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CHRONOLOGICAL SUMMARY -- DASA/DNA REPORTS

1. General Observations:

a. Dr. Saenger submitted ten reports to DASA/DNA from 1961 through 1972 in accordance with the terms of his contract.

b. The reports provide a means to trace the expansion of the research's scope, increased sophistication of techniques, and ambitiousness of future plans. The reports were similar in that they stated the purpose of and criteria for the research, research structure and techniques, how the work was conducted, the results of the experiments, observations and analysis of the data, plans for future study, and individual case histories of patients observed during the reporting period.

2. General information about DoD sponsorship of radiation experiments at the University of Cincinnati 1960-1971.

1958 In September, 1958 Dr. Saenger submitted an unsolicited research application to the Research and Development Division of the Army Surgeon General's Office. The application proposed to research metabolic changes in humans following total body radiation for the purpose of determining whether the presence of amino-acidura in humans after radiation would provide a reliable biological marker of radiation exposure. Dr. Saenger requested approximately $25,000 for the first year and $21,000 for two subsequent years.

1958-1959 Over the next year the proposal was reviewed within the Defense Department and a contract negotiated. Available documentation reveals that at least four Army Medical Corps and one Medical Service Corps officer reviewed the proposal. They recommended the contract application be approved. In October, 1959 the Defense Atomic Support Agency's (DASA) Deputy Chief of Staff, Weapons Effects and Test requested, thru the Chief, DASA, the Contract Management Branch, Directorate of Logistics negotiate a contract with the University of Cincinnati for the study of the metabolic changes in humans following total body radiation.

1960 In early 1960 a contract (DA-49-146-XZ-029, dated 1 January 1960) was signed between DASA and the University of Cincinnati Board of Directors. The contract provided $25,085 for the study. This contract, with supplements and modifications,

funded the study through February, 1964.

The first contract stated the technical scope of the research was "to study the phenomen of amino-acidura following irradiation, a condition which has been reported in humans and animals, to clarify some of the mechanisms responsible for amino-acidura and to determine whether it is a practical biological test of radiation exposure." The search for a biological marker of radiation exposure was one constant of Dr. Saenger's research effort over the next decade.

1961 On 28 February 1961 the Cincinnati project's contract was modified for the first time. The contract was modified to establish a new date for work completion to provide additional time for research on amino-aciduria following irradiation; amended the technical scope of the work to meet additional objectives of the government; provided additional funds to meet research requirements under the amended scope of work; altered portions of the contract to bring the contract in accordance with Armed Services Procurement Regulations that became effective subsequent to the signing of the original contract. The contract amount increased almost $30,000 from $25,000 to $54,000 and the length of the project was extended from February, 1961 to April, 1962. The scope of the work was expanded by three requirements: a breakdown of desoxyribonucleic acid and is derivatives in patients receiving total body radiation; DNA studies on patients who received partial irradiation and radiomimetic chemotherapeutic agents; and preliminary determination of appropriate psychometric tests.

1961 In June, 1961 the contract was modified for the second time. An additional $650 was allocated to use the technical services of a French authority on radiobiology at a Whole Body Radiation Conference to be held by DASA at the University of Cincinnati in October, 1961.

1962 In April, 1962 the project's contract was modified for the third time. The contract total was increased approximately $39,000 to $94,400. The project completion date was extended to April 30, 1963. The scope of work was also further expanded. Three additional objectives were added. Additional studies were to be made of--increasing the upper range of radiation dose to 150-200 rad,

and single doses of nitrogen mustard or other radiomimetic drug using .4mg/kilo. The following tests were to be conducted for 9 days post-treatment--urinary taurine for correlation with leukocyte count, BAIBA in urine, Kynurenic and xanthurenic acids, deoxycytidine, DNA fragments in urine, et al, xanthine and hypoxanthine in urine, urinary phosphate, and glutathione. The test were to be done over a 30 day period--routine electrophresis, immunoelectrophoresis, quantitative precipitin studies, serum urea nitrogen and/or serum creatine once weekly, urinalysis once weekly and as needed, routine hematology, and completion of the manuscript of the DASA Conference on Total Body Irradiation of October, 1961.

1963 On April 1, 1963 the contract was modified for the fourth time. The contract was extended through April 30, 1964. Funding was increased $40,000 to $134,56. The scope of the work was further amended. Tests to be conducted over a 30 day period between March 1, 1962 and February 28, 1963 were to be: (1) routine electrophesis, (2) immunoelectrophesis, (3) quantitative precipitin studies, (4) serum urea nitrogen and/or serum creatine once weekly, (5) urinalysis once weekly or as needed, and (6) routine hematology. During the same year the following tests were to be conducted over a 42 day period included 3,4,,5,6 and chromosome cultures of peripheral blood.

