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WASHINGTON, DC 20301-3050

ATOMIC ENERGY

Honorable Rob Portman
House of Representatives
Washington, D.C. 20515-3502

Dear Mr. Portman:

Thank you for your recent letter and the kind sentiments you expressed regarding my appearance before the Subcommittee in Cincinnati. The Subcommittee's direct and thought-provoking questions, and comprehensive approach to the issues surrounding the University of Cincinnati research, created an excellent forum for discussing the many aspects of this issue. Also, I appreciated the opportunity to represent the Department of Defense and explain our role in the University of Cincinnati research.

Your continued interest in this matter, and the Department of Defense's role, provide an opportunity to further explore the issues associated with the University of Cincinnati research and, thus, develop a better understanding of the context in which the research was conducted. In that respect, attached are answers to the first set of questions that you forwarded to me on 13 April, subsequent to my appearance. I hope that you find them helpful.

On a more personal note, I want to thank you for your patience regarding our responses to these questions. The depth and complexity of the questions required that detailed background research be conducted in order to develop thorough responses. If I can be of further assistance, please contact me.

Best regards.

Gordon K. Soper
Principal Deputy

Congressman Portman:

I know this has been a long time in getting to you. It's important to be responsive -- we'll do better in the future. GKS

QUESTIONS FROM REPRESENTATIVE PORTMAN

QUESTION 1:

Was it typical for other DoD funded projects, where experiments were being conducted on humans, that reports submitted to DoD would only (or primarily) refer to information of interest to DoD? To what extent, in other DoD funded studies, would there be mention of the treatment or therapeutic benefits to patients involved? Colonel Isherwood stated in his October 20, 1958 Memorandum concerning the Application for Research Contract that, "Any correlation of tumor response to total dose of irradiation by such means as proposed in this project would be of great value in the field of cancer." Is there any evidence that this was in response to written or verbal references concerning the value of the experiments to the patients?

ANSWER TO QUESTION 1:

1.) DoD Reports.

a.) DoD Directive 3200.8, *Standards for Documentation of Technical Reports under the DoD Scientific and Technical Information Program*, dated February 18, 1964 defined a technical report as "documents written for the permanent record to document results obtained from and recommendations made on scientific and technical activities relating to a single project, task, or contract or relating to a small group of closely-connected efforts within the DoD R&D program."

b.) The contracts between the Defense Atomic Support Agency and the University of Cincinnati directed that upon the completion of the research a final report was to be submitted to the Project Officer, "making full disclosure of all research conducted including the results and conclusions thereof with appropriate recommendations. The Contractor will prepare the final report and all others reports required in the form and manner directed by the project officer."

c.) From these two excerpts there appears to be two consistent requirements for DoD reports. The Department wanted to be informed of the <u>results</u> of the research and provided with recommendations. In this context, the reports submitted by Dr. Saenger, and others submitted by researchers who studied the effects of total body radiation for the Department of Defense during the 1950's and 1960's, are similar. A review of Dr. Saenger's reports and of nine reports submitted by researchers at Sloan-Kettering Memorial Hospital in New York, and the M. D. Anderson Hospital and the Baylor University College of Medicine in Texas reveal that they generally reported the same type of information. The reports described how the research was conducted, the number of patients studied during the reporting period, individual case histories of the patients, the techniques used to conduct the research, dosimetry, recommendations and future plans.

It should be noted, however, that some reports mentioned the therapeutic aspect of the treatment, while another specifically excluded such a discussion. A 1955 report submitted by Baylor researchers stated, "this department has been occupied in a continuing program directed toward a better understanding of the role of total body radiation in therapy, the systemic response of the patient, and particularly the effect upon iron metabolism." In their introduction to a 1957 report, researchers at M.D. Anderson Hospital noted that their "present study, originating from therapeutic considerations alone, attempts to contribute... additional information" on the effects of human whole body irradiation. However, in the conclusion the researchers stated that a "critical evaluation of the procedure as a therapeutic tool was excluded from the report; its scope was limited essentially to acute and subacute effects, so far as they were systemic in nature."

2.) Colonel Isherwood.

Colonel Isherwood was a medical doctor who was the Chief of Radiological Services at Walter Reed Army Hospital at the time he endorsed the project. Walter Reed Army Medical Center was contacted to inquire if Radiology Department files circa 1958 were available. The files were transferred long ago and their subsequent disposition was not readily available, although efforts to discover their disposition are still ongoing.

However, as Director of Radiology Services at the Army's premier teaching, research, and medical treatment facility, and with his professional credentials, Dr. Isherwood was in a position to be cognizant of the research being conducted in the field of radiology and its application to cancer treatment. Also, Dr. Isherwood possessed personal knowledge of Dr. Saenger's capabilities and expertise. Records indicate that when Dr. Saenger was on active duty and assigned to the Isotope Section of the Radiology Department of Brooke Army Hospital in San Antonio, Texas in 1955, Dr. Isherwood was the chief of the Radiology Department at Brooke Army Hospital and Dr. Saenger was his subordinate.

