[Use of human volunteers in experimental research by the Department of Defense]

PREPARED

STATEMENT

BY

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THE SURGEON GENERAL

DEPARTMENT OF THE ARMY

BEFORE THE

SUBCOMMITTEE ON INVESTIGATIONS

OF THE

ARMED SERVICES COMMITTEE

HOUSE OF REPRESENTATIVES

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BIOGRAPHICAL SKETCH OF WITNESS: Lieutenant General Richard R. Taylor, M.D., was born in Prairieburg, Iowa, on November 21, 1922. After completing premedical studies at the University of Chicago in 1944, he graduated in 1946 with a doctor of medicine degree.

General Taylor attended the Army Medical Department officer's basic course, after com pleting an internship at the Highland Alameda County Hospital, Oakland, California, in 1947. His first medical assignment was as a general medical officer at the Army-Nav General Hospital in Hot Springs, Arkansas. After attending the company grade medical officer's course, he completed his residency training at Letterman General Hospital in internal medicine and cardiology.

In 1953, General Taylor was assigned to Korea, first as Assistant Division Surgeon, then as Commander, 7th Medical Battalion, 7th Infantry Division, later serving as an interni at the Hemorrhagic Fever Center, 45th Evacuation Hospital. In 1955, General Taylor returned to the United States as a resident in pulmonary disease at Fitzsimons General Hospital and later became Chief, Non-TB Chest Disease Service.

In 1957, he became Commanding Officer, US Army Medical Research and Development Unit, Fitzsimons General Hospital.

Following a fellowship in tropical medicine at Louisiana State University in 1959, Gene Taylor became Chief, Biophysics and Astronautics Research Branch of the US Army Medi Research and Development Command. After successive staff assignments, he was named Deputy Commander of the Command in 1963.

September 1964 saw General Taylor serving as Staff Surgeon of the Joint US Military Assistance Group in Thailand and Command Surgeon of the Military Assistance Commanc Thailand. After attending the Army War College at Carlisle Barracks, Pennsylvania, he served in the Office of the Secretary of Defense as Chief, Biological and Medical Scier Division, Office of the Director of Defense Research and Engineering.

He served as Command Surgeon, Headquarters, Military Assistance Command, Vietnam, from 1969-70, where he was promoted to Brigadier General on October 1, 1969. In September 1970, he became Commanding General of the US Army Medical Research and Development Command. He was sworn in as the Deputy Surgeon General on March 1, 1973, and became The Surgeon General, US Army, on October 1, 1973.

He is certified by the American Board of Internal Medicine, and is a Fellow of both the American College of Physicians and the American College of Chest Physicians. He is a member of the American Medical Association, the Association of Military Surgeons of the US (Past President), and the New York Academy of Science.

His awards and decorations include the Distinguished Service Medal, the Legion of Merit with oak leaf cluster, the Bronze Star Medal, the Joint Services Commendation Medal with oak leaf cluster and the Army Commendation Medal with oak leaf cluster.

Mr. Chairman:

I am pleased to appear before you to review Department of Defense policies and procedures to protect the rights and welfare of human subjects of biomedical and behavioral research conducted under its sponsorship. I believe that your invitation was based upon a desire to know whether the Department of Defense has sponsored or is now sponsoring medical research which exposes human beings to unreasonable risks. I refer to the risks of death or likely permanent damage to the mind, personality, or physical well-being as a result of research. I assure you that Department of Defense policy prohibits research carrying this degree of risk as well as research on humans who have not given their free and informed consent. I believe that you also wish to know whether the Department of Defense meets current standards for conduct of research in human subjects. The Department of Defense and the military departments today follow standards for protection of research subjects which equal or exceed those followed by other Federal agencies and the medical community at large.

The basic Department of Defense policy governing medical experiments was promulgated by the Secretary of Defense on 26 February 1953 (Incl 1). This policy is based on the Nuremberg Code of 1947, which followed the war crimes trials (Incl 2). The Chief of Staff published an implementing Memorandum in 1953. The departmental regulations implementing the tightening Federal controls of studies using investigational drugs, use of volunteers in medical research, and clinical investigations are listed at Incl 3. Copies of these regulations are available to your staff.

Some impacts of these various regulations are that an individual participating as a subject is required to be fully informed of the nature, purposes, and the effects of the experimentation; he must give voluntary written informed consent without coercion; and he must be allowed to withdraw at any point from the experiment.