1964 Contract DA-49-146-XZ-315 came into effect and funded the research from February, 1964 to April, 1969.

1965 Ralph C. Rursiek and Dr. Eugene L. Saenger wrote a letter, dated May 17, 1965, to Director, Defense Atomic Support Agency, ATTN: STMD requesting that NWER No. 03.009 be funded at an estimated cost of $45,000 for FY65. The overall objective was to study various phenomena of desoxyribonucleic acid breakdown and other abnormalities following whole or partial body irradiation of human beings. Fifteen patients were to be studied. The project intended to study patients for 5-14 days prior to irradiation and for as long as possible after to evaluate clinical hematological and psychological changes. Investigation of the metabolism and urinary excretion of deoxycytidine was to be continued. Bone marrow was also to be stored prior to

irradiation. All serum was to be sent to Dr. Luzzio at Fort Knox.

1967 In 1967 a member of the University of Cincinnati research team, Dr. James G. Kereiakes, attended an Atomic Energy Commission sponsored conference at Oak Ridge, Tennessee. A purpose of the conference was to refine the dosimetric aspects of whole and partial body irradiations being used by the medical community to treat leukemia and widely disseminated cancers. The aim of the conference was to standardize the dosimetry being used to report patient dose. Information developed at the conference revealed 1,835 patients at about 35 institutions had received whole or partial body irradiations for the palliation or treatment of cancers. The use of radiation was widely spread and acknowledged as an effective modality.

1969 The final contract (DASA-01-69-C-0131), effective May, 1969 funded the research until March, 1972 when the University of Cincinnati refused DASA's offer for additional contract funding.

1971 Dr. Eugene L. Saenger wrote a letter, March 22, 1971, to Dr. Robert Loind, DASA, Attn: STMD. The cover letter with attachments forwarded the projects proposal for FY 73. The proposal requested $70,000 for a study entitled "An Appraisal of Human Studies In Radiobiological Aspects of Weapons Effects". A six page description of the study's philosophy, the role of future human research in relation to the remainder of the radiobiology program, specific areas of endeavor (eight--clinical evaluation, metabolic effects, behavioral effects, dose response studies, partial body studies, prognosis, therapeutic methods, use of healthy volunteers), and future plans regarding funding.

1960-1971 Through 1971 DoD ultimately spent over $650,000 on Dr. Saenger's endeavors which treated 85 adults whole- or partial-body radiation. Three children with localized Ewing's tumor were also treated with whole-body radiation. DoD funds were provided for laboratory, psychological and psychiatric tests to assess the effects of varying doses of whole and partial body irradiation. No funds were paid to the University of Cincinnati for direct patient care.

3. Report Summaries

1960-1961

The report for the first research period (February 19, 1960 to October 31, 1961) was DASA 1422 Supplement, which was entitled Metabolic Changes in Humans Following Total Body Irradiation. This title was used for the reports through 1967. The report provides a detailed itemization of the investigations and study projects. The aim of the studies was "to obtain new information about the metabolic effects of total body and partial body irradiation so as to have a better understanding of the acute and subacute effects of irradiation in the human." During this period ten patients received total body irradiation in doses that ranged from 16 to 150 rads. Patients were selected for the study were those with "proven metastatic or far advanced cancer...in relatively good nutritional status, i.e., able to maintain their body weight....[and] have normal hematological values." An explanation of one of the study's technique stated "the patient is told that he is to receive treatment to help his sickness. There is no discussion of subjective reactions resulting from the treatment. Other physicians, nurses and ward personnel are instructed not to discuss these aspects with the patient." The remainder of report discussed on-going studies, clinical observations, dosimetry, and other study techniques supplemented with tables and patient case histories.

1961-1963

The second report, DASA 1422 reported on the research from November, 1961 to April, 1963. Ten patients were treated with total body radiation in doses that ranged from 150-200 rad during the report period. The study's statement of aims was identical to that of the previous report except that it was expanded. The added aim stated "This information is necessary to provide knowledge of combat effectiveness of troops and to develop additional methods of diagnosis, prognosis, prophylaxis and treatment of these injuries." Patient selection criteria was more refined. In addition to those already stated new criteria was that "patients with lymphoma [were] excluded...Patients with solid neoplasms not radiosensitive are sought." The technique reported previously remained in use. Verbal consent of the patients was obtained prior to treatment.