QUESTION 2:

What were the names of the Contracting Officer's Representatives who were responsible for overseeing the University of Cincinnati General Hospital project during the period from 1960 through 1971? Are any of them still alive or are there any other DOD or DASA personnel, active or retired, who would have any information concerning this project?

ANSWER TO QUESTION 2:

The contracting officer's representative (COR) for the various contracts, and the documents which identified them as such, are as follows:

Contract DA-49-146-XZ-315: Commander George P. Douglas is identified in acquisition management logs as the COR.

Contract DA-49-146-XZ-029: Commander R.L. Gade is identified in acquisition management Contract logs as the COR.

Contract DASA 01-69-C-0131: Lieutenant Stephen Kessler, USN, was designated as the COR in an unsigned letter dated May 9, 1969, from John Watson, Contracting Officer to Lieutenant Kessler. Lieutenant Warren O. Kessler, USN, was identified as the COR in a disposition form dated March 23, 1970, signed by Colonel Edward J. Huycke, Chief, Medical Directorate. Lieutenant Robert C. Loynd, USN, was designated as the COR in an unsigned letter dated October 26, 1970, from John Watson to Lieutenant Loynd. The letter provided that Lieutenant Loynd was replacing Lieutenant W. Kessler.

The status of Lieutenants Stephen Kessler and Loynd and Commanders Douglas and Gade is unknown at this time. We are continuing our efforts to determine their status. Lieutenant Warren Kessler is alive and has been named a defendant in the ongoing University of Cincinnati litigation. His request for representation by the Department of Justice is pending.

The names of other DoD or DASA personnel who might have information about the project include Dr. Northrup, the former Deputy Director for Science and Technology in the 1971 time- frame. He was one of the DASA employees who met with a Washington Post reporter in 1971 to discuss Contract DASA 01-69-C-0131. Also in attendance were Lieutenant Colonel Johansen, Public Information Office, and Lieutenant Colonel John W. Cable, USAF, Veterinary Corps, Medical Directorate. Although it is not clear from the files available what Lieutenant Colonel Cable's position was, he appears to have had some responsibility with regard to Contract DASA 1-69-C-0131. In addition, Colonel Huycke, Chief of the Medical Directorate in 1970, Colonel H. B. Mitchell, USAF, Acting Chief of the Medical Directorate in 1969 and Captain J. E. Stark, USN, Chief, Medical Directorate in 1969 may have knowledge of the technical aspects of the project. At this time, we do not know if any of these individuals are alive, but we will attempt to determine their status and provide that information to you.

These names have been gleaned from the contract files, a copy of which you have, and are those individuals who appear to have had knowledge of the subject matter of the project, rather than those who performed duties related to the processing of the contract, i.e., the logistical, security, or financial aspects of the contracts. As the Defense Nuclear Agency (DNA) continues to search for files, more names may surface. We will be happy to provide further information as it becomes available.

QUESTION 3:

Please confirm the existence or non-existence of a DOD report, classified or unclassified, summarizing the effects of radiation on humans that has incorporated any of the findings of the UC General Hospital project....

ANSWER TO QUESTION 3:

The following unclassified reports, which summarize the effects of radiation on humans, cite the University of Cincinnati General Hospital findings:

Anno, G.H., H.L. Brode, and R. Washton-Brown, Initial Human Response to Nuclear Radiation, DNA-TR-237, April 1982.

Anno, G.H., Weapons Effect Research at PSR - 1982, Vol. XIV, Acute Radiation Response in Humans: Informal Comments by Physicians and Radiobiologist, DNA-TR-82-179-V14, June 1983.

Baum, S.J., G.H. Anno, R.W. Young, and H.R. Withers, Nuclear Weapon Effect Research at PSR - 1983, Vol. 10, Symptomatology of Acute Radiation Effects in Humans After Exposure to Doses of 75 to 4500 Rads (cGY) Free-in-Air, DNA-TR-85-50, August 1984.

Anno, G.H., G.E. McClellan, M.A. Dore, and S.J. Baum, Biological Effects of Protracted Exposure to Ionizing Radiation: Review, Analysis, and Model Development, DNA-TR-90-157, November 1991.

Anno, G.H., S.J. Baum, H.R. Withers, and R.W. Young, "Symptomatology of Acute Radiation Effects in Humans After Exposure to Doses of 0.5 - 30 Gy" Health Physics, Vol. 56, No. 6, June 1989, pp. 821-838.

