APPENDIX Y

MAY 1, 1987

LETTER FROM FRANK E. YOUNG, M.D., PH.D., COMMISSIONER OF FOOD AND DRUGS, FOOD AND DRUG ADMINISTRATION, TO WILLIAM MAYER, M.D., ASSISTANT SECRETARY OF DEFENSE FOR HEALTH AFFAIRS, DEPARTMENT OF DEFENSE

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

May 1, 1987

William Mayer, M.D.
Assistant Secretary of Defense
for Health Affairs
Department of Defense
Washington, D.C. 20301-1200

Dear Bud:

I am very pleased to be able to send you the Memorandum of Understanding (MOU) between the Department of Defense and the Food and Drugs Administration (FDA) concerning the investigational use of human drug products and medical devices by the DoD. Under the joint direction of FDA's Associate Commissioner for Health Affairs and DoD's Deputy Assistant Secretary of Defense for Health Affairs, agreement on the content of this MOU has been reached. I believe that this MOU serves as an excellent example of interagency cooperation which meets both the needs of national defense and health concerns.

I have approved and signed two copies of the MOU on behalf of the FDA and am forwarding them for your signature. After DoD acceptance and signature, please retain one copy and return the other for FDA's files.

With my best personal regards,

Sincerely yours,

Frank E. Young, M.D., Ph.D.
Commissioner of Food and Drugs

Enclosures

MEMORANDUM OF UNDERSTANDING

Between the

FOOD AND DRUG ADMINISTRATION

and the

DEPARTMENT OF DEFENSE

CONCERNING INVESTIGATIONAL USE OF
DRUGS, ANTIBIOTICS, BIOLOGICS, AND
MEDICAL DEVICES BY THE DEPARTMENT OF DEFENSE

I. PURPOSE

This agreement between the Department of Defense (DoD) and the Food and Drug Administration (FDA) establishes the procedures to be followed regarding the investigational use of drugs, including antibiotics and biologics, and medical devices by DoD. This Memorandum of Understanding (MOU), when signed by the representatives of the agencies, replaces the previous MOU on this subject signed in 1974.

II. BACKGROUND

Sections 505(a) and 507 of the Federal Food, Drug, and Cosmetic Act ("the Act") establish procedures for the approval required before a new drug or antibiotic can be introduced into interstate commerce. Sections 505(i) and 507(d) of the Act (21 U.S.C. 355(i), 357(d)) provide authority for the Secretary to exempt from the drug approval procedures new drugs and antibiotics which will be used for investigational purposes. Section 520(g) of the Act (21 U.S.C. 360(g)) provides authority for the Secretary to exempt from the device approval procedures devices which will be used for investigational purposes. Section 351 of the Public Health Service Act establishes procedures for the approval required before a biological product can be introduced into interstate commerce.

Regulations governing investigational new drugs, investigational antibiotics, and investigational biologics are published at 21 CFR 312; for investigational medical

devices at 21 CFR 812 and 813; for protection of human subjects at 21 CFR 50; and for institutional review boards at 21 CFR 56. These regulations establish the procedure and prescribe the necessary forms to be filed in order to exempt drugs and devices to be used for investigational purposes from, inter alia, the approval procedures of the Federal Food, Drug, and Cosmetic Act and the biologic licensing provisions of the Public Health Service Act.

Pursuant to Title 5, Section 301, of the United States Code, DoD regulations on protection of human subjects in DoD-supported research in 32 CFR Part 219 and DoD Directive 3216.2 generally adopt the system of Institutional Review Boards (IRBs) established under 21 CFR 56. However, the functions of research protocol review and approval are separate in the Department of Defense. The function of protocol review remains with the IRB which recommends approval. The function of approval is held by the commander to whom the review committee reports. In addition, the Surgeon General of each Service may require that the final review and approval for use of investigational drugs, biologics, or medical devices, remain within his or her office. The Surgeons General have the authority to delegate this final review and approval authority to a "Headquarters Review Board" (HRB), or the medical department component holding the IND or IDE. In no case can an approving authority or HRB give final approval to a protocol which has been disapproved by a local IRB, nor can an approving authority or HRB reduce safeguards or special conditions imposed by the local IRB.