These basic moral, ethical, and legal principles, identified above, are common to the regulations of the military departments. The Department of Defense has demonstrated a continuing concern in this area and has reviewed the procedures and taken corrective action where it was needed.

In 1964, HEW and DOD entered into a Memorandum of Understanding related to new regulatory authority and responsibilities of the FDA concerning investigational drugs. This Memorandum and subsequent DOD Directives and service regulations established Investigational Drug Review Boards within the Offices of the Surgeons General. The boards provide professional review of proposed investigations with new drugs and biologicals. With these boards, the DOD was permitted certain exceptions from ordinary FDA review, including military requirements work which was classified, for reasons of national security. The DOD agreed to discuss its classified investigations of drugs periodically with FDA personnel who had proper security clearance and to report to FDA findings associated with such studies which FDA should be aware of to make a sound evaluation of non-classified studies proposed on the same or similar drugs.

In May 1974, the Army staff responsibility for research involving life sciences was transferred from the Army Research Office, Office of the Chief of Research and Development, to The Surgeon General. In July of 1974, the approval authority for all research involving human subjects in the Army, except for nuclear and chemical warfare related studies, was transferred from the Office of the Chief of Research and Development to The Surgeon General. Proposals for research with nuclear or chemical warfare agents are forwarded by The Surgeon General with recommendations on the medical aspects to the Secretary of the Army for approval.

In October 1974, The Surgeon General established the Human Use Review Office under the direction of the Assistant Surgeon General for Research and Development. The Human Use Review Office was charged with administering and coordinating activities of the Army Investigational Drug Review Board, the US Army Medical Research and Development Command Contract Review Board, and The Surgeon General's Human Use Committee and Clinical Investigation Committee to insure uniform application of ethical standards for human research studies conducted within or sponsored by the Army Medical Department and other Army agencies.

The Human Use Review Committee is the central Army processing point for all extramural and intramural human subjects research which require approval under provisions of Army Regulations. The staff includes a full time physician, two pharmacists with advanced training in pharmacology and a biostatistician. Legal advice is provided by attorneys in the Army Medical Research and Development Command. This medical,

scientific, and legal staff identifies problem areas and requests review by expert professional consultants, clarifications and/or revision before protocols are submitted to appropriate committees for review and recommendations to The Surgeon General. The Deputy Surgeon General has been delegated authority for final approval. The Human Use Review Office is the authorized channel through which Army investigators communicate with the Food and Drug Administration (FDA). The Army committees on human subjects research reviewed and made recommendations on over 300 research proposals during fiscal year 1975. Provisions for the protection of human subjects and the detailed content of consent agreements were the primary concern of the members. The careful review is reflected by the fact that a large number of proposals were disapproved or deferred pending revision of the consent procedures. The Human Use Review Office staff and committees apply the standards contained in current Department of Defense and Department of Health, Education, and Welfare (DHEW) regulations. For example, when the recent HEW moratorium on fetal research was promulgated, the files were searched to be sure such research was not being conducted within the Army Clinical Investigation Program. The Human Use Review committees have paid particular attention to special classes of subjects involved in Army research i.e. children, pregnant women, and prisoners, and have often required special consent procedures appropriate to a particular project.

Within the Army, increased emphasis has been placed on insuring that agencies outside the Army Medical Department follow the same high standards as those within it. We have insisted that other Army agencies interpret the language of AR 70-25

broadly to include all experiments which may expose participants to risk even though the project proponents may consider the testing to be primarily an operational examination of prototype machinery or equipment. If a test of a new uniform or vehicle, for example, may expose subjects to risks from heat stress, noise, or fumes, the protocol is examined in detail to be sure that the subjects are fully informed volunteers and to reduce risk as much as possible. A large amount of time and effort is often required to adequately review tests of this type since their uniquely military setting sometimes makes it difficult to distinguish clearly what tasks are reasonably "in the line of duty."

Scope of Department of Defense Research Involving Human Subjects

Within this context, I would like to discuss in broad terms the present Department of Defense research effort involving human subjects. Military missions expose troops to extremely diverse hazards and stresses, including "exotic" infections such as malaria and scrub typhus, great pressure variations, as in deep diving, and crash forces; and high and low velocity missile combat wounds. The effectiveness of even our most "automated" military systems still is intimately linked to proper human performance. The rising cost of defense manpower means that efforts to decrease non-effectiveness of military personnel are increasingly important. Within our military health care systems we must conserve the fighting strength, and maintain quality health care. It should not be surprising that a defense environment of this kind generates requirements for research and investigation which can only be met by the use of human subjects.

