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Oak Ridge Operations
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September 5, 1980

Dr. Charles R. MacKay, Deputy Director
Office for Protection from Research Risks
Office of the Director
Department of Health and Human Services
3A18 Westwood Building
5333 Westbard Avenue
Bethesda, Maryland 20205

Dear Dr. MacKay:

This is in response to your letter of June 17, 1980, to Dr. C. C. Lushbaugh, Oak Ridge Associated Universities (ORAU), and our subsequent telephone conversation requesting an investigation and report concerning involvement of individuals as subjects of research at the Oak Ridge National Laboratory (ORNL).

Before discussing the results of our investigation, it may be helpful to clarify the role of the two institutions referred in your letter. The Oak Ridge National Laboratory is a Federally owned facility operated for the Department of Energy (DOE) by the Union Carbide Corporation, Nuclear Division. Research at ORNL for other government agencies is conducted under the DOE contract with Union Carbide Corporation. Oak Ridge Associated Universities is also a prime operating contractor of DOE. Since there are two DOE research centers in Oak Ridge, both of whom have work funded by NIH, a bi-institutional General Assurance was sought and granted by NIH with both institutions sharing the General Assurance (G01716). The ORAU/ORNL Committee on Human Studies is chaired by Dr. Robert Lange of the University of Tennessee Memorial Research Center in Knoxville, Tennessee. For continuity, Dr. Lushbaugh has agreed to have all matters relating to the Committee be addressed to him. The fact that Dr. Lushbaugh is listed as the Institutional Officer to whom correspondence concerning Board affairs should be addressed does not change the bi-institutional nature of the Committee as shown in Enclosure 1. For ORNL, Dr. John Storer is the Institutional Representative. This block diagram was included as Annex 6

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in the letter of January 17, 1977, from Dr. C. C. Lushbaugh to Dr. Roy Kinard. In view of the somewhat complex bi-institutional involvement, we determined that the best method to obtain the information you requested was for DOE to undertake this investigation and report the results directly to you.

I will address your questions in the order in which they appear in your letter of June 17, 1980.

1. "confirmation from the institution of the reported incidents, including whether or not IRB review of the activities took place and, if so, minutes of the review":

In the Spring of 1979, Dr. Thomas Slaga, a member of the Senior Staff at the Oak Ridge National Laboratory, did apply 12-O-tetradecanoyl phorbol 13-acetate (TPA) to a small area of his skin as did four other members of Dr. Slaga's research group. The application occurred only once, away from the Laboratory and during off-duty hours.

Prior to this exposure, no IRB review had occurred. Unfortunately, a formal investigation and report were not made at the time ORNL first learned of the exposure. We have already informed ORNL of our position that such an investigation should have been made immediately and the results reported to us promptly. Subsequently, Dr. Slaga did submit an application to the ORAU/ORNL Committee on Human Studies and the application was disapproved. Dr. Slaga's application and the Minutes of the Committee's review and related correspondence is contained in Enclosure 2.

2. "in the event that there had been no prior IRB approval, a report of any follow-up or corrective action taken by the institution including measures to prevent the recurrence of similar incidents":

Following a determination by the Director of the ORNL Biology Division that exposure to TPA had occurred without

prior IRB or Laboratory approval, Dr. Slaga was informed in the strongest possible terms that this was an unacceptable practice and its occurrence away from the Laboratory did not relieve Dr. Slaga of his professional responsibility. Dr. Slaga was again informed of ORNL policies with regard to human use experimental procedures which require that any proposed research involving human subjects be approved in advance by the ORAU/ORNL Committee on Human Studies. As indicated previously, Dr. Slaga did subsequently submit an application which was not approved.

As a result of this incident, all ORNL policies and procedures regarding human use experiments have been reviewed to insure that they could be reasonably expected to prevent any such future occurrence. Following this review, it has been emphasized to all ORNL Senior Research staff the importance of these procedures and their individual responsibility to see that all investigators and staff under their supervision are fully aware of the policies and adhere to them. Further, an additional administrative check has been introduced into the ORNL procedures.

3. "a statement of the institutional policy regarding IRB review of such activities and what is being done administratively to insure understanding of, and compliance with, the policy on the part of researchers":

As indicated above, the Oak Ridge National Laboratory is a Federally owned facility of the Department of Energy and must observe all regulations of the DOE and the other Federal agencies where they apply. The DOE regulations for "Protection of Human Subjects" (10 CFR, Part 745) conform to the Department of Health and Human Services' regulations and clearly require the Institutional Review Board review and approval of any activity involving human subjects. These regulations are covered at ORNL and ORAU by the "Implementing Guidelines for Research on Human Subjects", Enclosure 3. These guidelines are being updated to reflect the change from DHEW to HHS and from ERDA to DOE. Some other minor changes may also be made subject to review and approval of the Committee on Human Studies. When approved by the Committee, the revised guidelines will be promptly forwarded to you for your review.

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We have emphasized to ORNL Senior Management the importance of these regulations and their responsibility to see that they are fully complied with. Subsequently, one additional administrative check has been added to the ORNL procedures. All proposed research which has been reviewed and approved by the IRB must still be approved by the ORNL Institutional Representative before any such research activity can actually be initiated. We believe this additional decision point is administratively very useful in a Laboratory as large as ORNL.

4. "how the current institutional policies regarding use and handling of know carcinogenic and other hazardous materials adequately cover research involving human subject":

Prior to obtaining permission to work with any known carcinogenic or other hazardous materials, a research protocol must be submitted to the ORNL Biohazards Review Committee. This Committee functions similar to the Institutional Review Board and must review and approve the research proposed, determine that the Laboratory in which the material will be used meets all applicable safety standards and that the protocol clearly contains all procedures for handling, storage and disposal of the materials. Review and approval of the proposal for scientific merit must precede submission to the Biohazards Review Committee. The Minutes of the Biohazards Review Committee are reviewed by a professional member of the DOE staff. The DOE-Oak Ridge staff also conducts periodic occupational safety audits of the facilities used for such research to insure full compliance with all Federal regulations and standards.

If the Biohazards Review Committee approves the proposed research, it would then be submitted to the ORAU/ORNL Committee on Human Studies if human subjects were to be involved.

We have devoted considerable effort to providing the fullest possible answers to your letter request. I regret that it has taken so long and appreciate your patience. If you have suggestions or comments to improve these procedures, we would be most glad to receive them or to provide other information you might require.

Sincerely,



William R. Bibb, Director
Research Division

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Enclosures:

1. Committee Block Diagram
2. Application/Minutes
3. Guidelines

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