A Memorandum of Understanding (MOU) on this subject was first executed by the Departments of Defense and Health, Education, and Welfare in 1964. It was revised in 1974 to state the procedures that would be followed to ensure that the requirements of the Federal Food, Drug, and Cosmetic Act and its implementing regulations are fully met without jeopardizing or impeding the requirements of national security. Experience in operating under these MOUs from 1964 to 1987 indicates that the DoD and FDA have a record of cooperation; that human subject concerns have been adequately addressed in DoD-sponsored studies; that the DoD has been able to carry out effectively its responsibilities for national security without compromising the intent of the above-cited statutes and regulations; and that certain exemptions, relieving the DoD from the need to meet the

ordinary requirements of the Investigational New Drug (IND) and Investigational Device Exemption (IDE) regulations are no longer necessary. Accordingly, the DoD and the FDA agree to the following new procedures concerning investigational use of drugs and devices by the DoD.

III. SUBSTANCE OF AGREEMENT

The FDA and the DoD agree that:

A. Clinical testing of investigational drugs, biologics, or medical devices under programs sponsored by the DoD and conducted either by the DoD within its own research facilities, or for the DoD by a contractor or grantee will follow the provisions of 21 CFR 312 or 21 CFR 812 governing the investigational use of new drugs and medical devices in human beings, and FDA's informed consent and Institutional Review Board regulations (21 CFR 50 and 21 CFR 56).

B. They will continue to cooperate in meeting the requirements of the Federal Food, Drug, and Cosmetic Act and its implementing regulations without jeopardizing the mission of the DoD. To accomplish this goal, they agree that an expeditious review of special DoD requirements to meet national defense considerations will be carried out by FDA. This review would consist of an FDA review of available data on a drug, biological, or device under IND or IDE to determine if stockpiling for future use, or use in an expanded military population is appropriate. When necessary, special reporting requirements would also be established by FDA.

C. It is the general policy of the DoD not to classify medical research and development. However, should it become necessary to classify for reasons of national security the clinical testing of a drug, biologic, or medical device that would normally fall under the provisions of 21 CFR 312 or 812, these studies will be handled under the special provisions of this MOU. The DoD will be solely responsible for determining the security classification of such research projects. If classified studies are required DoD will submit a classified IND or IDE application to be reviewed by

appropriate FDA personnel who hold the required security clearances. It will be the responsibility of the FDA to maintain an appropriate cadre of personnel who have security clearances. In the event that a request is made under the Freedom of Information Act for records concerning the research DoD has classified, FDA will refer such requests to DoD for processing and response under DoD regulations.

IV. NAME AND ADDRESS OF PARTICIPATING AGENCIES

A. Department of Defense
Washington, D.C. 20301

B. Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

V. LIAISON OFFICERS

A. Senior Program Specialist for Medical Research
Office of the Assistant Secretary of Defense
(Health Affairs)
Washington, D.C. 20301
Telephone: (202) 695-6800

B. Military Assistant for Medical and Life Sciences
Office of Under Secretary of Defense (Acquisition)
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C. Associate Commissioner for Health Affairs, HFY-1
(currently Stuart L. Nightingale, M.D.)
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857
Telephone: (301) 443-6143

VI. PERIOD OF AGREEMENT

This agreement becomes effective upon acceptance by both parties, and will remain in effect indefinitely. It may be amended by mutual written consent or terminated by either party upon a 30-day advance written notice.

APPROVED AND ACCEPTED FOR THE DEPARTMENT OF DEFENSE

By William Mayer M.D.

ASSISTANT SECRETARY OF DEFENSE (HEALTH AFFAIRS)

Date 21 May 1987

APPROVED AND ACCEPTED FOR THE FOOD AND DRUG ADMINISTRATION

By

COMMISSIONER FOOD AND DRUG ADMINISTRATION

Date May 1, 1987