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Faculty, Staff, and Student Guide to Research Involving Human Subjects

I. HISTORY OF THE HUMAN SUBJECTS PROTECTION SYSTEM

The modern story of human subjects protections begins with the *Nuremberg Code,* developed for the Nuremberg Military Tribunal as standards by which to judge the human experimentation conducted by the Nazis. The *Code* captures many of what are now taken to be the basic principles governing the ethical conduct of research involving human subjects. The first provision of the *Code* states that "the voluntary consent of the human subject is absolutely essential." Freely given consent to participation in research is thus the cornerstone of ethical experimentation involving human subjects. The *Code* further provides the details implied by such a requirement: capacity to consent, freedom from coercion, and comprehension of the risks and benefits involved. Other provisions require the minimization of risk and harm, a favorable risk/benefit ratio, qualified investigators using appropriate research designs, and freedom for the subject to withdraw at any time. Similar recommendations were made by the World Medical Association in its *Declaration of Helsinki: Recommendations Guiding Medical Doctors in Biomedical Research Involving Human Subjects*, first adopted by the 18th World Medical Assembly in Helsinki, Finland, in 1964, and subsequently revised by the 29th World Medical Assembly, Tokyo, Japan, 1975, and by the 41st World Medical Assembly, Hong Kong, 1989. The Declaration of Helsinki further distinguishes **therapeutic** from **nontherapeutic** research.

In the United States, regulations protecting human subjects first became effective on May 30, 1974. Promulgated by the Department of Health, Education and Welfare (DHEW),

those regulations raised to regulatory status NIH's Policies for the Protection of Human Subjects, which were first issued in 1966. These regulations established the Institutional Review Board as one mechanism through which human subjects would be protected.

In July of 1974, the passage of the National Research Act established the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. The Commission met from 1974 to 1978. In keeping with its charge, the Commission issued reports and recommendations identifying the basic ethical principles that should underlie the conduct of biomedical and behavioral research involving human subjects and recommending guidelines to ensure that research is conducted in accordance with those principles. The Commission also recommended DHEW administrative action to require that the guidelines apply to research conducted or supported by DHEW. The Commission's report that sets forth the basic ethical principles that should underlie the conduct of biomedical and behavioral research involving human subjects is titled *The* Belmont *Report*, and is discussed in depth below.

In 1981, in response to the Commission's reports and recommendations, both the Department of Health and Human Services (DHHS, formerly DHEW) and the Federal Drug Agency (FDA) promulgated significant revisions of their human subjects regulations. As Levine (1986) points out, these revisions "do not alter the general principles of IRB review as they had evolved over the preceding three decades. Rather, they are concerned with some of the details of what the IRB is expected to accomplish and some of the procedures it must follow" [p. 324].

The DHHS regulations are codified at Title 45 Part 46 of the Code of Federal Regulations. Those "basic" regulations became final on January 16, 1981, and were revised effective March 4, 1983, and June 18, 1991. The June 18, 1991, revision involved the adoption of the Federal Policy for the Protection of Human Subjects. The Federal Policy (or "Common Rule," as it is sometimes called) was promulgated by the 16 federal agencies that conduct, support, or otherwise regulate human subjects research; the FDA also adopted certain of its provisions. As is implied by its title, the Federal Policy is designed to make uniform the human subjects protection system in all relevant federal agencies and departments.

Additional protections for various vulnerable populations have been adopted by DHHS, as follows:

> Subpart B, "Additional Protections Pertaining to Research, Development, and Related Activities Involving Fetuses, Pregnant Women and Human in Vitro Fertilization" became final on August 8, 1975, and was revised effective January 11, 1978, and November 3, 1978.
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> Subpart C, "Additional Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects" became final on November 16, 1978.
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> Subpart D, "Additional Protections for Children Involved as Subjects in Research" became final on March 8, 1983, and was revised for a technical amendment on June 18, 1991.

FDA regulations on the protection of human subjects are codified at Title 21 Parts 50 and 56 of the Code of Federal Regulations. Part 50, which sets forth the requirements for

informed consent, became final on May 30, 1980, and was revised effective January 27, 1981, March 3, 1989, and June 18, 1991. Subpart C, which provides special protections for prisoners, was adopted on July 7, 1981; the effective date of Subpart C has been stayed until further notice. Part 56, which sets forth the provisions for institutional review boards, was adopted on January 27, 1981, with revisions to some sections effective February 27, 1981, March 3, 1989, and June 18, 1991.

Additional FDA regulations that are relevant to IRB review of research are Parts 312 (Investigational New Drug Application), 812 (Investigational Device Exemptions), and 860 (Medical Device Classification Procedures).

The President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research, which met from 1980 to 1983, produced numerous reports on various aspects of medical ethics and biomedical and behavioral research. Its mandate with respect to the protection of human subjects was, first, to review the federal rules and policies governing human subjects research, and second, to determine how well those rules were being implemented or enforced.

Several excellent sources trace the history of human subjects research and the development of the IRB system as a mechanism for the protection of human subjects. An account of the history of human subjects research and the human subjects protection system in the United States can be found in David J. Rothman's *Strangers at the Bedside: A History of How Law and Bioethics Transformed Medical Decision Making* and in Dennis Maloney's *Protection of Human Research Subjects*. Rothman details the abuses to which human subjects were exposed, culminating in Henry Beecher's 1966 article, "Ethics and Clinical Research," published in the *New England Journal of Medicine*, and ultimately contributing to the impetus for the first NIH and FDA regulations. Other equally useful sources include Robert J. Levine's *Ethics and Regulation of Clinical Research*, Joan E. Sieber's *Planning Ethically Responsible Research*, Robert M. Veatch's "Human Experimentation Committees: Professional or Representative?," and William J. Curran's "Government Regulation of the Use of Human Subjects in Medical Research: The Approaches of Two Federal Agencies."

