

OAK RIDGE NATIONAL LABORATORY

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UNION CARBIDE CORPORATION  
NUCLEAR DIVISION



POST OFFICE BOX X  
OAK RIDGE, TENNESSEE 37830

OFFICE OF THE DIRECTOR

September 2, 1980

Department of Energy, Oak Ridge Operations  
Attention: Mr. J. A. Lenhard, Assistant Manager  
for Energy Research and Development  
Post Office Box E  
Oak Ridge, Tennessee 37830

REPOSITORY MMES / X-10 / 4500 N  
COLLECTION Director's Files  
BOX No. \_\_\_\_\_  
FOLDER \_\_\_\_\_

Gentlemen:

ORNL HUMAN USE EXPERIMENTAL PROCEDURES

Your letter of July 21, 1980, expressed concern with regard to the exposure of several ORNL employees to 12-O-tetradecanoyl phorbol 13-acetate (TPA). We fully share your concern with regard to this matter and would like to apprise you of the steps we have taken since the exposure.

When this matter first came to our attention in the Spring of 1979, the Director of the Biology Division informally met with Dr. Slaga to establish the facts. It was determined that exposure to TPA had occurred after hours and away from the Laboratory and without prior Laboratory approval. Dr. Slaga was informed in the strongest possible terms that this was an unacceptable practice and that its occurrence away from the Laboratory did not relieve him of his professional responsibility. Dr. Slaga was also informed again of ORNL policies with regard to human use experimental procedures which require that any proposed research involving human subjects must be approved in advance by the Human Use Committee.

We subsequently reviewed all our policies and procedures regarding human use experiments to insure that they could be expected to reasonably prevent any such future occurrence. Following this review, we emphasized to our senior research staff the importance of these procedures and their individual responsibility to see that all investigators and staff under their supervision were fully aware of the policy.

Since receiving your letter, we have again reviewed the ORNL policies and procedures to see if they are adequate and have made some changes to broaden the policy. A copy of the latest ORNL policy is enclosed. As a result of this detailed review, we are convinced that the ORNL practices and procedures

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Human Subjects Project

Mr. J. A. Lenhard

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concerning research involving human subjects can reasonably be expected to prevent such occurrences in the future.

We trust this information is fully responsive to your request and that it will be adequate for the Office for Protection from Research Risks, NIH.

Sincerely,

A handwritten signature in black ink that reads "Herman Postma". The signature is written in a cursive, slightly slanted style.

Herman Postma  
Director

HP:jnw

Enclosure

cc: A. S. Garrett  
R. A. Griesemer  
R. F. Hibbs  
C. C. Hopkins  
C. R. Richmond  
File - RC

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ORAU/ORNL Committee on Human Studies

IMPLEMENTING GUIDELINES FOR RESEARCH ON HUMAN SUBJECTS

(In Compliance with DHEW and ERDA Regulations on Protection of Human Subjects)

(March 1977)

A. Basic Principles (See Definitions, Annex 1.)

The Committee on Human Studies for Oak Ridge Associated Universities and Oak Ridge National Laboratory has officially adopted the code of ethics adopted by the World Medical Association, known as the Declaration of Helsinki. It accepts as amplification of this document the statement of the British Medical Research Council. The guiding principles of operation of this Committee are, however, those set forth in detail by DHEW in Federal Register, March 13, 1975, Vol. 40, No. 50, Part II, Protection of Human Subjects, Technical Amendments, pp. 11854-11858, and by ERDA in an August 17, 1976 document titled "Protection of Human Subjects Proposed Regulations" (10 CFR Part 705) as amended in 10 CFR, Part 745 (FR 41, November 30, 1976, pp. 52434-52438). (See Annex Items 2 and 3.) Wherever these guidelines appear to differ substantively from those in the Federal Register, those in the Federal Register should be understood to be dominant and to be followed.

