will be recorded and maintained by the RSO.

The aforementioned statements should complete our application but should you have additional questions, please call (317) 845-2386.

Sincerely,

Iva Sue Smith
Manager
Regulatory Affairs

Patricia Jemison
Radiation Safety Officer

ISS:reg

cc: G. Evanega

Enclosures

I. Statement of Boehringer Mannheim Philosophy

Boehringer Mannheim will institute a program of radiation safety that will insure that all employees will be exposed to radiation as low as reasonably achievable. (ALARA)

II. The NRC

A. History

1. Manhattan Project started 1939 to investigate military development of atomic energy.

2. 1946, Manhattan Project became the AEC, which announced availability of radioactive isotopes for medical use.

3. 1954, the AEC received total control of byproduct materials.

4. AEC split into NRC and ERDA (Energy Research and Development) in 1975. ERDA is now Department of Energy.

B. NRC Role and Function

1. Establishes minimum standards of all radiation use for anyone who makes or uses radiation.

III. Radiation

A. Definition: propagation of energy waves through space or matter.

1. Examples: light, heat, sound, microwaves, radio, et al.

B. Ionizing radiation: capable of altering molecules by taking away electrons from atomic orbits.

1. 3 Types: alpha, beta, X or gamma.
   a. Gammas originate in nucleus and are emitted as radioactive material (material with excess energy) returns to stable state. Gammas are photons which share the characteristics of particles and waves. As radioactive atoms give off gammas they return to a more stable energy state.

IV. Units of Radiation Can Be Quantitated

A. Roentgen: measures photons in air only, measures ion pairs produced in kg. of air.

IV. Units of Radiation Can Be Quantitated (continued)

B. Rad: radiation absorbed dose, developed because of restriction of R in air, measures all radiations other than photons, measure of absorbed dose.

C. Rem: radiation equivalent man, developed because evidence found that biological effects of exposure differed for different types of radiation. Film badge exposure reported in rems.

D. Curie: measure of disintegrations per time. Boehringer Mannheim employees will only be exposed to microCurie amounts.

V. Monitoring Devices: Devices Used to Measure Amounts of Radiation

A. GM Survey meter: measures mR in air, used for lab and equipment surveys and surveys checking for contaminated clothing and hands.

B. Pocket dosimeter: ionization chamber in small cylinder, a charge placed across electrodes of chamber and radiation entering chamber decreases this charge proportional to amount of incident radiation. Characterized by eyepiece through which a graduated scale and quartz fiber can be seen. Periodic checks on weekly basis to measure exposure in mR.

C. Film badges: film 1 1/2 by 2" in plastic container, clipped to clothing, or rings worn on finger. Film developed by commercial firms monthly -- degree of darkening shows dose received. Filters in badge allow reporting in rems.

VI. Biologic Effects of Ionizing Radiation

When biological tissue is radiated, a certain amount of energy is absorbed from the radiation. Path of ionization or excitation of molecules occurs along path of incident radiation.

A. Radiation effects on cellular level: no living cell is completely radioresistant.

1. Growth suppression, restriction of motility, alterations in gland secretions, inactivation of enzymes.

2. Effect on chromosomes: adhesions, clumping or breaking of DNA leading to gene mutations.

VI. Biologic Effects of Ionizing Radiation (continued)

B. Radiation effects on biological systems

1. Blood system: bone marrow, spleen, lymph nodes are radiosensitive. Drop in lymphocytes indicator of damage, hemmorhage, platelet drop.

2. Reproductive systems: sterility only occurs in high doses, 300 R and up. Radiation does not cause impotency, which is a popular misconception.

3. Lymphatic system: spleen, lymph nodes, thymus, all exhibit high degrees of radiosensitivity. Loss of spleen weight is sensitive indicator of dose of radiation, plus cessation of production of both red and white blood cells.

4. GI tract: edema, degeneration and necrosis of cells lining GI tract lead to GI syndrome. Exhibited by nausea, vomiting, diarrhea.

5. Skin: about as radiosensitive as GI tract. Effects exhibited by erythema and changes in appendages (hair and nails). Epilation occurs at low doses, depigmentation, ulcerations and dermatitus at higher levels.

6. Eyes: cataracts with high doses -- noted in radiation workers who developed cyclotron and Japenese survivors of atomic bomb.

7. CNS: most radioresistant in mammals. Takes thousands of Rs for effects to be noted.

8. Other organs including heart, kidney, liver and pancreas are extremely radioresistant. Hemmorrhage, infarcts, necrosis occur only after massive doses.

C. Acute effects of radiation: large single, short-term dose results in a complex of clinical symptoms, collectively called Acute Radiation Syndrome (ARS). Depletion of radiosensitive cells from organs causes a variety of symptoms. Evidence gathered by nuclear bombing attacks and radiation therapy accidents.

1. ARS: initially loss of appetite, nausea, sweating, fatigue, fever. Two days may become normal and remain that way for 2-8 weeks. Fever, infection, epilation, hemmorrhage, lethargy, cardiovascular problems arise. Human LD50/30 is approximately 500 rems. In bats the LD50/30 is 16,000 rems.

VI. Biologic Effects of Ionizing Radiation (continued)

D. Chronic effects of radiation

1. Shortening of life span -- due to malignancies and leukemia in animals. As of yet, no data for man providing satisfactory basis for quantitative estimation of overall life-shortening effects.

2. Leukemias increases evidence that has been reported in radiologists and survivors of atomic bombs, people with thymus gland x-ray treatment.