These documents were part of the output from the Intermediate Dose Program (IDP) whose purpose was to predict the performance of humans and units on the nuclear battlefield. There are no classified documents in this series.

QUESTION 4:

Please state your understanding of DOD's oversight role during the period from 1960 through 1971; specifically, what the standards for oversight were for experiments on humans, the extent of DoD's compliance with such standards, and how DoD oversight with respect to the UC General Hospital project compared to other similar funded projects. I would also appreciate a statement of the procedures that DoD would follow today (both for approval of the project and for monitoring compliance with informed consent and other requirements) if the same project were submitted to the DoD today.

ANSWER TO QUESTION 4:

Current research cannot identify any DoD directives or instructions that explicitly address DoD oversight functions for the type of contracted research conducted at the University of Cincinnati. However, there were DoD instructions issued in 1964 which established guidelines for human research which employed the investigational use of drugs. The guidelines were for DoD's internal components and DoD contractors. Also, for research within the Department of Defense, a policy was promulgated in 1953 by a memorandum from Secretary of Defense Charles Wilson. The memorandum's title was *Use of Human Volunteers in Experimental Research*. The memorandum established the policy for the participation of "Armed Services personnel and/or civilians on duty at installations engaged in" experimental research in the fields of atomic, biological, and/or chemical warfare.

There are several considerations when evaluating DoD oversight policy during this era. The University of Cincinnati Ad Hoc Committee Report of January 1972 noted the DASA-sponsored research conducted at the University of Cincinnati "was carried out with the complete scientific freedom appropriate for research conducted in University facilities."

The Ad Hoc Committee report does not explain the basis of this observation, however, these extracts from DoD Instruction 3210.3, *Administration of Basic Research Grants*, dated August 25, 1959 may provide some perspective. This instruction was formulated to provide general information to institutions of higher education and nonprofit organizations regarding DoD grants for the support of basic research. The forward to the instruction noted that "the Department of Defense's approach to the administration of grants for basic research rests on the belief that institutions and scientists alike wish to share, with the Department of Defense, responsibility for the administrative, financial, and scientific integrity of the program."

The instructions later stated, "the Department of Defense assumes that, once a grant is made, the principal investigator, operating within the policies of the grantee institution, is in the best position to determine the means by which the research may be conducted most effectively. Accordingly, the primary responsibility for the administration of any grant is one that is shared by the grantee and the principal investigator. The Department of Defense wishes to avoid any action that might diminish the responsibility of the grantee and the investigator for making sound scientific and administrative judgements.... The primary concern of the Department of Defense is that the granted funds be used in a manner that will make the maximum contribution to the progress of science--and it is expected that grantees and investigators will also direct their efforts to this end."

The DoD instruction appears to provide some basis for the observation by the Ad Hoc Committee and also provides a possible partial explanation for DoD's lack of a formally promulgated oversight policy. Some thirteen years later a similar sentiment was echoed by the Department in a report to a congressional staff which was entered into the *Congressional Record* for August 1, 1972, page 26232.

In February 1972, the Senate Armed Services Committee staff asked the Department what controls existed to ascertain the need for human experiments, the impact of such experiments on patients and adherence to accepted medical standards. As part of its response, the Department of Defense stated, "the most important control does not exist in any regulation or bureaucratic procedure. It exists in the integrity and ethical standards of the physicians charged with conducting and supervising such research."

Along this line the three contracts between DASA and the University of Cincinnati included a statement of work clause that required the contractor to agree "that the performance of work and services pursuant to the requirements of this Contract shall conform to high professional standards."

Another clause in all of the contracts required the contractor to agree "to utilize, in the performance of the research work under this Contract, such supervisory personnel as are highly qualified in the research fields involved; whose professional standards are of the

highest; and whose opinions in such research fields are entitled to respect and confidence of recognized experts in the field."

The Department's requirement that DoD-sponsored research be conducted by highly qualified personnel with high professional standards was also evident in the application forms/format to be submitted when requesting a research contract. In the 1958 standard application for research contract, part of the application was devoted to describing the professional biographies of the responsible investigator and the principal professional assistants. Required information included educational background; research training (institutions, research director, subject, and dates); other information bearing on their qualifications (hospital appointments, professional societies, specialty boards, etc.); and bibliography (of not more than ten publications.) Available documentation reveals that, in subsequent applications, general qualification information was also submitted.

Another aspect of DoD oversight involves contracting officer and contracting officer representative responsibilities that were generally delineated in the *Armed Service Procurement Regulations (ASPR)*and *Army Procurement Policies (APP)*. The *APP* was relevant because during the early years of the Saenger contracts the Department of the Army was tasked to provide procurement authority to the Defense Atomic Support Agency. The Army's support was to "be exercised in accordance with Department of Defense policies and regulations, and to the extent appropriate, policies and regulations of the Department of the Army." (DoD Directive 5158.2 *Administrative Arrangements for the Defense Atomic Support Agency*, dated 2 February 1960) These general responsibilities were supplemented by department/agency guidance.