B. Committee Membership and Structure

The Committee shall consist of persons of either sex and any race with varying backgrounds, training, vocation and community interests who, while cognizant of the research goals and programs of the two sponsoring institutions (ORNL and ORAU), are sufficiently qualified to safeguard the rights and welfare of human subjects and review the relative merit of human studies in respect to any risks involved. The Committee will be composed of at least two lay persons, two research scientists and two clinicians. Two of the medical professionals, however, must be from institutions other than ORNL or ORAU, the institutions from which will emanate applications for permission to conduct a particular human study. Because of the dual sponsorship of this Committee, the Medical Director of the Health Division, ORNL; Director of Biology Division, ORNL; and the Chairman of the Medical and Health Sciences Division of ORAU shall be members of the Committee. The Directors of the two sponsoring institutions (ORAU and ORNL) shall designate to these divisional directors the responsibility for seeing that their respective staffs comply with HEW and ERDA regulations for the protection of human subjects. The Chairman and Secretary of the Committee shall be elected at one (January) of two annual meetings of the Committee. A person nominated for Committee membership by a member of the Committee or a sponsoring institution shall be made a member only with the concurrence of the other Committee members. Because of the complexity of modern laws and regulations protecting human rights, governing contractual obligations and guiding the use of government funds and facilities for research, at least one member will be a lawyer cognizant of the Federal Regulations. A lawyer consultant will be

agreed upon and will be readily available to counsel the Committee if the Committee membership does not include a lawyer member. Similarly, if the membership does not contain a minister or a psychologist (or psychiatrist), some person with a related vocation who is interested in protecting persons from emotional and psychologic trauma must be available to the Committee for consultation on individual projects whether or not psychologic stress or risk is obviously involved. (See Annex 4, 5, and 6.)

C. Procedures for Carrying out Initial and Continuing Review of Applications and Projects

1. Initial Review

All applications for support of research, training, demonstration or general research support projects, including those of fellows and trainees, which involve the use of human subjects, must be presented to and approved by the Committee on Human Studies, prior to submission for funding, and with the identical experimental design used for grant submission or ERDA "189" proposals. Regardless of the nature or degree of risk anticipated, the application must be presented in writing on the proper form (Annex 7). The application should not contain extraneous material; that is, the investigator should not submit a copy of an IND or ERDA-189 as a substitute for the form specified. The applicant must be prepared to discuss in person before the Committee detailed information on the following points:

- a. The possible risk to the rights and welfare of human subjects, including the rights of privacy, freedom from harassment and confidentiality of data. A description of the provisions made to minimize these risks must also be presented.
- b. Methods used to acquire informed consent. The form on which it is obtained and the risk described. Special emphasis shall be placed on the appropriateness of a consent form to the particular situation inherent in the study plan in question (Annex 8).
- c. The relative risks of the project as compared to the probable benefits to the subjects and to society. For each application, the Committee will document whether or not physical or psychological risks are likely to ensue as a result of the proposed research study, and further, that such potential risks have been evaluated in respect to the subject and his rights, needs and benefits. In addition, informed consent documents must be submitted to and approved by the Committee for each study so that members can be ensured that each human subject will receive candid explanations of specific procedures and their purposes, of attendant specific discomforts and risks, and possible benefits, if any. In addition, the Committee must be satisfied in

each study evaluation that the subjects will be instructed that they are free to withdraw their consent to participate and to discontinue their participation in the proposed project at any time without prejudice to them. No informed consent form will be considered acceptable if it contains any exculpatory clauses or attempts in any way to absolve the Principal Investigator's responsibility for the health (physical or mental) and welfare of the human subjects to be involved.

Specific deficiencies in a proposal will be identified by the Committee in writing for the proposer and also directed to the attention of that Committee member (the Director of the Health or Biology Division, ORNL, or Chairman of the Medical and Health Sciences Division, ORAU) who also has the responsibility designated to him by the Director of his sponsoring institution (either ORNL or ORAU) to obtain staff compliance with DHEW and ERDA Regulations and Guidelines for Protection of Human Subjects. Such a statement of deficiency by the Committee will be understood to require (1) delay in submission of the proposed grant or contract application to HEW or ERDA, and (2) resubmission for Committee approval before the project proposals are allowed to go forward in the funding process. A statement of approval by the Committee will be accompanied by HEW-596 (Annex 9) for the institutional director's signature for simultaneous submission with an NIH, NSF or ERDA grant proposal.

