UNITED STATES
NUCLEAR REGULATORY COMMISSION
REGION III
801 WARRENVILLE ROAD
LISLE, ILLINOIS 60532-4351

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JAN 1 4 1994

MEMORANDUM FOR: Hugh L. Thompson, Jr., Deputy Executive Director for Nuclear Materials Safety, Safeguards and Operations Support, EDO

FROM: John B. Martin, Regional Administrator, Region III

SUBJECT: REGION III REVIEW OF LICENSE FILES FOR RECORDS RELATED TO RESEARCH INVOLVING HUMAN SUBJECTS

This is in response to your memorandum in which you requested each Region to conduct a review of materials license files. The purpose of the review was to identify licensees likely to have conducted medical or scientific radiation effects research on humans prior to dissolution of the Atomic Energy Commission in 1975.

Based upon the criteria identified in your memorandum, we reviewed 25 license files. The files reviewed encompassed those licenses issued prior to 1975 with a focus on medical institution broad scope licenses. This included all broad scope Veterans Administration Hospitals as well as the major broad scope universities. Our review also included the one remaining military hospital in Region III. The Wright Patterson Air Force Base Hospital license file is no longer available in the region since that facility is now authorized by the broad scope authority granted to the United States Air Force and issued from Region IV. The other military hospital identified was Great Lakes Naval Hospital, however this license has been terminated and is no longer available for review.

Please note that due to the time constraints placed on this project, we only reviewed license files that fit the criteria as set forth in your memorandum for licensees that we believe performed human research studies. Region III staff believes there may be other licensees who conducted such research but do not fall into your criteria (i.e., non-medical broad scope R&D Facilities), and we believe additional agency effort may be warranted to conduct more reviews. We also wish to bring to your attention the fact that some pertinent information may not be available in the files due to the fact that in 1982 the materials license files were purged pursuant to NMSS guidance. Therefore, in many cases we could not determine if licensee's were actually conducting human research.

Enclosure A summarizes the results of our review. This summary lists the licensee name, license and docket number as well as a brief summary of our review. As indicated, we identified 22 licensees with license authorization for medical research on humans. With the exception of Mayo Foundation, University of Michigan, Cleveland Clinic Foundation, Henry Ford Hospital, University of Cincinnati, and V.A. Hines we found no evidence in the license files of the remaining licenses reviewed that would indicate they had actually initiated research activities as authorized in their license.

In addition to reviewing the license files we also polled various members of our staff to see if there was any recollection of licensees that may have been involved with research on humans. Four licensees that our staff believes may have conducted some human medical research activities were identified. The licensees were Proctor and Gamble, UpJohn Corporation, Borgess Medical Center Hospital and the University of Cincinnati (Dr. Eugene Saenger's research activities). The staff members had no specifics pertaining to the first three licensees. Concerning the University of Cincinnati, we believe that Dr. Saenger had been involved with human research studies in the 1950's. With exception of the University of Cincinnati, the three other licensees were not authorized to perform medical research, nor did we identify any documents in the file that would indicate medical research was conducted. In particular, and as summarized in Enclosure A, we noted that the University of Cincinnati file authorized medical research, including research with 100 millicuries of americium-241 in the form of a sealed source; there was no indication of Dr. Saenger's association with that or any other research.

Our review also generated a list of those terminated licensees who were active prior to 1975. The license files for those licensees are no longer available in Region III and more than likely are in the agency archives. It should be noted, however, that there are some State of Illinois licensees on that list that some staff believe may have performed human research studies (i.e., University of Chicago and Michael Reese Hospital). For your information we are enclosing a list of those terminated licenses.