One of the issues the researchers encountered involved complications in trying to determine the

effects of radiation. The report stated "Physicians assess patient to be certain that the underlying disease can be evaluated. Thus, there was difficulty in selection of patients for assessment of radiation effects because of underlying disease. Patients previously treated by radiation or chemotherapy were excluded because previous treatment confounded the response to radiation in several early patients."

Throughout the narrative and near the conclusion with the researchers thoughts on "Human Effectiveness Following Whole-Body Irradiation". Several of their observations included:

"Marked hematological changes occur generally between the 25th and 35th day following exposure. Maximum recovery to be obtained generally requires about 100 days."

"Human beings recover slowly and are quite sensitive to radiation with multi-system involvement."

"Prodromal acute effects such a nausea, vomiting, anorexia, and lassitude are of the duration hours. Intermediate effects such as hematologic complications are to be conceived of in weeks."

"A previous dose of radiation does influence the incidence of acute effects. Therefore the incidence of 'combat effectiveness' will be significantly increased on re-exposure of an individual."

"...individuals with previous exposure to radiation will be less tolerant of subsequent exposures. Hence troops previously exposed to 150-300r of whole body radiation will tend to show more combat ineffectiveness in the prodromal period than will those who are unexposed."

"This field of investigation has obvious important implications. Breakdown of DNA has long been implicated as the fundamental biochemical change of radiation and there is an impressive literature bearing on this point...The observation cited above of decrease of DOC after the administration of protective agents indicates the possibility of the use of specific prophylactic agents for the protection of humans in nuclear warfare."

A final observation was offered on future study:

"It is our opinion that human radiation studies need to be expanded.

We propose to establish facilities for withdrawal, storage, and reinfusion of autologous bone marrow. As indicated elsewhere in this report we have encountered significant hematological difficulties with a dose range of 200-325r. Therefore, to proceed with higher doses, we feel the need to protect our patients even if we might sacrifice their value for hematological evaluation after 2-3 weeks since the hematological effects are well documented. Once this technique has been developed as a support procedure we then anticipate increasing doses to higher levels."

Tables, figures and case histories rounded out the report.

1963-1964

DASA 1633 was the report submitted for the period May 1, 1963 to February 29, 1964 during which six patients were treated with total body radiation doses between 100 to 150 rad. The aims of the study remained as previously reported. "Normal renal function' was added to patient selection criteria. The technique to limit subjective reactions treatment was unchanged. Proposals for human study expanded on the previous report's discussion of autologous bone marrow reinfusion. The report stated:

"Storage and reinfusion of autologous bone marrow will be accomplished in the facility which has been established...The purpose of marrow storage and reinfusion is to protect subjects who receive doses in excess of 150 rad in the event of bone marrow failure. We hope to utilize doses between 200-300 rad."

Tables and case histories once again accompanied the report.

1964-1966

DASA 1844 covered not only the study years 1964 to 1966 but also provided a summary of the first six years of the experiment. Midway through the decade the aims of the project were stated as:

"This program is designed to obtain new

information regarding the metabolic, physiologic, immunologic, hematologic, and biochemical effects of TBR and PBR in human beings. It will then be possible to understand better the influence of radiation on combat effectiveness of troops and to develop more suitable methods of diagnosis, prognosis, prophylaxis and treatment of radiation injuries. It is our belief that information concerning radiation effects in the human being can be determined as well or better in these subjects as in the laboratory animal even though the characteristic of cancer must be kept in mind in the evaluation of the data."

On page 2 the aims were once again addressed in terms of the original scope of the study:

"A major objective of these studies has been a search for a suitable biological indicator of radiation dose in human beings....At this time the urinary excretion of deoxycytidine seems to be promising as a biological indicator."

Another aim was stated on pages 2 and 3.

"Psychological and psychiatric testing has been started in 14 patients....This approach will provide information on another important parameter of combat effectiveness of troops."

Later in the report an aspect of the psychiatric evaluation is further discussed.

"One of the most difficult aspects of radiation injury requiring evaluation is that of performance decrement. This term is loosely used but in our laboratory it is defined as any decrease in ability to carry out assigned tasks."

Patient selection criteria was more specific:

"Patients with metastatic or incurable neoplasms are given whole partial body radiation for palliative treatment of their disease. Patients for the studies described in this report are selected from patients treated as described above providing that they satisfy the following criteria:

1. The patients have solid tumors. Patients with lymphoma are excluded.
2. Relatively good nutritional status

(ability to maintain weight).
3. Normal renal function
4. Stable hemogram in the control period."