A member of the Committee who is from the institution (ORNL or ORAU), from which the research proposal is being submitted, will be expected to attend the Committee only for his information, and will have no persuasive or voting powers concerning the acceptability of that proposal and its level of compliance with HEW and ERDA guidelines.

Approval of a proposal for a study involving human subjects shall be formalized only after a majority of the qualified (see paragraph above) Committee members have had a chance to review the written proposal, discuss it with the other members of the Committee, obtain adequate answers from the author to their questions, and reach complete agreement of acceptability. No proposal will be approved to which any Committee member objects on the basis of consideration of the physical or mental welfare of any human subject. In special cases where a Committee member cannot attend, his comment and vote can be obtained by mail.

The Committee's findings will be transmitted in writing to the appropriate officer of the laboratory proposing the research and to the applicant. Release of funds shall be controlled by the guidelines to HEW-596 (Annex 9). The applicant's administrative superior shall maintain continuing review of the project activities. If a responsible investigator plans a change in study protocol, he must submit the proposed changes to the Committee for approval before putting them into practice.

D. Procedures of the Committee to Provide Advice and Counsel to Investigators

On request, senior investigators will appear before the Committee at its called meetings to answer any questions concerning a proposal. The question and replies will form part of the official minutes of the Committee and will be distributed to the concerned staff members, together with recorded actions of the Committee on a Review and Action Form (Annex 10).

Committee Meetings

The Committee will meet at least twice a year. The first meeting of the year will be early in January, if possible, to meet the following administrative needs:

1. Election of Chairperson and Secretary,
2. Reelection of members and replacement of those members no longer able to serve,
3. Report of the Secretary on the previous year's Committee activities and on the number of approved studies that are still active and therefore require critical review in the new year. Establishment of the calendar for scheduled review of continuing projects, documented by an annual status report that reports any emergent problems and indicates the need for changes in research protocols or forms for obtaining informed consent.

The second biannual meeting will address any problems in these administrative areas that have risen since the first meeting.

Other meetings will be called to meet the scheduled annual critical reviews, and as needed, to consider a specific new proposal(s) involving humans as subjects where HEW, ERDA, NSF or other governmental funding agencies have fixed deadlines which the research applicant is trying to meet. In special cases where time is short, and particularly where the defined risk to the human subject is a commonly accepted one (i.e., a physical examination by a licensed physician) and does not require discussion with the project proposer, the appropriate members of the Committee (Annex 6) may be polled by phone by the Secretary under the Chairman's direction after the members have had a chance to review the proposal sent to them by mail.

E. Requirements for Reporting any Emergent Problems or Proposed Precedural Changes to the Committee

All senior investigators with proposed or active projects will receive notice of Committee meetings and will appear before the Committee in person. At this time they shall present in writing any proposed changes in procedures and shall describe any new risks and benefits, and any methods for safeguarding patients' rights and procedures for informed consent in advance of instituting these changes.

All investigators with active research programs involving human subjects that have been approved by the Committee must be kept aware of the need for an immediate report to the Committee secretary, Chairperson, or institutional representatives of emergent problems bearing on the health and welfare of human subjects and of needs for protocol modifications, restrictions or termination.

F. Procedures to Maintain an Active and Effective Committee

1. The chairman will ensure an active Committee by calling, in addition to the regular Annual Meeting, at least one additional meeting each year.
2. The members will be enjoined to assess every ongoing project as well as new proposals.
3. Extramural Committee members will be paid a consultant's fee, providing they are able to accept it, and travel expenses.
4. Full Committee Minutes will be distributed promptly to all members in draft form for corrections and review, so that the opinions and actions can be recorded accurately.
5. On a regular basis, at least annually, at some full Divisional professional staff meeting, the respective institutional representative will explain this program for protection of human subjects to his staff and reinforce the importance to his division of his staff following the HEW and ERDA Regulations and Guidelines on the use of human subjects in research.

G. Location of Records

The records of this Committee will be kept in the office of the Executive Secretary and will be available to the Committee, staff, and government auditors on demand.