3. Cancer: definite chronic effect from radiation. Ca's noted in early occupational workers (eg. radium watch dial painters 1914-1925). Thorotrast used in diagnostic radiology 1928-1945 caused liver tumors 10-20 years later.

VII. Radiation Safety

Field devoted to protection of individuals from ionizing radiation.

A. Early limits were arbitrary and usually voluntary and related to observed acute effects (eg. 1925, .2R/day for 30 days was limit).

B. Modern era ushered in with Manhattan Project. Doses have been steadily decreased since then as more people enter the nuclear field not because of evidence of damage due to earlier limits.

C. Current philosophy is ALARA, or "as low as reasonably achievable".

1. All exposure to radiation may be harmful, thus all doses must be minimized.

2. Exposure of large numbers of people to small amounts of radiation can produce the same genetic effects in a population as the exposure of a small number of people to a large dose of radiation.

D. Maximum permissable dose (MPD) exposures have been established by National Radiation Council. Philosophy is not how one might avoid exceeding the MPD but how to achieve the lowest exposure with reasonable cost and effort.

1. Combined whole body = 5 rems/year or 1.25 rems/quarter, or 100 mRem/week.
   Skin = 15 rems/year or 2.75 rems/quarter.
   Hands = 75 rems/year or 18.75 rems/quarter.
   Fertile Women = .5 rem in gestation period.
   Non-occupational Workers = .1 of above.
   Cumulative Dose = 5(n-18) rems.

VI. Radiation Safety (continued)

E. Ways of achieving ALARA:

1. Time: handle radiation quickly, don't rush but don't lag either.

2. Distance: most routine, effective way to limit exposure. Follows inverse square law -- amount of radiation at a given distance from a source is inversely proportional to the square of the distance (double the distance from the source, dose is 1/4 the original). By halving the distance, dose received is 4 times the original.

3. Shielding: body of material used to prevent or reduce the passage of radiation. Effectiveness depends upon the density and thickness of the shield.

F. Prevention of internal and external exposure:

1. No eating or smoking where unsealed radionucleides are open.

2. Do not pipette radioactivity by mouth.

3. Wear protective clothing and gloves while working -- dispose of gloves before leaving the area.

4. Clean up spills immediately and dispose of wastes properly.

5. Survey the work area routinely.

6. Wash hands before eating, drinking or smoking.

7. Work areas should be covered with glass, plastic, stainless steel or absorbant paper, and cleaned regularly.

8. Keep all radionucleides in sealed containers when not in use.

9. Wear film badges when working in radiation area.

10. Lab coats should be monitored before placing them in the laundry.

11. Wounds should be protected.

VII. Accidental Spills

A. Notify all persons in the room immediately.

B. Confine the spill.

1. Drop absorbant paper on the spill, being careful not to spread the spill.

C. Restrict the number of people in the spill area until the extent of shoe and clothing contamination can be ascertained.

D. Notify the radiation safety officer (RSO).

E. Decontaminate the area under the direction of the RSO.

F. Monitor all persons involved in the spill -- decontaminate them if necessary under the direction of the RSO.

B. The RSO will permit no one to resume work in the area until survey is made and the area is sufficiently free of contamination.

IX. NRC (Part 10, Title 10, Chapter 1, CFR)

A. Notices to workers:

1. Licensee must post or have available Parts 19 and 20, copy of license and conditions, operating procedures, any notice of violations.

B. Instructions to workers:

1. Must be kept aware of radiation storage and use.

2. Must be instructed in health protection problems associated with exposure.

3. Must be instructed on responsibility to report to licensee any condition which may lead to a violation of regulations.

4. Must be advised of radiation exposure reports.

IX. NRC (Part 10, Title 10, Chapter 1, CFR) (continued)

C. Reports to workers:

1. Any worker can request and obtain current exposure records and records of past exposures with a different employer.

D. Inspections: "each licensee shall afford to the commission at all reasonable times opportunity to inspect materials, activities, facilities, premises and records."

1. Inspectors may consult privately with workers during the inspection.

2. An individual may be authorized by the workers to represent them and accompany the inspector during the inspection.

3. During the inspection the workers may notify the inspectors of any past or present condition which may have caused any violation (license) or any unnecessary exposure of an individual to radiation.

4. Any worker may request an inspection if he believes a violation exists by giving notice of the alleged violation to Commission Inspectors or Regional Commission Office.

Units of Radiation

Roentgen	Ionizing radiation in air only. Abreviation = R.
Rad	Radiation asorbed dose.
Rem	Radiation equivalent man.
Curie	Disintegrations per time. One Curie = 3.7×10^{10} disintegrations per second. Abbreviation = C.
Millicurie	One thousandth of a Curie, or 3.7×10^{7}. Abbreviation = mCi.
Microcurie	One millionth of a Curie, or 3.7×10^{4} dps. Abbreviation = Ci.

ALARA	As low as reasonably achievable.
Radiation	Propagation of energy waves through space or matter.
Ionizing Radiation	Radiation capable of altering molecule by removal of electrons from atoms.
RSO	Radiation Safety Officer. Person responsible for maintaining radiation worker records and enforces radiation regulations set by the NRC concerning receipt, handling and disposal of all radioactive materials. The RSO for Boehringer Mannheim is Ms. Patrician Jemison, Extension 2302.
NRC	Nuclear Regulatory Commission, branch of federal government which sets standards for radiation protection, and rules and regulations pertaining to the production and use of radioactive materials.