All Department of Defense work using human subjects is conducted to meet requirements of the Department of Defense. There are two main divisions of this work. First, and by far the largest, is the RDTE funded program. The second, and newer program is that of clinical investigations funded in operations and maintenance accounts.

The RDTE program is reviewed by the Director of Defense Research and Engineering and conducted by the Military Departments. Its requirements are generated by military unique needs of the Department of Defense and the Military Departments.

The Assistant Secretary of Defense (Health and Environment) is the DOD proponent of the clinical investigation program. The requirement for this program is generated by the Department of Defense mission of providing health care and training of medical personnel. The work here more nearly resembles civilian (university) research programs. Professional postgraduate medical training requires the experience of research or clinical investigation, while the opportunity to participate in clinical investigations remains an important career incentive. While the work may not be unique to the Military Departments, it is usually of considerable relevance and aimed at improving the care in military hospitals.

Some examples of military medical research are:

Casualty Care

a. Use of electrical anesthesia in surgery.

b. Tissue (bone) transplantation in the treatment of severe maxillofacial wounds.

Infectious Disease. This area is one of great importance and interest in the Department of Defense and accounts for the largest use of human subjects, chiefly in vaccine development.

a. Development and testing of a meningococcal meningitis vaccine to protect recruit populations.

b. Development and testing of new antimalarial drugs against malaria resistant to conventional medications.

Following tests for safety and effectiveness in experimental animals, humans must be involved initially in small and later larger scale tests.

Hazard Protection

Human testing of physiological techniques to improve tolerance to sustained high acceleration forces encountered in combat aircraft.

Evaluation of body heat loss encountered in cold-water diving in various protective suits.

This area of research is primarily performed by active duty military personnel who are skilled in operating in these unusual environments and who have volunteered for hazardous duty, for which they receive extra pay. This area of research is potentially the most hazardous of Department of Defense research and the one with the most highly trained subjects.

Defense Against Chemical Weapons

This research is conducted in service and under contract by Edgewood Arsenal, which is a part of the US Army Materiel Command. Research involving defense against chemical and biological weapons was authorized by the Secretary of the Army in 1953 and has been governed by Department of Defense and Army directives originally written in 1953 containing the language of the Nuremberg Code which I referred to earlier. This work was reviewed in open hearings before the House Committee on Science and Astronautics, 16 and 22 June 1959, and on several later occasions by Congressional Committees. The major research effort is involved with trying to find more effective antidote drugs to counteract chemical weapons that we know are in the arsenals of potential enemies. Many of the drugs that are used do temporarily affect performance and ability to do complex tasks but this is a side effect and not an intended purpose of using the drug. I am sure you may have many questions about the history of this type of research and I will do my best to answer them. I would like to point out, however, that no drug is tested if there is any suspicion from pre-chemical testing in animals that it will have serious adverse or long lasting effects. Furthermore, the review mechanisms applied to Edgewood have been tightened over the last two years so that protocols are reviewed by the Army Investigational Drug Review Board and Human Subjects Research Review Board and relevant Department of Defense and Food and Drug Administration regulations are followed. A case in point is the newly developed antidote called "TAB" which will replace the traditional atropine antidote carried by US Armed Forces. A meeting was held with the FDA in

November 1974 regarding the deployment of this new drug. Since that time, further clinical studies have been postponed pending submission of further data to FDA.

Other Work with Investigational Drugs

There is presently no classified work with investigational drugs being conducted in the Department of Defense. The large majority of this work has always been open and reported fully to the Food and Drug Administration. Presumably all use of investigational drugs in the Department of Defense is formally on file with the FDA and projects are subject to that agency's review before projects are begun. In addition to the 1974 meeting, mentioned above, representatives of the Food and Drug Administration reviewed the Medical Research activities at Edgewood Arsenal in 1967, pursuant to the HEW/DOD agreement, and a liaison visit by FDA was made to the Biomedical Laboratory, Edgewood Arsenal in 1972. More detailed information about Department of Defense research involving human subjects will be provided for the record. Historical information which you may desire will be promptly retrieved.