Twenty three additional patients were treated during the research period between 1964 and 1966. Of these patients 13 received total body radiation treatments with dosages between 25 and 150 rads. Partial body radiation doses between 100 and 300 rads were used in the treatment of 10 patients.

The technique to "isolate" patients from discussions of subjective reactions remained the same.

Discussion of hematology stated:

"Since severe hematological depression was found in most patients who expired, autologous bone marrow storage has been performed for 13 patients. In only two patients has infusion been carried out. The method is being refined so as to include filtration prior to infusion. Although we have not encountered morbidity...filtration appears to decrease the probability of incidence of pulmonary emboli."

Accompanying the 35 page report were 122 pages of tables, and case histories of the all patients treated to date.

1966-1967

DASA 2179 described the treatment of four patients between May 1, 1966 and April 30 1967. Of the four patients treated one received total body radiation (150 rad) while the other three received partial body radiation doses in the range of 100-200 rad. Aims, patient selection criteria, and technique remained as previously reported. Three accomplishments were reported. The first involved "the completion of an infusion filtration system for reinfusion of autologous stored human bone marrow." As a result of the development the researchers stated "Since this instrumentation will make infusion of marrow a safer and more easily controlled procedure we feel that earlier infusion to prevent the hematological depression from radiation should be investigated." The text noted that the methods were described in a paper presented in Paris, France which cited DASA support.

The second accomplishment was the "perfection

by Dr. I-Wen Chen of a new, much improved method for the determination of deoxycytidine (CdR) in urine from humans and from rats."

The third involved "the growth of two strains of phage on synthetic culture medium." This development made it "possible to titrate antibody production in experimental animals and man before and after irradiation."

Future plans included the evaluation of "alterations in antibody production and /or destruction in human beings due to radiation." Observations of this nature on "the effects of radiation exposure will yield a better understanding for military planning and triage."

Tables, figures, and case histories supplemented the text.

1967-1968

The report for the period May 1, 1967 to April 30, 1968 was DASA 2168. The report's title changed to Radiation Effects in Man: Manifestations and Therapeutic Efforts. Reports carried this title for the remainder of research. This report recounted the treatment of seven patients. Four patients were treated with total body radiation doses between 100 and 200 rad. Three patients were treated with lower body partial body radiation doses of 200 to 300 rad. The report's forward noted "these studies were performed in conformation with the 'recommendations guiding doctors in clinical research' as stated in the Declaration of Helsinki of the World Medical Association (1964). Reported aims, criteria and techniques were as previously reported. Updated information from the psychiatric-psychological team noted "the number of patients who have been evaluated by the psychiatric-psychological team now totals 20." Hematology research continued. The researchers reported "seven patients received autologous bone marrow transfusions at completion of DADA 2168. Guidelines for quantity of marrow cells to be infused for successful transfusion and bone marrow protection were developed."

Case histories and tables provided additional information.

1968-1969

The research over the period between May 1, 1968 and April 30, 1969 was the subject of DADA 2428. Eight patients were treated during this period. Total body radiation doses of 100-200 rad were given to six patients. Two patients were treated with 200-300 rad doses of partial body radiation.

Once again the forward noted that the studies conformed to the recommendations of the Declaration of Helsinki. Aims and goals remained unchanged. In the field of hematology the report stated "success has finally been obtained in autologous marrow infusion which will permit us to employ higher doses of radiation in the coming year. Several new biological dosimeters are under evaluation." Tables and case histories accompanied the report.

1969-1970

DASA 2599 reported on the research based on observations of twelve patients between May 1, 1969 and April 30, 1970. The recommendations of the Declaration of Helsinki were once again noted. A presentation by Dr. Edward B. Silberstein on the team's earlier work and the data contained in this report at the IAEA-WHO Conference in Paris on 24 June 1970 was reported.

During this period six patients were treated with doses of 100-230 rad of total body radiation. The other six patients received partial body radiation doses between 150 to 300 rad. Regarding these patients the report stated "Most of the patients had inoperable metastatic carcinoma which was not amenable to conventional chemotherapy. Nevertheless, these patients were all clinically stable, many of them working daily. Several of the subjects, apparently tumor free and clinically normal after regression of regionally irradiated tumors (Ewing's tumor), received prophylactic whole body radiation."

Hematological work, specifically related to biological dosimetry, was discussed. Several biological dosimetry issues were discussed.

"We are pursuing this goal at whole-body radiation doses up to 250 rad with even higher doses planned with the support of marrow autotransfusions and laminar-flow 'sterile' rooms. Large-volume partial-body irradiation is also being performed to learn more about the efficacy of chromosome aberrations as a radiation dosimeter in the more frequent situation of inhomogeneous exposure. With a linear accelerator, we hope to study the effects of various dose rate <u>in vivo</u> as well."