A. The Belmont Report

On September 30, 1978, the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research submitted its report entitled "The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research." The Report, named after the Belmont Conference Center at the Smithsonian Institution where the discussions that resulted in its formulation were begun, sets forth the basic ethical principles underlying the acceptable conduct of research involving human subjects. Those principles, **respect for persons, beneficence**, and **justice**, are now accepted as the three quintessential requirements for the ethical conduct of research involving human subjects.

> **Respect for persons** involves recognition of the personal dignity and autonomy of individuals, and special protection of those persons with diminished autonomy.

Beneficence entails an obligation to protect persons from harm by maximizing anticipated benefits and minimizing possible risks of harm.

Justice requires that the benefits and burdens of research be distributed fairly.

The Report also describes how these principles apply to the conduct of research. Specifically, the principle of *respect for persons* underlies the need to obtain informed consent; the principle of *beneficence* underlies the need to engage in a risk/benefit analysis and to minimize risks; and the principle of *justice* requires that subjects be fairly selected. As was mandated by the congressional charge to the Commission, the Report also provides a distinction between "practice" and "research." The text of the *Belmont Report* (http://**www.med.umich.edu/irbmed/ethics/belmont/belmontr.htm**) is thus divided into two sections: (1) boundaries between practice and research and (2) basic ethical principles.

B. Boundaries Between Practice and Research

While recognizing that the distinction between research and therapy is often blurred, *practice* is described as "interventions that are designed solely to enhance the well-being of an individual patient or client and that have a reasonable expectation of success. The purpose of medical or behavioral practice is to provide diagnosis, preventive treatment, or therapy to particular individuals." Research is defined as systematic observation and data collection which is (1) intended for release to the scientific community as a contribution to knowledge or (2) portrayed (explicitly or implicitly) by university students, faculty, or staff as “research” or “experimental” investigation or (3) intended to fulfill requirements for a masters thesis, doctoral dissertation, or other research requirements of the university. If a proposed activity can be defined as “research” by one or more of these criteria, the protocol must receive the appropriate review by the DRC and be assigned a docket number by UT Martin’s ORGC. If a protocol activity cannot be defined as “research” by one or these criteria, then the protocol does not have to be reviewed by the DRC or UT Martin IRB. Examples of observation or data collection activities involving human participants that do not require departmental review committee or IRB review include:

- Data collection for internal departmental or other university administrative purposes (e. g., teaching evaluations, student evaluations, staff evaluations)
- Program evaluation carried out under independent contract for an external organization that is for their internal purposes only (i. e., no external reporting to any funding or public agency). Examples of program evaluation include: personnel studies, staff effectiveness studies, human cost benefit analysis, treatment effectiveness studies, or human engineering studies.

Course activities that involve the use of human participants, but have no connection of research beyond the instructional function preclude the need for certification or IRB review; **however, efforts that lead to presentation outside of the classroom, and/or the publicizing of the student-prepared documents in any manner are considered research.** If the investigator intends to use the data from such activities as the basis for a scientific contribution, or portrays the activities as “research” or “experiment,” then the activity will be considered research involving human participants

and will be subject to DRC review and possibly IRB review and must receive a docket number from UT Martin's ORGC. If the investigator intents to use the data for purposes of a maters thesis or required research project, then the activity will be considered research involving human participants and will be subject to DRC and possibly IRB review and must receive a docket number from UT Martin's ORGC.

C. Classroom-Related Activities

The collection of information from respondents for the purpose of class discussion or for the purpose of training in research or research methods does not require IRB review. In this situation, instructors are responsible for the protection of human subjects. The ORGC recommends that instructors who plan to have their students conduct research complete the IRB 101 training. Instructors will need to contact the ORGC, 881.7015, for instructions to access training. **Class-related projects that must be approved are**:

- All master's theses and research projects that involve human subjects
- All projects for which findings may be published or otherwise disseminated. **Since publication will require consent of the participants, it would be prudent to seek IRB review of the informed consent form and other project materials in advance if there is any chance of publication later.**
- Class-related projects for which the data collected are archived for any purpose other than administrative evaluations. For instance, if a student developed an exemplary plan and collects data that could be impressive enough that the instructor wants to use it as an example for subsequent projects, this would be archived and subject to IRB approval before it can be used. Without IRB approval, these data must be destroyed and cannot serve as an example.