If you have any questions or if we can provide further assistance please contact William Axelson or Roy Caniano of my staff at 708-829-9500.

for

John B. Martin
Regional Administrator

Enclosures: As stated

cc w/enclosure:
T. T. Martin, RI
S. D. Ebneter, RII
L. J. Callan, RIV
K. E. Perkins, RV
R. Bernero, NMSS
C. J. Paperiello, NMSS
A. Dauginas, RIII
J. Lynch, RIII

Enclosure A

1. Mayo Foundation
License No. 22-00519-03
Docket No. 030-02195

In a May 15, 1956 letter to the AEC addressing renewal of the institution's license, the following statement was made: "Serial tracers of I-132 are being administered soon after therapeutic doses of I-131 to demonstrate the early radiation effects on thyroidal iodine accumulating capacity."

a. dates of the studies - Unable to determine
b. types and purpose of research studies - As described above
c. identification of research subjects - Unable to determine
d. range of activity or doses - Unable to determine
e. sponsor of research - Unable to determine

2. V.A. Medical Center, Ann Arbor, MI
License No. 21-00159-04
Docket No. 030-01987

In an application dated October 24, 1972, the licensee requested authorization to perform non-routine human use - clinical research and evaluation. The application was approved. The licensee did not provide specific description of studies to be performed.

a. dates of the studies - Unable to determine
b. types and purpose of research studies - Unable to determine
c. identification of research subjects - Unable to determine
d. range of activity or doses - Unable to determine
e. sponsor of research - Unable to determine

3. University of Michigan
License No. 21-00215-04
Docket No. 030-01988

In 1967, the licensee was authorized to perform medical research on patients at the Jackson State Penitentiary. The studies used Se-75 and Cr-51 to evaluate red blood cell survival. The licensee was also authorized to perform research using I-131 to obtain information that may explain and help prevent certain cases of mental deficiency and deaf-mutism. The study involved 100 deaf or deaf-mute children and 100 mentally deficient individuals and a maximum of 50 cretins.

a. dates of the studies - Authorized in 1967
b. types and purpose of research studies - As described above
c. identification of research subjects - Unable to determine
d. range of activity or doses - Both studies in microcurie range
e. sponsor of research - Unable to determine

4. Harper Hospital
License No. 21-04127-02
Docket No. 030-02045

In 1969, the licensee was authorized for 15 curies of gadolinium-153 as a sealed source "to be used in General Motors Research Laboratories portable radiography exposure units for purposes of evaluating its suitability for producing radiographs of adult patients." The referenced correspondence was not in the file.

In 1970, the licensee was authorized for 600 millicuries of I-125 as a sealed source to "study the effect of sodium etidronate on acute astroporosis in quadriplegics as measured by bone absorptiometry using a shielded external source of radiation." The referenced protocol was not in the file.

a. dates of the studies - Unable to determine
b. types and purpose of research studies - As described above
c. identification of research subjects - Unable to determine
d. range of activity or doses - Unable to determine
e. sponsor of research - Unable to determine

5. V.A. Lakeside Medical Center, Chicago, IL
License No. 12-02642-06
Docket No. 030-01435

License documents issued prior to 1975 verify the licensee was authorized to use radioactive materials for medical/human use. Examples include the use of S-35 to "study 5 normal individuals of 40 years of age, 5 individuals undergoing surgery with local anesthesia and 5 patients undergoing surgery with general anesthesia." Patients with extensive burns, hypofibrinogenemia and pancreatic fistulas will also be studied.

a. dates of the studies - Unable to determine
b. types and purpose of research studies - As described above
c. identification of research subjects - Unable to determine
d. range of activity or doses - Millicurie range
e. sponsor of research - Unable to determine

6. V.A. Medical Center, Minneapolis, MN
License No. 22-01859-01
Docket No. 030-02205

Prior to 1975, the licensee was authorized to perform medical research. An example is the use of magnesium-28 for metabolism studies in 10 normal patients and 10 diseased patients, all over 40 years of age.

a. dates of the studies - Unable to determine
b. types and purpose of research studies - As described above
c. identification of research subjects - Adults over age of 40
d. range of activity or doses - Millicurie range
e. sponsor of research - Unable to determine

7. Indiana University
License No. 13-02752-03
Docket No. 030-01609

The University was authorized to perform medical/human research prior to 1975. Examples include use of I-132 to study the effects of varying agents on the uptake of iodine by the thyroid, and C-14 for metabolism studies in patients with anxiety state, schizophrenia and other psychosomatic disorders.