As you have heard, there is evidence that the sound ethical principles directed in past and present DOD regulations appear not always to have been followed, particularly in the 1950's. Where this has been true, I believe that the problem has not been lack of guidelines but lack of compliance with them. We all deplore any instances in which the welfare of human subjects was not properly protected. Procedures have been implemented that tighten control of this work so that the future will not provide more incidents. I assure you that no contract or in service projectscalling for experimentation upon human beings will be done in the future by

any part of the Department of Defense without the proper safeguards. In addition, action has been taken to insure that any participation in volunteer studies under the sponsorship of Fort Detrick or Edgewood Arsenal by service personnel will be carefully documented in individual medical records.

My aim has been to give you an overview of the subject. I assure you that when we ask people to assume any degree of risk as part of a Department of Defense medical or behavioral research project, we do it in the context of a long tradition of ethical responsibility. I believe our past efforts to protect subjects have been vigorous but we are always striving to improve.

SECRETARY OF DEFENSE
Washington

26 Feb 1953

MEMORANDUM FOR THE SECRETARY OF THE ARMY
SECRETARY OF THE NAVY
SECRETARY OF THE AIR FORCE

SUBJECT: Use of Human Volunteers in Experimental Research

1. Based upon a recommendation of the Armed Forces Medical Policy Council, that human subjects be employed, under recognized safeguards, as the only feasible means for realistic evaluation and/or development of effective preventive measures of defense against atomic, biological or chemical agents, the policy set forth below will govern the use of human volunteers by the Department of Defense in experimental research in the fields of atomic, biological and/or chemical warfare.

2. By reason of the basic medical responsibility in connection with the development of defense of all types against atomic, biological and/or chemical warfare agents, Armed Services personnel and/or civilians on duty at installations engaged in such research shall be permitted to actively participate in all phases of the program, such participation shall be subject to the following conditions:

a. The voluntary consent of the human subject is absolutely essential.

(1) This means that the person involved should have legal capacity to give consent; should be so situated as to be able to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress, over-reaching, or other ulterior form of constraint or coercion; and should have sufficient knowledge and comprehension of the elements of the subject matter involved as to enable him to make an understanding and enlightened decision. This latter element requires that before the acceptance of an affirmative decision by the experimental subject there should be made known to him the nature, duration, and purpose of the experiment; the method and means by

~~TOP SECRET~~

Encl 1

which it is to be conducted; all inconveniences and hazards reasonably to be expected; and the effects upon his health or person which may possibly come from his participation in the experiment.

(2) The concept of the human subject shall be in writing, his signature shall be affixed to a written instument setting forth substantially the aforementioned requirements and shall be signed in the presence of at least one witness who shall attest to such signature in writing.

(a) In experiments where personnel from more than one Service are involved the Secretary of the Service which is exercising primary responsibility for conducting the experiment is designated to prepare such an instrument and coordinate it for use by all the Services having human volunteers involved in the experiment.

(3) The duty and responsibility for ascertaining the quality of the consent rests upon each individual who initiates, directs or engages in the experiment. It is a personal duty and responsibility which may not be delegated to another with impunity.

b. The experiment should be such as to yield fruitful results for the good of society, unprocurable by other methods or means of study, and not random and unnecessary in nature.

c. The number of volunteers used shall be kept at a minimum consistent with item b., above.

d. The experiment should be so designed and based on the results of animal experimentation and a knowledge of the natural history of the disease or other problem under study that the anticipated results will justify the performance of the experiment.

e. The experiment should be so conducted as to avoid all unnecessary physical and mental suffering and injury.

f. No experiment should be conducted where there is an a priori reason to believe that death or disabling injury will occur.

g. The degree of risk to be taken should never exceed that determined by the humanitarian importance of the problem to be solved by the experiment.

h. Proper preparation should be made and adequate facilities provided to protect the experimental subject against even remote possibilities of injury, disability, or death.

i. The experiment should be conducted only by scientifically qualified persons. The highest degree of skill and care should be required through all stages of the experiment of those who conduct or engage in the experiment.

j. During the course of the experiment the human subject should be at liberty to bring the experiment to an end if he has reached the physical or mental state where continuation of the experiment seems to him to be impossible.

k. During the course of the experiment the scientist in charge must be prepared to terminate the experiment at any stage, if he has probable cause to believe, in the exercise of the good faith, superior skill and careful judgment required of him that a continuation of the experiment is likely to result in injury, disability, or death to the experimental subject.

l. The established policy, which prohibits the use of prisoners of war in human experimentation, is continued and they will not be used under any circumstances.