D. Applying the Ethical Principles

1. Respect for Persons. Required by the moral principle of respect for persons (*see* definition, above), **informed consent** contains three elements: information, comprehension, and voluntariness.

b .Information: First, subjects must be given sufficient information on which to decide whether or not to participate, including the research procedure(s), their purposes, risks and anticipated benefits, alternative procedures (where therapy is involved), and a statement offering the subject the opportunity to ask questions and to withdraw at any time from the research. Responding to the question of what constitutes adequate information, the *Report* suggests that a "reasonable volunteer" standard be used: "the extent and nature of information should be such that persons, knowing that the procedure is neither necessary for their care nor perhaps fully understood, can decide whether they wish to participate in the furthering of knowledge. Even when some direct benefit to them is anticipated, the subjects should understand clearly the range of risk and the voluntary nature of participation." Incomplete disclosure is justified only if it is clear that: (1) the goals of the research cannot be accomplished if full disclosure is made; (2) the undisclosed risks are minimal; and (3) when appropriate, subjects will be debriefed and provided the research results.

b. Comprehension: Second, subjects must be able to comprehend the information that is given to them. The presentation of information must be adapted to the subject's capacity to understand it; testing to ensure that subjects have understood may be warranted. Where persons with limited ability to comprehend are involved, they should be given the opportunity to choose whether to participate (to the extent they are able to do so), and their objections should not be overridden, unless the research entails providing them a therapy unavailable outside of the context of research. [*See* discussions on this issue in other sections of the Guidebook]. Each such class of persons should be considered on its own terms (*e.g.*, minors, persons with impaired mental capacities, the terminally ill, and the comatose). Respect for persons requires that the permission of third persons also be given to protect them from harm.

c. Voluntariness: Finally, consent to participate must be voluntarily given. The conditions under which an agreement to participate is made must be free from coercion and undue influence. IRBs should be especially sensitive to these factors when particularly vulnerable subjects are involved.

2. Beneficence. Closely related to the principle of beneficence (*see* definition, above), **risk/benefit assessments** "are concerned with the probabilities and magnitudes of possible harms and anticipated benefits." The *Report* breaks consideration of these issues down into defining the nature and scope of the risks and benefits, and systematically assessing the risks and benefits. All possible harms, not just physical or psychological pain or injury, should be considered. The **principle of beneficence** requires both protecting individual subjects against risk of harm and consideration of not only the benefits for the individual, but also the societal benefits that might be gained from the research.

In determining whether the balance of risks and benefits results in a favorable ratio, the decision should be based on thorough assessment of information with respect to all aspects of the research and systematic consideration of alternatives. The Report recommends close communication between the IRB and the investigator and IRB insistence upon precise answers to direct questions. The IRB should: (1) determine the "validity of the presuppositions of the research;" (2) distinguish the "nature, probability and magnitude of risk...with as much clarity as possible;" and (3) "determine whether the investigator's estimates of the probability of harm or benefits are reasonable, as judged by known facts or other available studies."

Five basic principles or rules apply when making the risk/benefit assessment: (1) "brutal or inhumane treatment of human subjects is never morally justified;" (2) risks should be minimized, including the avoidance of using human subjects if at all possible; (3) IRBs must be scrupulous in insisting upon sufficient justification for research involving "significant risk of serious impairment" (e.g., direct benefit to the subject or "manifest voluntariness of the participation"); (4) the appropriateness of involving vulnerable populations must be demonstrated; and (5) the proposed informed consent process must thoroughly and completely disclose relevant risks and benefits.

3. Justice. The principle of justice mandates that the **selection of research subjects** must be the result of fair selection procedures and must also result in fair selection outcomes. The "justness" of subject selection relates both to the subject as an individual and to the subject as a member of social, racial, sexual, and to ethnic groups.

With respect to their status as individuals, subjects should not be selected either because the researcher favors them or because they are held in disdain (*e.g.*, involving "undesirable" persons in risky research). Further, "social justice" indicates an "order of preference in the selection of classes of subjects (*e.g.*, adults before children) and that some classes of potential subjects (*e.g.*, the institutionalized mentally infirm or prisoners) may be involved as research subjects, if at all, only on certain conditions."

Investigators, institutions, or IRBs may consider principles of distributive justice relevant to determining the appropriateness of proposed methods of selecting research subjects that may result in unjust distributions of the burdens and benefits of research. Such considerations may be appropriate to avoid the injustice that "arises from social, racial, sexual, and cultural biases institutionalized in society."

Subjects should not be selected simply because they are readily available in settings where research is conducted, or because they are "easy to manipulate as a result of their illness or socioeconomic condition." Care should be taken to avoid overburdening institutionalized persons who "are already burdened in many ways by their infirmities and environments." Nontherapeutic research that involves risk should use other, less burdened populations, unless the research "directly relate[s] to the specific conditions of the class involved."

E. Suggestions for Further Reading

- **Beauchamp**, Tom L., and Childress, James F. *Principles of Biomedical Ethics*, 3d ed. New York: Oxford University Press, 1989.
- **Beecher**, Henry K. "Ethics and Clinical Research." *New England Journal of Medicine* 274 (1966): 1354-1360.
- **Curran**, William J. "Government Regulation of the Use of Human Subjects in Medical Research: The Approaches of Two Federal Agencies." In *Experimentation with Human Subjects*, edited by Paul A. Freund, pp. 402-454. New York: George Braziller, 1970.
- **Fried**, Charles. Medical Experimentation: *Personal Integrity and Social Policy*. New York: American Elsevier Company, 1974.
- **Levine**, Robert J. *Ethics and Regulation of Clinical Research*. 2d ed. Baltimore: Urban and Schwarzenberg, 1986. *See* especially Chapter 14, "The Institutional Review Board."
- **Maloney**, Dennis M. *Protection of Human Research Subjects: A Practical Guide to Federal Laws and Regulations*. New York: Plenum Press, 1984.
- **McCarthy**, Charles R. "Experience with Boards and Commissions Concerned with Research Ethics in the United States." In *Research Ethics*, edited by Kare Berg and Knut Erik Tranoy, pp. 111-122. New York: Alan R. Liss, 1983.
- **McCarthy**, Charles R. "Current Regulations for the Protection of Human Subjects." In *Alzheimer's Dementia: Dilemmas in Clinical Research*, edited by Vijaya L. Melnick and Nancy N. Dubler, pp. 13-18. Clifton, NJ: Humana Press, 1985.