a. dates of the studies - Unable to determine
b. types and purpose of research studies - As described above
c. identification of research subjects - Unable to determine
d. range of activity or doses - Both studies in millicurie range
e. sponsor of research - Unable to determine

8. University of Cincinnati
License No. 34-06903-05
Docket No. 030-02764

The license authorized medial research prior to 1975. Many referenced documents prior to 1975 were not in the file. Amendment No. 43 authorizes 100 millicuries Am-241 as a sealed source for medical research. The referenced document pertaining to the use of Am-241 was not in the file.

a. dates of the studies - Unable to determine
b. types and purpose of research studies - Unable to determine
c. identification of research subjects - Unable to determine
d. range of activity or doses - 100 millicurie sealed source
e. sponsor of research - Unable to determine

9. V.A. Medical Center, Allen Park, MI
License No. 21-04234-01
Docket No. 030-02050

The license authorized medical research prior to 1975 and it appears the licensee performed various types of studies. Examples include: (1) use of zinc for absorption studies on 25 patients - a report was required to be submitted to AEC; (2) use of Cs-137 acetate for myocardial scanning on 10 volunteers over 40 years and 25 patients; and (3) use of C-14 to study the influence of digitalis on cardiac metabolism.

a. dates of the studies - Unable to determine
b. types and purpose of research studies - As described above
c. identification of research subjects - Unable to determine
d. range of activity or doses - microcurie to millicurie
e. sponsor of research - Unable to determine - possibly the AEC

10. V.A. Medical Center, Cleveland, OH
License No. 34-00203-03
Docket No. 030-02639

The licensee was authorized to perform medical research prior to 1975. An example is use of I-125 to evaluate the use of radioiodionated - fibrinogen for detection of phlebothrombosis in the lower extremities in 25 patients. A report has to be submitted to the Commission. Also, the use of C-14 in 1 patient with enterocholic fistula to investigate the excretion of bile acids.

a. dates of the studies - Unable to determine
b. types and purpose of research studies - Unable to determine
c. identification of research subjects - Unable to determine
d. range of activity or doses - I-125 - millicurie
C-14 - microcurie
e. sponsor of research - Unable to determine - possibly the AEC

11. Cleveland Clinic Foundation
License No. 34-00460-01
Docket No. 030-13931

Inspection reports issued prior to 1975 indicate that human research was conducted.

12. Henry Ford Hospital
License No. 21-04109-16
Docket No. 030-02043

Inspection reports issued prior to 1975 indicate that human research was conducted.

13. V.A. Edward Hines, Jr., Medical Center, Hines, IL
License No. 12-01087-01
Docket No. 030-01391

Inspection reports issued prior to 1975 indicate that human research was conducted.

14. University of Wisconsin
License No. 48-09843-18
Docket Nos. 030-03465/030-17753/070-00052

The license authorizes medical research, however a review of the file did not reveal any evidence that the licensee was performing radiation studies on humans.

15. Milwaukee County Medical Complex
License No. 48-04193-01
Docket No. 030-03444

The license authorizes medical research, however a review of the file did not reveal any evidence that the licensee was performing radiation studies on humans.

16. University of Missouri
License No. 24-00513-32
Docket No. 030-02278

The license authorizes medical research, however a review of the file did not reveal any evidence that the licensee was performing radiation studies on humans.

17. Ohio State University
License No. 34-00293-02
Docket No. 030-02640

The license authorizes medical research, however a review of the file did not reveal any evidence that the licensee was performing radiation studies on humans.

18. Washington University Medical School
License No. 24-00167-11
Docket No. 030-02271

The license authorizes medical research, however a review of the file did not reveal any evidence that the licensee was performing radiation studies on humans.

19. V.A. Medical Center, Iowa City, IA
License No. 14-00822-01
Docket No. 030-01680

The license authorizes medical research, however a review of the file did not reveal any evidence that the licensee was performing radiation studies on humans.