As for the continued research into the utility of deoxycytidine the report noted "deoxycytidinuria appears to be related to general

tissue catabolism from several causes, including radiation. Other problems in using urinary CdR include variations in excretion due to race (57) and age (63)." [Note: Numbers in () are bibliographic reference numbers.]

Tables and case histories were included with the report. Table XII provided "a summary of demographic and other pertinent data...for the entire group of 36 patients" observed since the start of testing.

1970-1971

DNA 2751T was the report for the period May 1, 1970 to April 30, 1971. Eight patients underwent treatment. Three received total body radiations dosages of 100-200 rad. Five underwent partial body radiation with doses of 300 rad. The research aims were restated.

"The University of Cincinnati studies in radiation effect in man continues as a carefully integrated effort to maximize clinical, psychiatric, therapeutic, biochemical, and theoretical approaches to whole and partial therapeutic irradiation as given for palliation of certain selected cancers."

To achieve these aims "the methods of applying radiation have remained essentially the same since the inception of these studies."

Acknowledgement was made of guidance provided.

"The nature of the specific projects undertaken in our laboratories reflects the consideration of many of our faculty and the thoughts and problems of the other DNA conferences organized over the past several years by Col E.J. Huycke. Valuable interchange of ideas have been stimulated by visitors from Department of Defense laboratories who give our staff a more practical insight into military problems than we might otherwise have."

Future plans were described.

"Many of the new directions in our investigation stem from concurrent advances in cytogenics, organ transplantation, bio-chemical aspects of molecular biology, and clinical aspects

of cancer therapy."

"A renewed interest is manifested in chromosome aberrations as being eventually an index of 'effective radiation dose,' particularly since almost all exposures encountered in nontherapeutic circumstances will have varying degrees of nonuniformity of dose rate and dose distribution."

"As an outgrowth of our needs to afford maximum protection to patients receiving doses in the LD_{50} range, some new technical advances have been developed in bone marrow transfusion in patients."

Regarding biological dosimetry the report stated:

"Yet in severely burned individuals deoxycytidine ((deoxycytidine excreted in urine)) occurs late (in 2 to 4 weeks) and in the several patients studied the levels seemed directly related to the extent and depth of the burn. Radiation induced deoxycytidinuria when found occurs within 2-3 days and then disappears. Additional studies may suggest this test as a way of differentiating relative contribution of these two modalities of injury."

The usual tables and case histories supplemented the narrative.

1971-1972

The final report in the series was DNA 3024F which was to be for the period April 1, 1971 to March 31, 1972. However, its was really a summary of the entire research effort and was a "scientific communication presented at the meeting of the American Roentgen Ray Society in Washington on 3 October 1972." It was further noted that "this report has been accepted for publication in the American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine."

As stated in this report the research were "to improve the treatment and general clinical management and if possible the length of survival of patients with advanced cancer. Systemic effects of radiation therapy have been given particular attention in our work."

The issue of informed consent was addressed.

"All patients gave informed consent in

accordance with directives of the Faculty Research committee of the University of Cincinnati College of Medicine and those of the National Institutes of Health. The use of formal informed consent forms in this study antedated the above requirements by two years. The project is reviewed and approved regularly by the above committee."

The report noted that "patients become eligible for this form of treatment if they have advanced cancer for whom cure could not be anticipated....Chief among the reasons for elimination was an indication in the pretreatment phase that some risk from wide-filed radiation might ensue or that another method of treatment was considered preferable."

From an analysis of radiation mortality "one can identify eight cases in which there is a possibility of the therapy contributing to the mortality."

A comparison is later made between times of death of those that entered the study and received radiation treatments, and those that entered the study and did not receive radiation treatments. From this comparison the report noted:

"Fisher's exact probability test yields a p value of 0.16, indicating that there is no difference between the two groups. Therefore, one may conclude that in other patients described, the effect of whole- and partial-body radiation therapy was less important in contributing to death than was the extent of disease in these patients. Another interpretation would be that a physician selecting far advanced cancer patients for a given treatment would have about the same degree of difficulty in selecting any form of treatment for these very ill patients."

Tables and figures accompanied the report as did a section entitled "Thermography as a Radiobiological Dosimeter".

1971-1972 Issues arise that lead to the termination of the contractual relationship between DNA and the University of Cincinnati.