- **Marshall**, Ernest. "Does the Moral Philosophy of the Belmont Report Rest on a Mistake?" *IRB* 8 (No. 6, November/December 1986): 5-6.
- **Rothman**, David J. *Strangers at the Bedside: A History of How Law and Bioethics Transformed Medical Decision Making*. New York: Basic Books, 1991.
- **Rothman**, David J. "Ethics and Human Experimentation: Henry Beecher Revisited." *New England Journal of Medicine* 317 (No. 19, November 5, 1987): 1195-1199.
- **Sieber**, Joan E. *Planning Ethically Responsible Research: A Guide for Students and Internal Review Boards*. Applied Social Research Methods Series, vol. 31. Newbury Park, CA: Sage Publications, 1992.
- **Twenty Years After:** The Legacy of the Tuskegee Syphilis Study. *The Hastings Center Report* 22 (No. 6, November/December 1992): 29-40. Includes articles by Arthur L. Caplan, Harold Edgar, Patricia A. King, and James H. Jones.
- **U.S. National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research.** A complete list of the National Commission's reports and recommendations is provided in Appendix 1.
- **U.S. President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research.** A complete list of the President's Commission's reports is provided in Appendix 1.
- **Veatch**, Robert M. "Human Experimentation Committees: Professional or Representative?" *Hastings Center Report* 5 (No. 5, October 1975): 31-40.

II. INTRODUCTION

The University of Tennessee at Martin (UT Martin) is committed to the furthering of human understanding. Research is regarded as a major avenue leading to the advancement of such knowledge, especially when freedom of inquiry is available to investigators. Such freedom, however, must be earned through the conduct of research in a competent, moral, and responsible manner by investigators who not only hold to scientific values but also have the highest regard for the implications and consequences of their research on society and the individuals therein. At times, it is possible that the scientist's quest for knowledge may endanger the right and welfare of individuals; guaranteeing these rights must be a focus of constant concern and scrutiny. It is the investigator's responsibility to assess research procedures regularly to insure the protection of the individual and, when appropriate, to review them with associates and other responsible members of society.

With due regard for the freedom of inquiry, but with the highest regard for the safeguarding of individual rights and welfare, the following code and procedures are offered to serve as guidelines to be followed at UT Martin for all research. This research includes that conducted by University faculty, staff, or students, on or off campus, whether funded or not. Non-UT Martin personnel conducting research on the UT Martin campus must also follow these guidelines. To be effective, such guidelines will have to be flexible enough to allow for changes in our value systems and for those modifications that necessarily will be required with experience.

III. JURISDICTION OF THE INSTITUTIONAL REVIEW BOARD (IRB)

The IRB is an administrative body established to protect the rights and welfare of human research subjects recruited to participate in research activities conducted under the auspices of the institution with which it is affiliated. The IRB has the authority to approve, require modifications in, or disapprove all research activities that fall within its jurisdiction as specified by both the federal regulations and local institutional policy. Research that has been reviewed and approved by an IRB may be subject to review and disapproval by officials of the institution. However, those officials may not approve research if it has been disapproved by the IRB [Federal Policy §___.112].

The IRB also functions independently of, but in coordination with, other committees. For example, an institution may have a research committee that reviews protocols to determine whether the institution should support the proposed research. The IRB, however, makes its independent determination whether to approve or disapprove the protocol based upon whether or not human subjects are adequately protected.

Whenever the IRB reviews a protocol, an initial question is whether the IRB has jurisdiction over approval of the research. That is, the IRB must ask, "Is the research subject to IRB review?" The federal regulations apply "to all research involving human subjects conducted, supported, or otherwise subject to regulation by any federal department or agency" that has adopted the human subjects regulations [Federal Policy §___.101(a)].

The first two questions the IRB faces are whether the activity involves *research*, and second, whether it involves *human subjects*. These terms are defined under Section IX of this Guide. In addition, some research that involves human subjects may be **exempt** from the regulations requiring IRB review [Federal Policy §___.101(b)]. See Section XI of this Guide for discussion of exempt review.

Jurisdictional questions arise, however, in that the regulations also require that, as part of their Assurances, institutions agree to protect the welfare of all human subjects involved in research, whether or not the research is conducted or supported by a federal department or agency [Federal Policy §___.103(b)(1)]. While the regulations further specify that this requirement "need not be applicable to any research exempted . . . under §___.101(b)," many institutions' human subjects policies provide that all research, even research that is exempt from review under the federal regulations, is to be reviewed by the IRB. In such cases, the IRB has jurisdiction over all human subjects research, thereby providing broader protection for subjects than that required by the regulations. It is crucial that IRBs keep in mind that their authority to approve, require modifications in, or disapprove research derives from both federal law and institutional policy.

Research that has been reviewed and approved by an IRB may be subject to further review and disapproval by officials of the institution. Those officials, however, may not approve research if it has been disapproved by the IRB [Federal Policy §___.112]. Furthermore, approved research is subject to continuing IRB review and must be reevaluated at least annually (and more frequently, as specified by the IRB) [Federal Policy §___.109(e)].

Research versus Therapy. The fact that much biomedical research is conducted for evaluating new therapies or treatments leads to two problems for IRBs. The first is, to some degree, a problem of IRB jurisdiction; the second is a problem of risk/benefit assessment.