20. Hennepin County Medical Center
License No. 22-11070-01
Docket No. 030-02244

The license authorizes medical research, however a review of the file did not reveal any evidence that the licensee was performing radiation studies on humans.

21. V.A. Medical Center, Indianapolis, IN
Richard L. Roudebush
License No. 13-00694-03
Docket No. 030-01583

The license authorizes medical research, however a review of the file did not reveal any evidence that the licensee was performing radiation studies on humans.

22. V.A. Medical Center, Madison, WI
License No. 48-01183-01
Docket No. 030-03418

The license authorizes medical research, however a review of the file did not reveal any evidence that the licensee was performing radiation studies on humans.

TERMINATED LICENSES WITH PCODE 02110 ISSUED PRIOR TO 1975

CHICAGO, UNIVERSITY OF 12-00509-03	STREET CITY STATE_CODE	5801 SOUTH ELLIS AVENUE CHICAGO IL	DATE_ORG_LIC	0
COOK CTY. HOSPITAL 12-00010-05	STREET CITY STATE_CODE	1835 W. HARRISON STREET CHICAGO IL	DATE_ORG_LIC	0
MICHAEL REESE HOSPITAL & MEDICAL CT 12-00074-04	STREET CITY STATE_CODE	29TH AND ELLIS AVENUE CHICAGO IL	DATE_ORG_LIC	0
MICHAEL REESE HOSPITAL & MEDICAL CT 12-00074-05	STREET CITY STATE_CODE	29TH STREET AND ELLIS AVENUE CHICAGO IL	DATE_ORG_LIC	0
ILLINOIS, UNIVERSITY OF AT CHICAGO 12-00088-06	STREET CITY STATE_CODE	P.O. BOX 6998 CHICAGO IL	DATE_ORG_LIC	0
EVANSTON & GLENBROOK HOSPITALS 12-00437-01	STREET CITY STATE_CODE	2650 RIDGE AVE EVANSTON IL	DATE_ORG_LIC	0
RUSH-PRESBYTERIAN-ST. LUKE'S 12-00929-13	STREET CITY STATE_CODE	1753 WEST CONGRESS PARKWAY CHICAGO IL	DATE_ORG_LIC	0
ILLINOIS MASONIC MEDICAL CTR. 12-02349-05	STREET CITY STATE_CODE	836 WELLINGTON AVENUE CHICAGO IL	DATE_ORG_LIC	0
CHRIST HOSPITAL 12-09239-01	STREET CITY STATE_CODE	4440 W. 95TH ST. OAK LAWN IL	DATE_ORG_LIC	0
MINNESOTA, UNIVERSITY OF 22-00218-29	STREET CITY STATE_CODE	410 CHRUCH ST. S.E. MINNEAPOLIS MN	DATE_ORG_LIC	0
LOYOLA UNIVERSITY MEDICAL CTR. 12-11355-04	STREET CITY STATE_CODE	2160 S. FIRST AVENUE MAYWOOD IL	DATE_ORG_LIC	0
NORTHWESTERN MEMORIAL HOSPITAL 12-02501-03	STREET CITY STATE_CODE	250 E. SUPERIOR STREET CHICAGO IL	DATE_ORG_LIC	0
CHILDREN'S MEMORIAL HOSPITAL 12-02184-05	STREET CITY STATE_CODE	2300 CHILDRENS PLAZA CHICAGO IL	DATE_ORG_LIC	0

TERMINATED LICENSES WITH PCODE 02110 ISSUED PRIOR TO 1975

CLEVELAND CLINIC FOUNDATION	STREET	9500 EUCLID AVENUE -B060	DATE_ORG_LIC	0
34-00466-04	CITY	CLEVELAND		
	STATE_CODE	OH		

TIME SENSITIVE INFORMATION

JAN 10 1994

ALL AGREEMENT STATES

TRANSMITTAL OF STATE AGREEMENTS PROGRAM INFORMATION (SP-94-011)

Your attention is invited to the attached correspondence which contains:

INCIDENT AND EVENT INFORMATION.....