3. The Secretaries of the Army, Navy and Air Force are authorized to conduct experiments in connection with the development of defenses of all types against atomic, biological and/or chemical warfare agents involving the use of human subjects within the limits prescribed above.

4. In each instance in which an experiment is proposed pursuant to this memorandum, the nature and purpose of the proposed experiment and the name of the person who will be in charge of such experiment shall be submitted for approval to the Secretary of the military department in which the proposed experiment is to be conducted. No such experiment shall be undertaken until such Secretary has approved in writing the experiment proposed, the person who will be in charge of conducting it, as well as informing the Secretary of Defense.

5. The addresses will be responsible for insuring compliance with the provisions of this memorandum within their respective Services.

/signed/
C.E. WILSON

Copies furnished:
Joint Chiefs of Staff
Research and Development Board

NUREMBERG CODE*

1. The voluntary consent of the human subject is absolutely essential.

This means that the person involved should have legal capacity to give consent; should be so situated as to be able to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress, over-reaching, or other ulterior form of constraint or coercion; and should have sufficient knowledge and comprehension of the elements of the subject matter involved as to enable him to make an understanding and enlightened decision. This latter element requires that before the acceptance of an affirmative decision by the experimental subject there should be made known to him the nature, duration, and purpose of the experiment; the method and means by which it is to be conducted; all inconveniences and hazards reasonably to be expected; and the effects upon his health or person which may possibly come from his participation in the experiment.

The duty and responsibility for ascertaining the quality of the consent rests upon each individual who initiates, directs, or engages in the experiment. It is a personal duty and responsibility which may not be delegated to another with impunity.

2. The experiment should be such as to yield fruitful results for the good of society, unprocurable by other methods or means of study, and not random and unnecessary in nature.

3. The experiment should be so designed and based on the results of animal experimentation and a knowledge of the natural history of the disease or other problem under study that the anticipated results will justify the performance of the experiment.

4. The experiment should be so conducted as to avoid all unnecessary physical and mental suffering and injury.

5. No experiment should be conducted where there is an *a priori* reason to believe that death or disabling injury will occur; except, perhaps, in those experiments where the experimental physicians also serve as subjects.

6. The degree of risk to be taken should never exceed that determined by the humanitarian importance of the problem to be solved by the experiment.

Proper preparations should be made and adequate facilities provided to protect the experimental subject against even remote possibilities of injury, disability, or death.

8. The experiment should be conducted only by scientifically qualified persons. The highest degree of skill and care should be required through all stages of the experiment of those who conduct or engage in the experiment.

9. During the course of the experiment the human subject should be at liberty to bring the experiment to an end if he has reached the physical or mental state where continuation of the experiment seems to him to be impossible.

10. During the course of the experiment the scientist in charge must be prepared to terminate the experiment at any stage, if he has probable cause to believe, in the exercise of the good faith, superior skill, and careful judgment required of him that a continuation of the experiment is likely to result in injury, disability, or death to the experimental subject.

*Copied from Experimentation with Human Beingsby Jay Katz, Russell Sage Foundation, New York 1972.

June 2

CURRENT REGULATIONS

Army

AR 40-7	Use of Investigational Drugs in Humans and the Use of Schedule I Controlled Drug Substances, 4 Apr 75
AR 40-38	Clinical Investigation Program, 23 Feb 73
AR 70-25	Use of Volunteers as Subjects of Research, 15 Sep 74

Navy

BUMEDINST 6000.4B	Clinical Investigation Program, 15 Jan 75
BUMEDINST 6710.49D	Investigational Use of New Drugs in Human Beings, 9 Jul 73
SECNAVINST 3900.39	Use of Volunteers as Subjects in Research, Development, Test and Evaluation, 28 Apr 69

Air Force

AFR 169-6	Clinical Investigation, 26 Jun 74
AFR 169-8	Use of Human Test Subjects in the Medical Service, 19 Aug 74
AFR 80-33	Use of Volunteers in Aerospace Research, 28 Aug 69

Encl 3

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