The distinction between **research and treatment** can become blurred in patient care settings as well as in some educational and training settings. This distinction raises questions of IRB jurisdiction over the research: *Is the proposed activity one that requires IRB review (pursuant either to federal regulations or institutional policy)?* Research itself is not therapeutic; for ill patients, research interventions may or may not be beneficial. Indeed, the purpose of evaluative research is to determine whether the test intervention is in fact therapeutic. The support of an activity by a research grant may sometimes provide a practical, if somewhat artificial, operational answer to the question of whether or not that activity is research. IRBs that review only activities whose review is mandated because of the source of funding (*e.g.*, by DHHS regulations 45 CFR 46), can be confident that the intent of the activity is research rather than therapeutic (although subjects may obtain some therapeutic benefit from the research). But an IRB that reviews all research, regardless of the source of support, may sometimes face questions about whether or not a particular activity performed with therapeutic intent is, therefore, research and should be reviewed. Or it may face the difficult question of whether a formal research **protocol** should be developed (and reviewed by the IRB) for a new or non-validated procedure that is being used for therapeutic purposes within the institution. IRBs should be prepared to play such a role; some prominent commentators have pointed out the dangers of allowing new procedures to come into widespread use without having been systematically validated in well-controlled trials.

The second distinction between **research and therapies** that may pose a problem for IRBs concerns risk/benefit assessments in research on therapies. Often, the risks of a study may seem justified by a therapy provided as part of the study. IRBs should determine, however, whether the anticipated therapeutic benefits would be available to persons who are not participating in a study that presents additional risks. Such benefits should not be used to justify risks presented by the research.

IV. STRUCTURE OF THE INSTITUTIONAL REVIEW BOARD (IRB) – CFR 45 §46.107

An Institutional Review Board (IRB) can have as many members as necessary for it to perform its duties effectively. Care should be taken, however, to ensure that it does not become so large that its management becomes cumbersome. The IRB shall be sufficiently qualified through the experience and expertise of its members, and the diversity of the members, including consideration or race, gender, and cultural backgrounds and sensitivity to such issues as community attitudes, to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects. In addition to possessing the professional competence necessary to review specific research activities, the IRB shall be able to ascertain the acceptability of proposed research in terms of institutional commitments and regulations, applicable law, and standards of professional conduct and practice. The IRB shall, therefore, include persons knowledgeable in these areas. If an IRB regularly reviews research that involves a vulnerable category of subjects (i. e., children, prisoners, pregnant women, or handicapped or mentally disabled persons), consideration

minutes should reflect whether these requirements have been met. Additionally, the IRB, in its discretion, may invite individuals with competence in special areas to assist in the review of issues that require expertise beyond or in addition to that available on the IRB. These individuals may not vote with the IRB.

The UT Martin IRB shall meet at a **regularly scheduled time** and place. This time and place will be published in the *Addenda* and on the RGC Web page by July 1 of each year, and Board members will be notified in writing and through email of the schedule. In the event that no IRB application is submitted for full review within 10 working days of the regularly scheduled meeting, the Authorized Institutional Official shall cancel the meeting and notify the IRB accordingly.

The **Expedited Review Board, composed of the IRB Chair and IRB Secretary**, shall review all protocols it can as expeditiously as possible, sending only protocols necessary for full Board review to the entire Board. It is proposed that an Expedited Review will take 10 – 12 days of receipt of the Application to review. Applications during the summer will take longer to review since many faculty do not teach on a regularly scheduled basis and are, therefore, not on campus.

The Board members shall be identified to the U.S. Department of Health and Human Services by name, earned degrees, if any, position or occupation, representative capacity, and by other pertinent indications of experience, sufficient to describe each member's chief anticipated contribution to Board deliberations [Federal Policy §§___.103(b)(3) and ___.115(a)(5)]. Any employment or other relationship between each member and UT Martin shall be identified (i. e., full-time employee, part-time employee, member of governing panel or board, paid consultant, unpaid consultant). Also, changes in Board membership shall be reported to the Department of Health and Human Services in such form and at such times as the Secretary may require [Federal Policy § __.103(a); 103(b)(3) and 115(a)(5)]

The UT Martin IRB is empowered to call in outside consultants and/or UT Martin faculty consultants and may utilize review subcommittees where it deems appropriate.

VI. RESPONSIBILITIES

A. Responsibilities of UT Martin

In accordance with federal guidelines for the protection of human subjects in research, UT Martin has established a university institutional review board (IRB) and departmental review committees (DRC) in those departments that would be more likely to conduct research utilizing human subjects. This review board and these departmental review committees review and approve research involving human subjects performed at UT Martin. Before any human subjects research can be conducted, UT Martin shall provide the department or agency a written **Assurance** that it will comply with the requirements of the Policy; the Assurance must be approved by the department or agency; and UT Martin shall certify to the department or agency head that the research has been reviewed and approved by an IRB established in accordance with the requirements of the Policy [Federal Policy §___.103]. Note, however, that the FDA does not require the submission and approval of an Assurance.

Specification of quality standards in the conduct of research is an important function of UT Martin's leadership. Insistence upon well-conceived and -conducted research is evident both in written policies and in actions of UT Martin officials. Research that is conducted so poorly as to be invalid exposes subjects and the institution to unnecessary risk. Approval procedures have been devised such that UT Martin supports only well-designed and properly executed research.