Although there was no formally stated DoD oversight policy regarding the use of humans in contracted research during this era, the documents such as the *ASPR*, *APP*, and the contracts themselves delineated some specific oversight responsibilities. These, in turn, required an intimate involvement in the administration and performance of work conducted under a DoD contract.

It also should be noted that the clauses contained in the contract(s) were standard clauses specified by the *ASPR* for a fixed-fee research and development contract. As they were standard clauses, the contract responsibilities outlined therein were applicable whenever such a type contract was entered into.

Another aspect to consider is that for the period of the contractual relationship between DASA and the University of Cincinnati the contracts were renewed annually. The annual renewal required the submission of updated applications to be evaluated by DoD personnel. Also, each contract required the submission of periodic letter-type progress reports(the first two contracts required quarterly submissions while the last contract required semiannual reports).

TODAY'S PROCEDURES

As I stated in my testimony in Cincinnati, under current regulations a proposal like Dr. Saenger's would require more supporting documentation and justification to be considered for funding support by the Department of Defense.

Since the promulgation of Secretary Wilson's 1953 Memorandum, and paralleling developments in the civil sector, Department policy towards supporting research that utilized human subjects evolved, and more detailed procedures were established. These steps included the incorporation, in 1991, of the *Department of Health and Human Services Regulations for the Protection of Human Subjects, 45 C.F.R. Part 46.*

DoD-supported research is governed by the so-called *Common Rule*--the Federal Policy for the Protection of Human Subjects--which is part of DoD regulations at *Title 32, Code of Federal Regulation, Part 219.* DoD is a full partner in the Government's commitment to this standard and has further defined its human use regulation in DoD Directive 3216.2, *Protection of Human Subjects in DoD Supported Research*, January 7, 1983, and Department of Defense Guidance for the *Assurance of Compliance with the Federal Policy for the Protection of Human Subjects*, June 10, 1993. The latter instructions state, "the additional DHHS protection regulations found in Subparts B-D, while not part of the Common Federal Policy, contain basic protection concepts which should be adopted for research that involves protected classes of human subjects."

Contractors or grantees are informed of Departmental policy with regard to human use by several mechanisms. A notice of Federal requirements with regard to human use experimentation is often included in the Broad Agency Announcement soliciting research proposals. In addition, all contract and grant proposals using human subjects must provide either written assurance of compliance, hold assurance numbers issued by National Institute of Health (NIH), or other Federal Agencies, or undergo scrutiny by appropriate human use review committees at the funding organization. In general, there must be evidence of IRB review and approval of the research protocol, and of the informed consent document, prior to the award of any funds.

More specifically, under the aforementioned regulations, a proposal like that from the University of Cincinnati would require much more supporting documentation and justification to be considered for funding. This includes the following:

a) The therapy itself, separate from the research, would require more information on the possible benefits and the known side effects.

b) Several local committees (specifically, scientific, radiation, and institutional review boards [IRBs]), would have to review the proposed research protocol package, with proposed consent forms, before the DoD would review the proposal for acceptance.

c) The sponsor's IRB would have to include people from diverse backgrounds, including some members with non-scientific perspectives, who could objectively and fully assess the proposal.

d) The IRB record would have to document that the research design is sound, that risks to subjects are minimized, that the selection of subjects is equitable, and that, if applicable, special protections have been adopted for any vulnerable groups mentioned.

e) A written consent form signed by the patient/subject would be required for participation in the research. This consent form would require an explanation of the proposed therapy, all procedures and studies to be performed, and all expected outcomes and side effects in laymen's terms. The consent form must also state that the patient has been counseled about all of the above, and space provided for the patient to sign stating this has occurred and that the patient understands it.

f) The protocol would be required to justify withholding radiation in the control group of patients, if such radiation therapy were the standard of care for the patient's cancer.

g) The investigator would be required to give a more in-depth description of the known and suspected risks and the intended benefits of the research for the subject.

Approximately 104 Department full time employees (FTEs) are devoted to overseeing assurance and compliance with regulations governing the use of human subjects in research.

The Department has conducted approximately 199 announced site visits over the past 3 years. The site visits do not include the internal quality assurance committee monitoring programs, or periodic administrative and recordkeeping audits that are conducted.

The results of these visits can cause various administrative actions to be taken to correct minor discrepancies or provide consultative recommendations. The majority of corrective actions relate to documentation requirements and the training of researchers in documentation procedures. However, in five cases, the studies were halted to ensure adequate IRB review of the original protocol or modifications to the protocol submission, and to ensure adequate review of the informed consent documents.