Project Chronology
October 1971 - January 1973

October 8, 1971 -- An article appeared in *The Washington Post*, "Pentagon Has Contract to Test Radiation Effect on Humans", by Stuart Auerbach and Thomas O'Toole that prompted the subsequent governmental investigations of the Cincinnati project.

October 11, 1971 -- Dr. Eugene L. Saenger, Dr. Clifford G. Grulee, Dean of the University of Cincinnati College of Medicine, and Dr. Edward A. Gall, Vice President of the University of Cincinnati and Director of the University of Cincinnati Medical Center, were present at a press conference the subject of which was the impending Senate and Government Accounting Office (GAO) investigations of the conduct of the Cincinnati project.

October 11, 1971 -- A follow up article appeared in *The Washington Post*, "Pentagon's Radiation Experiments Defended". The article featured Dr. Saenger explaining the process of patients selection and Department of Defense (DOD) funding of the project.

Mid-October 1971 -- DOD developed a Fact Sheet on the Cincinnati project that discussed its contractual arrangements with the University of Cincinnati. A copy of the Fact Sheet was later entered into the Congressional Record on December 15, 1971 as an attachment to a letter from the Assistant Secretary of Defense (Legislative Affairs) to Senator Robert Taft, Jr.

October-November 1971 -- Senator Mike Gravel wrote a letter to Dr. Robert W. McConnell, President of the American College of Radiology (ACR) requesting the ACR to conduct an evaluation of the Cincinnati Project.

November 12, 1971 -- Dean Clifford G. Grulee appointed an Ad Hoc committee to review the "whole-body radiation study" which Dr. Eugene L. Saenger had been conducting at the University of Cincinnati Medical Center. The Ad Hoc committee, chaired by Dr. Raymond Suskind, Director, Environmental Health, University of Cincinnati, was made up of eleven members and was charged with reviewing the scientific content, methodology, and data treatment of this study, as well as other aspects which the committee deemed appropriate. All eleven committee members were professors at the University of Cincinnati. Ten committee members were medical doctors and one was a Ph.D. in Physiology.

December 6, 1971 -- Mr. Ellis R. Mottur, Science Adviser to the Senate subcommittee on Health, Senate Committee on Labor and Public Welfare and Dr. Caper, both of Senator Kennedy's staff interviewed Dr. Edward B. Silberstein, University of Cincinnati Medical Center, Dr. Eugene L. Saenger, and others at Cincinnati General Hospital.

December 6, 1971 -- Dr. Robert S. Daniels, Professor and Director, Department of Psychiatry, University of Cincinnati, wrote a letter

to Dr. Raymond Suskind. The letter forwarded a list of question to Dr. Suskind for inclusion in a "our [Ad Hoc Review Committee] report on 'Total Body Radiation' project".

December 7, 1971 -- Mr. Ellis R. Mottur of Senator Kennedy's staff requested the opportunity to conduct interviews with surviving project subjects.

December 7, 1971 -- Dr. Eugene L. Saenger wrote a letter to Dr. Raymond Suskind, which discussed the impending arrival of the ACR Committee to review the project.

December 13, 1971 -- The subject of interviewing patients was broached in a letter from Senator Edward Kennedy, acting in his role as Chairman of the subcommittee on Health, Senate Committee on Labor and Public Welfare, to Dr. Warren Bennis, President University of Cincinnati.

December 17, 1971 -- Dr. Eugene L. Saenger wrote a letter to Dr. Charles Barrett, Department of Surgery, University of Cincinnati Medical Center. The letter details Dr. Saenger's objections and concerns about providing patients to be interviewed.

December 20, 1971 -- Dr. Eugene L. Saenger authored "Comments on Differences Between Therapeutic and Non-Therapeutic Investigation". Dr. Saenger generally defended his research and methods by citing legal and medical opinions. He then went on to refute specific allegations that relate to DoD funding, informed consent techniques (Dr. Saenger made the point that since 1968 patients were told the information gained might be of use on the battlefield), follow-up, alleged contributory effects of radiation to patient deaths, racial composition of study group, and the below average intelligence level of the project subjects.

December 21, 1971 -- Dr. Eugene L. Saenger wrote a letter to Dr. Edward A. Gall. The letter was a response to Dr. Gall's request that Dr. Saenger identify patients that might be suitable for interviews by Mr. Mottur.

January 1972 -- The Ad Hoc Review Committee chaired by Dr. Raymond Suskind of the University of Cincinnati communicated its report to the Dean of the College of Medicine concerning Dr. Saenger's project. The Report contains seven sections,two of which are pertinent to DOD involvement; Section IV <u>Financial Support of Program</u> and Section V <u>Informed Consent and Human Rights</u>.