1. The Assurance. UT Martin as primarily an undergraduate institution would be more likely to be involved in behavioral research, but could be, at times, involved in biomedical research. The university has in place a set of principles and guidelines that govern the institution, its faculty, and staff, in the discharge of its responsibilities for protecting the rights and welfare of human subjects taking part in research conducted at, or sponsored by, UT Martin, regardless of the source of funding [Federal Policy §___.103(b)(1)]. Assurances applicable to federally supported or conducted research must, at a minimum, contain such a statement of principles, which may include an appropriate existing code, declaration, and/or statement of ethical principles as formulated by the institution. In the United States, most institutions cite *The* Belmont *Report*. Foreign institutions sometimes cite other codes, such as the *Declaration of Helsinki* (http://www.od.nih.gov/helsinki.php3).

This set of principles is in the form of a document that is readily available to all faculty, students, and/or staff who have need of it and can be a part of the staff or faculty manual. It is written in clear, concise, unambiguous language, understandable to its intended audience. This document can be accessed in hard copy from UT Martin's Office of Research, Grants, and Contracts, from the department chairs of each academic department, from the deans of each academic college, from each operating department/office on campus, and through the RGC web site (www.utm.edu/rgc).

2. Staff, Space, and Supplies. UT Martin will provide the IRB with sufficient meeting space and staff to support the IRB's review and record keeping duties [Federal Policy §___.103 (b) (2)]. Records will be kept in the Office of Research, Grants, and Contracts.

3. Communication. UT Martin's leadership assures that open channels of communication are maintained at all levels. It is important that staff, subjects, and other interested parties have a means of communicating information about the conduct of a research project directly to the appropriate institutional officials. It is vital that IRB members, department chairs, and other officials with responsibility for oversight of research have open and ready access to the highest levels of authority within the institution.

4. Record Keeping. UT Martin, or when appropriate the IRB, must prepare and maintain adequate documentation of IRB activities [Federal Policy §___.115]. In addition to the written IRB procedures and membership lists required by the Assurance process [Federal Policy §___.103], such documentation must include copies of all research proposals reviewed, minutes of IRB meetings, records of continuing review activities, copies of all correspondence between the IRB and investigators, and statements of significant new findings provided to subjects (as required by Federal Policy §___.116(b)(5)).

Minutes of UT Martin IRB meetings will be kept in sufficient detail to record the following information: attendance at each meeting; actions taken by the IRB; the vote on actions taken (including the number of members voting for, against, and abstaining); the basis for requiring changes in or disapproving research; and a written summary of the discussion of controverted issues and their resolution [Federal Policy §___.115 (a)(2)].

IRB records will be retained for at least three (3) years; records pertaining to research that is conducted will be retained for three (3) years after completion of the research. All records will be accessible for inspection and copying by authorized representatives of the department or agency supporting or conducting the research at reasonable times and in a reasonable manner [Federal Policy §___.115(b)].

The Office of Research, Grants, and Contracts at UT Martin shall maintain a file for each IRB application that contains the following: the original completed application with all required attachments, copies of any and all correspondence with the applicant including the authorization to conduct research and the IRB docket number, and originals of required forms (i. e., completion of research, changes in protocol/methods, continuation, etc.). The applicant shall maintain a file on his/her research with sensitive information kept under lock and key in his/her office. Correspondence authorizing the applicant to conduct the proposed research shall outline the responsibilities of the applicant for the data and any items pertaining to his/her research.

B. Institutional Procedures and Guidelines

1. **Federal Policy Requirements**. According to federal guidelines, as provided for in its **Assurance**, UT Martin has prepared written procedures and guidelines to be followed by the IRB when conducting its initial and continuing review of research, and for reporting its findings and actions to the investigator and the administration of UT Martin. The procedures provide guidance for determining which projects will require review more often than annually and which projects require verification from sources other than the investigator that no material changes have occurred since the last IRB review. The guidelines also delineate procedures for ensuring prompt reporting to the IRB, by the investigator, of proposed changes in a research activity. They must also provide procedures for ensuring that such changes in approved research, during the period for which IRB approval has already been given, may not be initiated without IRB review and approval except when necessary to eliminate apparent immediate hazards to the subject [Federal Policy §___.103(b)(4)].

UT Martin also has written procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, and the department or agency head of: (1) any unanticipated problems involving risks to subjects or others, or any serious or continuing noncompliance with the Federal Policy or the requirements or determinations of the IRB; and (2) any suspension or termination of IRB approval [Federal Policy §___.103 (b)(5)].

2. **The Authorized Institutional Official**. Within the institution there must be a point of responsibility for the oversight of research and IRB functions. This point should be an official of the institution who has the legal authority to act and speak for the institution, and should be someone who can ensure that the institution will effectively fulfill its research oversight function. UT Martin's Vice Chancellor for Academic Affairs has appointed the

Director of Research, Grants, and Contracts (in the role of Compliance Officer) as the institution's **Authorized Institutional Official**. The Director of RGC shall also vote in the selection of the chair of the IRB. Selection of appropriate personnel assures the protection of the rights and welfare not only of research subjects but also of UT Martin itself.

3. Other Institutional Personnel. Training new personnel is a basic responsibility of any institution. In facilities that conduct research, all personnel should be aware of the applicable institutional policies and mechanisms for the approval of research and for reporting problems with research projects in progress. Personnel involved in the conduct of research should receive additional training in institutional expectations and specific regulations pertaining to research. Training designed to enhance the development of high quality proposals should be encouraged. **IRB members and others charged with responsibility for reviewing and approving research should receive detailed training in the regulations, guidelines, and policies applicable to human subjects research.** Attending workshops and other educational opportunities focused on IRB functions are encouraged and supported to the extent possible. Training in good research practices and in methods for minimizing risk shall be provided to all faculty, students, and staff involved with research utilizing human subjects. Since research conducted by others may have a bearing on research projects conducted by or at the institution, journals and other research-related materials should be available to staff. The UT Martin Office of RGC will provide continual training and updated materials for the utilization of human subjects in research on an annual basis.