PROGRAM MANAGEMENT INFORMATION.....

TRAINING COURSE INFORMATION.....

TECHNICAL INFORMATION.....

OTHER INFORMATION.....XX Authorization for Human Use

Supplementary information: The NRC has recently requested its Regional Offices, by memorandum dated January 7, 1994 (enclosed), to conduct a review of available license files, including terminated license files, to obtain information on certain licensees who were likely to have conducted medical or scientific radiation effects research on humans prior to the dissolution of the Atomic Energy Commission (AEC) in 1975. The purpose of this review is to identify those files containing information on experiments in which humans were deliberately exposed to radiation for purposes other than radiopharmaceutical development. The enclosed memorandum further details the specific criteria to be considered in this review.

We are also requesting at this time that the Agreement States review their files as well to identify and report to the Office of State Programs those files containing information on experiments in which humans were deliberately exposed to radiation for purposes other than radiopharmaceutical development. Initial information would be most useful if provided by January 18, 1994, with follow-up of final information by January 25, 1994.

If you have further questions regarding this correspondence, please contact the individual named below.

POINT OF CONTACT: Rosetta Virgilio
TELEPHONE: (301) 504-2307
FAX (301) 504-3502

Original Signed By
RICHARD L. BANGART
Richard L. Bangart, Director
Office of State Programs

Enclosure:
As stated

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UNITED STATES
NUCLEAR REGULATORY COMMISSION
WASHINGTON, D.C. 20555-0001

January 7, 1994

MEMORANDUM FOR: Those on Attached List

FROM: Hugh L. Thompson, Jr.
Deputy Executive Director for Nuclear
Materials Safety, Safeguards and
Operations Support, EDO

SUBJECT: REVIEW OF LICENSE FILES FOR RECORDS RELATED TO RESEARCH INVOLVING HUMAN SUBJECTS

This memorandum is to request each Region to conduct a review of available license files for certain licensees likely to have conducted medical or scientific radiation effects research on humans prior to the dissolution of the Atomic Energy Commission (AEC) in 1975. The purpose of this review is to identify those files containing information on experiments in which humans were deliberately exposed to radiation for purposes other than radiopharmaceutical development. For example, experiments such as studies where volunteers were used to clean up deliberately contaminated sites or studies performed to determine the potential harmful and beneficial effects of radiation exposure to humans should be reviewed.

The regional staff should select the specific licensees meeting the following criteria and review the license files in their entirety, starting with the earliest available records:

1. Military (Department of Defense(DOD)) research facilities and affiliates

2. Military hospitals and medical centers

3. Broad scope facilities for licenses issued before 1975 to include:

   a) Land grant universities and colleges
   b) Department of Veterans Administration hospitals
   c) Large state and private medical research and teaching facilities.

Initially, the review should be targeted at research facilities that are associated with a long history of involvement in these types of experiments. It may also be beneficial to talk to long-time NRC staff members who may recall specific licensees who conducted human radiation biology experiments or other experiments on humans. For this initial review, you should try to review all of the most likely candidates but no fewer than five licenses.

The following information should be submitted to the Office of Nuclear Material Safety and Safeguards (NMSS) for each file reviewed: license number, docket number, institutional name, and whether there was evidence of radiation

studies involving humans. If no evidence of human research is identified, that fact should be reported. If evidence of human research is identified, provide a brief description of the research that includes: 1) dates of the studies; 2) types and purpose of research studies; 3) whether identification of individual research subjects is available; 4) range of activities or doses reported; and 5) sponsor of research (e.g., DOD, AEC, etc.). NMSS will share the information with the current Presidential Task Force via the Department of Energy (DOE) to assure a uniform federal response to inquiries. Similarly, if you otherwise obtain information regarding individual subjects of radiation experiments, that knowledge will be shared with DOE. The information will be reviewed to ensure that it can be made available pursuant to applicable Federal laws regarding disclosure of such information.