In Section IV it is reported that the request for financial support for the project was initiated by the University of Cincinnati. The systematic investigation of whole body radiation did not begin until the project was funded by the Defense Atomic Support Agency (DASA). Through March 1972 DASA had granted $651,483, 13% to 15% of the budget of the Radioisotope Division. Section IV also details the breakdown of expenditures. There is no evidence that the DASA funding was made contingent on work, ideas,

or suggestions proposed by DASA and that all the information reported to DASA was kept unclassified and publicly available. The work was also carried out by the University researchers with complete scientific freedom.

In Section V it was stated that the procedures for informed consent followed by Dr. Saenger's partial and whole body radiation project reflected the process characteristic of the University of Cincinnati and the nation. As the idea of informed consent developed nationally in the 1960's from informal, oral, and non-specific to formal, written, and more detailed, Dr. Saenger's project appropriately updated their procedure for informed consent to meet the more stringent levels required for good medical research.

January 3, 1972 -- The ACR responded to Senator Mike Gravel's request to conduct an inquiry into the whole-body radiation therapy project supervised by Dr. Eugene L. Saenger. The ACR Report concluded that the Cincinnati project was validly conceived, stated, executed, controlled and followed up. The process of patient selection was based upon clinical considerations and conformed with good medical practice. The procedures for obtaining patient consent was valid and consistent with the recommendations of the National Institutes of Health and with the practice of most cancer centers. The ACR Report indicated procedures for obtaining informed consent were likely performed better than the average institution because of the volume of projects generated by the medical facility and the quality of the people involved. ACR urged Senator Gravel to support the projects continuation. The ACR Report also noted that DOD funds were used to support the laboratory and psychological studies, but not the treatment or the care of the patients. The ACR Report discusses at length the subject selection procedures and notes that in both race and IQ the group is representative of the patients served at Cincinnati General Hospital. The ACR Report also agreed with Dr. Saenger that ". . . it seems reasonable to continue [whole-body radiation] therapy for the gravely ill individual since this method of treatment is less elaborate and with no greater risk than many present forms of chemotherapy."

January 11, 1972 -- Senator Edward Kennedy wrote a letter to Dr. Warren Bennis in reference to the University's refusal to identify patients to be interviewed by the committee. The Senator pointed out that some patients appeared in a documentary produced by National Education Television in September, 1971, and it was difficult to understand why the University allowed them to appear on TV and not before a Senate Subcommittee. Senator Kennedy stated that the University's decision was unfortunate because "the most crucial element in the inquiry is the patient's perception and understanding of the experiments in which they were participating..."

January 19, 1972 -- Dr. Edward A. Gall wrote a letter to Senator Kennedy responding to the Senator's January 11, 1972 letter. Dr.

Gall stated that names were provided to NET with the consent of the patients but points out that the situation had subsequently changed. In response to the Senator's request the University was sending letters to surviving patients to ask them if they would give their consent to being questioned by representatives of the subcommittee. He said that experts were consulted and they were of the opinion that any such questioning may have led to some unfavorable medical implications. Dr. Gall also asked the Senator if he would consent to a meeting with senior university officials.

January 21, 1972 -- Mr. Ellis R. Mottur wrote a letter to Dr. Edward A. Gall requesting copies of the letter (with names omitted) sent to patients or parents of surviving patients asking if they would consent to interviews.

January 25, 1972 -- Dr. Edward A. Gall wrote a letter to Mr. Ellis R. Mottur, Science Adviser, Senate Committee Labor Public Welfare, that forwarded the requested copies of letters sent to patients or parents to request interviews.

February 4, 1972 -- In a letter to Dr. Robert W. McConnell Senator Mike Gravel indicated his displeasure with the results of the ACR Report released on January 3, 1972. Senator Gravel felt the report was deficient in relevant information and poorly organized. The Senator pointed out the ACR report "confirms that the patients were not thoroughly informed about the extra discomfort, the military aspects, or the possible lethal effects."

February 4, 1972 -- Mr. Myrton Tom Stewart and Mr. Robert Murphy of the General Accounting Officer (GAO) met with Dr. Eugene L. Saenger. Dr. Saenger was asked nine questions: when did the project start; did he approach DoD or vice versa [he approached]; how were parts of research funded; where were Federal funds used, etc. In response to question 4 which asked about the use of federal funds for patient care, Dr. Saenger replied that "[n]o DOD funds under these contracts were at any time used for payment of patient days in any hospital. DOD funds were used for technical help, support of a biochemist, physicians, physicists and for psychological and psychiatric studies." In response to question 6 which asked if treatments were given for the benefit of the patients or DOD, Saenger responded, "that in all cases the treatment was given for the palliation of cancer of the patients and information for the Dod was a byproduct."