4. Internal Audits. Internal audit procedures assure UT Martin's administration that its policies and procedures are being adhered to and that they are proper in scope and content. Evaluation of activities and functions is an accepted management tool, and the monitoring of institutional high- risk areas such as research is good policy. Audits allow the early identification and correction of problems. UT Martin ensures that reporting of noncompliance is accomplished and that appropriate follow-up measures are taken [Federal Policy §___.103].

5. Points to Consider

a. Do institutional policies comply with applicable regulations and promote appropriate review and approval?

b. Are the relevant institutional channels of communication sufficiently open?

c. Do adequate procedures for monitoring research and conducting audits of the research process exist?

d. Does the institution adequately provide for the training of personnel in policies and procedures related to research with human subjects?

e. Does the institution support educational activities related to the design, conduct, and approval of research?

6. Applicable Laws and Regulations

Federal Policy §___.101 [To what does this policy apply?]
Federal Policy §___.102 [Definitions]
Federal Policy §___.103 [Assuring compliance with this policy C research conducted or supported by any federal department or agency]
Federal Policy §___.107 [IRB membership]
Federal Policy §___.108 [IRB functions and operations]
Federal Policy §___.109 [IRB review of research]
Federal Policy §___.110 [Expedited review procedures]
Federal Policy §___.111 [Criteria for IRB approval of research]
Federal Policy §___.112 [Review by institution]
Federal Policy §___.115 [IRB records]
21 CFR 50 [FDA: Protection of human subjects (informed consent)]
21 CFR 56 [FDA: Institutional review boards]
34 CFR 97 [ED: Protection of human subjects]
34 CFR 350.3 [ED: What regulations apply to these programs (IRB membership)]
34 CFR 356.3 [ED: What regulations apply to these programs (IRB membership)]

C. Responsibilities of the Investigator/Researcher

The qualifications of the principal investigator should be considered when reviewing proposals. The investigator's professional development should be taken into account and related to the degree of protocol complexity and risk to human subjects. IRBs may require less experienced research investigators to be sponsored by seasoned researchers. Proposals that require skills beyond those held by the principal investigator should be modified to meet the investigator's skills, have additional qualified personnel added, or be disapproved. While the Institutional Review Board (IRB) acts as the official review board, the investigator is not relieved of personal and ethical responsibility for the design and conduct of the research as it may affect the welfare of subjects involved. In addition to complying with the formal procedures for obtaining approval of a project by IRB, each investigator must:

1. be thoroughly familiar with ethical guidelines for conduct or research utilizing human subjects and comply with these guidelines both in fact and spirit;
2. be sensitive to ethical considerations related to his/her research which may not be specifically covered by the guidelines;
3. follow the established University procedures, along with those recommendations for alterations in procedure by the IRB which were given as part of the conditions of acceptance of the proposed project;
4. bring to the attention of the IRB any alterations in procedure which might conceivably have some relation to the rights or welfare of human subjects;
5. bring to the attention of the IRB during any phase of any project problems (e. g., adverse reactions to drugs or medical devices) for further disposition by the IRB and for reporting to the Department of Health and Human Services; and
6. submit a **Change and/or Termination Form** (see Appendix F), as required by the IRB.

Research investigators shall prepare protocols giving **complete descriptions of the proposed research.** The research plan must include provisions for the adequate protection of the rights and welfare of prospective subjects and ensure those pertinent laws and regulations are observed. Samples of informed consent documents must be included with protocols. Research investigators are responsible for obtaining informed consent and

Federal Policy §___.119 [Research undertaken without the intention of involving human subjects]

D. Responsibilities of the Office of Research, Grants, and Contracts (RGC)

1. UT Martin's Office of Research, Grants, and Contracts (ORGC) is responsible for determining if the research protocols qualify for **Exemption** from continuing review under the *Common Rule* regulations. If **Exempt**, the researcher will be notified in writing and no further reports are required except where changes in procedure arise. All nonexempt research protocols will be forwarded to the Expedited Review Committee of the IRB if they qualify for **Expedited** review under the regulations, or to the full IRB if they do not so qualify.

2. All appeals of IRB decisions shall be submitted to the ORGC for forwarding to the IRB for reconsideration.

3. The ORGC will report information, as appropriate, to the IRB; the Office of Protection from Research Risks (OPRR); and the Department of Health and Human Services (DHHS); research investigators; and department chairs.

E. Responsibilities of the UT Martin Institutional Review Board (IRB)

The **UT Martin IRB** (see Section V of this Guide for structure of IRB) is an administrative body established to protect the rights and welfare of human subjects recruited to participate in research activities conducted under the auspices of the institution with which it is affiliated. The IRB has the authority to approve, require modifications in, or disapprove all research activities that fall within its jurisdiction as specified by both the federal regulations and local institutional policy. The IRB is not concerned with a researcher's choice of topic, research design, methodology, and controls except as they have a bearing on (1) the rights or welfare of the subjects involved or (2) on an assessment of the potential benefits to society in studies posing a definite risk to the subjects. The review responsibilities of the IRB are to:

1. meet as a Board with at least a quorum present and approve or disapprove with or without specified modifications the applications brought to it. A quorum of the Board shall be defined as a majority of the total membership duly convened to carry out the Board's responsibilities under the terms of the **Assurance**. As necessary, the Board will arrange to have qualified consultants with special competencies relevant to the proposal participate in the review. Approval shall be contingent upon assurance that the risks are kept to an absolute minimum and that any risks are clearly outweighed by the potential benefits. The Board, at its discretion, may invite the principal investigator (and the supervisor in the case of supervised research activities) to be present at the meeting so that any modifications in procedure to protect subjects can be worked out directly between the Board and the investigator.