Although, at this time, the review is limited to available files, if there is evidence that information may be available in archived files, the region should make note of that for possible future use. Due to the heightened public awareness of many radiation studies, the requested information should be forwarded to this Office by noon January 14, 1994.

In addition, a summary, entitled "Background Information on Human Research involving Radioactive Materials," is enclosed. This summary should be read by your staff and referred to when responding to inquiries from the regulated community and members of the public.

The contact for this project is John E. Glenn of this staff. Any questions concerning this review should be directed to him at (301) 504-3418.

Hugh L. Thompson, Jr.
Deputy Executive Director for Nuclear
Materials Safety, Safeguards and
Operations Support, EDO

Enclosure: As stated

Background Information on Human Research
Involving Radioactive Materials

The NRC does not conduct or directly fund research on human beings. NRC issues licenses to authorize medical research by its licensees based on an applicant's representations that it performs research in accordance with regulations of the Food and Drug Administration. Other types of human research administrations of radiation or radioactive material may be authorized on an NRC license if the applicant demonstrates that the appropriate FDA approved committees have been established, such as a Radioactive Drug Research Committee or Institutional Review Board or Committee. The NRC currently does not have separate regulations or review procedures but depends upon FDA or FDA approved committees to review research protocols in accordance with FDA regulations on such matters as conflict-of-interest or informed consent. The NRC does not inspect its licensees for compliance with FDA regulations. If NRC becomes aware of information or allegations about violations of FDA requirements, it will share those findings with FDA as part of a Memorandum of Understanding. A Proposed Rule was published on June 17, 1993, which would require that human research be conducted only in accordance with the Uniform Federal Policy on Research in Humans, and any proposed research not in compliance with the Federal Policy must receive prior approval by NRC.

The Atomic Energy Commission (AEC) was established by the Atomic Energy Act of 1946 to develop programs for the production and distribution of fissionable materials, development of nuclear reactors primarily aimed at the production of power, and safe industrial use of nuclear materials. AEC operated several research laboratories to advance the field of nuclear science by providing large scale qualified staff and expensive equipment which private industry could not financially afford. At the direction of AEC, some laboratories conducted research studies to determine the potential harmful and beneficial effects of radiation exposure to humans. Most of this AEC work was done by AEC contractors or subcontractors on an unlicensed basis. In an effort to promote the safe use of radiopharmaceuticals for patient diagnosis and therapy at hospitals and other medical facilities, AEC established investigational radioactive drug approval procedures for new drugs or uses, including drug safety and efficacy. With the dissolution of AEC in 1975, licensed AEC activities were transferred to the newly established NRC while AEC-sponsored research activities were transferred to an organization later incorporated into the U.S. Department of Energy. Also in 1975, FDA revoked a 1963 exemption for radioactive drugs from FDA's investigational drug regulations. As a result, NRC took over the licensing of, possession and use of radioactive materials formerly performed by the AEC but not the safety and efficacy review of new radioactive drugs nor the AEC contractor oversight. Thus NRC became the regulator and custodian of AEC issued licenses.

Some of these license files may contain information regarding individuals who were the subjects of research investigations or experiments using licensed radioactive materials or radiation from these materials. NRC's regional offices have been asked to review those files which they believe are most likely to contain information about individual human subjects (large teaching hospitals or research labs). If NRC identifies, or otherwise learns of information regarding individual subjects of radiation experiments, it will share that information with the current Presidential Task Force via the Department of Energy to assure a uniform federal response to inquiries. Information will be made available in accordance with applicable Federal laws regarding disclosure of such information.

ENCLOSURE

MEMORANDUM FOR: Those on Attached List Dated:

SUBJECT: REVIEW OF LICENSE FILES FOR RECORDS RELATED TO RESEARCH INVOLVING HUMAN SUBJECTS

Thomas T. Martin,
Regional Administrator, Region I

Stewart D. Ebneter
Regional Administrator, Region II

John B. Martin
Regional Administrator, Region III

L. J. Callan
Regional Administrator, Region IV

Kenneth E. Perkins
Acting Regional Administrator, Region V