February 16, 1972 -- Dr. Warren Bennis wrote a letter to Senator Kennedy referring to meeting with the Senator and Ohio Governor Gilligan on February 24, 1972. Dr. Bennis included a copy of the Ad Hoc Review Committee's report, and advised the Senator that Dr. Gall would be responding within a few days to the Senator's request for an evaluation of the report by the Junior Faculty Association. The letter concluded with the promise that he was willing to cooperate with the Subcommittee in any way consistent with the health and legal rights of the patients.

February 17, 1972 -- Dr. Edward A. Gall wrote a letter to Senator Edward Kennedy which provided a copy of the Ad Hoc Committee Report and other documentation. Regarding the Junior Faculty Report, Dr. Gall wrote that since the Ad Hoc Committee report addressed the points raised by the Junior Faculty Association he considered the Ad Hoc report "a complete and authoritative response." He also informed the Senator that they had received responses from all the surviving patients and the parents of the children treated regarding interviews. All responses had declined to be interviewed. Dr. Gall further expounded on the point made in his January 19, 1972 letter that two cancer experts (not local and not associated with the University) had given as their opinion that there would be unfavorable medical implications if patients were interviewed.

February 17, 1972 -- Dr. Edward A. Gall wrote a letter to Dr. Warren Bennis forwarding the consultant opinions from the two cancer experts. Dr. Gall noted they were in concurrence with their own physicians about the undesirability of subjecting the patients to interviews.

February 22, 1972 -- Mr. Cyril W. Kupferberg, Chair of Radiation Response Team, wrote a letter in response to an individual who requested to know if a family member was part of the experiment that was reported to DoD. The individual was not a subject of Dr. Saenger. The letter included attachments - University of Cincinnati Guideline for releasing medical information on deceased patients, an authorization for release of information form, and an example of a "Consent for Special Study and Treatment" form.

March 31, 1972 -- The Cincinnati project contract number DASA-01-69C-0131 expired. The University of Cincinnati had earlier indicated that it did not want to continue conducting research under this contract with the Defense Nuclear Agency.

July 5, 1972 -- Dr. Eugene L. Saenger wrote a letter to Dr. Edward A. Gall. The three page letter appears to be Dr. Saenger's response to an article published in the *Cincinnati Post* on April 25, 1972. Dr. Saenger's response focuses on several points: University procedures for seeking Federal grants/contracts, issues associated with seeking DoD funds for research in FY 74 and the terminating of research utilizing FY 73 funds.

August 1, 1972 -- Several pieces of correspondence relating to the Cincinnati project were entered into the *Congressional Record*, including a letter from the Comptroller General of the United States to Senator Edward Kennedy summarizing the results of the GAO investigation of DOD policy regarding the protection of humans used in medical research projects and DOD responses to questions from Senate staffers concerning DOD policy relative to human experimentation policies and procedures. The letter from the Comptroller General indicated that DOD policy was set forth by DOD Instruction 5030.29, dated May 12, 1964. Instruction 5030.29 states that "The Department of Defense assumes full responsibility

for the protection of humans involved in research under its sponsorship whether this involves investigational drugs or other hazards." The letter also states, "[c]oncering the contract with the University of Cincinnati . . . [DNA] stated that the cost of radiation treatment and patient case had not been borne by their agency. They also stated that funds of the Defense Nuclear Agency had been used only to pay for supplementary laboratory analyses of patients who had received whole-body irradiation in order for the Defense Nuclear Agency to gain information in areas that were relative to national defense."

The questions from Senate staffers focused on (1) the level of human experimentation funded by DOD, (2) what authorization was needed to conduct human experiments, (3) the adequacy of information given to prospective subjects and (4) were there differing standards applied to military personnel than to civilians. DOD responded to question one that only a very small portion of its medical R&D budget was given to human experimentation. In response to question two DOD stated that although there was no standardized authorization process, all human experimentation was guided by DOD instructions and service regulations and instructions. In response to question three DOD stated that informed consents was a primary ethical and legal requirements for all DOD use of human volunteers. In response to question four DOD responded that in terms of supervision, volunteering, informed consent and freedom to terminate there was no difference.

January 11, 1973 -- Mr. Lawrence Elish released a 26 page paper titled, "Legal Rights of Human Subjects in the University of Cincinnati Whole-Body Radiation Study", that examined the legal and ethical implications of the Saenger experiments.