2. offer consultation and advice on safeguarding the rights and welfare of human subjects;

3. review requests for exceptions or modifications to any University policy and procedures on research with human subjects;

4. periodically review certain projects, when the Board deems review appropriate, with the principal investigator and collect annually a Review Statement for all projects involving human subjects to assure procedural compliance. With respect to the latter, each investigator must submit a **Change and/or Termination Form (Appendix F)** on an annual basis and at the completion or termination of the project. This form can be obtained from the Office of Research, Grants, and Contracts or may be accessed online at the RGC web site. If in the judgment of the IRB Chair some problem may exist, the responsible investigator will be asked to appear before the Board for a comprehensive review; and

5. keep records and maintain a file of all projects reviewed for a period of at least three (3) years following completion of the project. All records shall be accessible for inspection and copying by authorized representatives of the federal government, or the IRB or ORGC, at reasonable times and in a reasonable manner.

VII. APPEALS

Researchers or investigators may appeal a decision of the IRB by presenting additional material to or requesting an appearance before the Board. All appeals should be submitted in writing to the IRB in care of UT Martin's Office of Research, Grants, and Contracts.

VIII. NONCOMPLIANCE BY INVESTIGATORS, INSTITUTIONAL REVIEW BOARDS, AND INSTITUTIONS

A. Investigators

Research investigators are the most frequent source of noncompliance with human subjects regulations. The most common lapses in investigator compliance include:

1. unreported changes in protocols,

2. misuse or nonuse of the informed consent document, and

3. failure to submit protocols to the IRB in a timely fashion. Problems such as these are often caused by communication difficulties. With investigator goodwill, these cases can be resolved by the IRB without jeopardizing the welfare of research subjects.

Occasionally, an investigator will either avoid or ignore an IRB. Such cases present a more serious challenge to the IRB and to the institution. Regardless of investigator intent, unapproved research involving human subjects places those subjects at an unacceptable risk. When unapproved research is discovered, the IRB and the institution should act promptly to halt the research, assure remedial action regarding any breach of regulatory or institutional human subject protection requirements, and address the question of the investigator's fitness to conduct human subject research. Beyond the obvious need to protect the rights and welfare of research subjects, the credibility of the IRB is clearly at stake. In addition, any serious or continuing noncompliance with DHHS human subjects regulations or the determinations of the IRB **must be promptly** reported to the Office of Human

Research Protections (OHRP) or the department or agency head [Federal Policy §___.103(b)(5)].

B. Institutional Review Boards

IRB noncompliance occurs whenever the IRB deviates from the duties imposed upon it by the federal regulations. Such deviations include:

1. the inadequate review of research protocols by failing to ensure that the consent document and process provide sufficient information to allow prospective subjects to make an informed decision whether to participate in the research;

2. failing to ensure that the research design includes adequate monitoring of the data and any additional safeguards necessary to protect the welfare of particularly vulnerable subjects; and

3. failing to conduct continuing review of research at intervals appropriate to the degree of risk.

4. failing to maintain adequate records of IRB business, and

5. failing to hold their meetings with a majority of members present, including a nonscientific member.

A demonstrated inability to carry out IRB responsibilities in accordance with DHHS regulations can be cause for the suspension or withdrawal of approval of an institution's Assurance.

C. Institutions

Although institutions are accountable for the actions of individual investigators and the IRB, institutional noncompliance is more broadly described as a systemic failure of the institution to implement practices and procedures contained in the institution's Assurance. Prime examples are (1) the failure of the institution to ensure that the IRB is appropriately constituted and functions in accordance with the regulations, (2) that the IRB receives appropriate institutional support and staffing, and (3) that investigators meet their obligations to the IRB. Systemic failure to abide by the terms and conditions of an institution's Assurance will result in withdrawal of approval of the Assurance.

D. Applicable Laws and Regulations

Federal Policy for the Protection of Human Subjects

21 CFR 56.108(b) [FDA: IRB functions and operations]
21 CFR 56.120-124 [FDA: Administrative actions for noncompliance]

Federal Register 56 (June 18, 1991): 28026 [FDA]

45 CFR 46.103 [DHHS: Assuring compliance with this policy]
45 CFR 46.123 [DHHS: Early termination of research support]

IX. DEFINITION OF TERMS

A. **Research** means a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge [Federal Policy §___.102 (d)]. Activities that meet this definition constitute "research" for purposes of these regulations, whether or not they are conducted or supported under a program that is considered research for other purposes. For example, some "demonstration" and "service" programs may include research activities. Classroom activities may also include research activities. Contact UT Martin's Office of Research, Grants, and Contracts if you are not certain if your activity fits the *research* definition.

1. **Educational Considerations**

a. Research Methods Instruction: Course activities that involve the use of human participants, but have no connection with research beyond the instructional function preclude the need for certification or IRB review. **However, efforts that lead to presentation outside the classroom and/or publicizing of the student-prepared documents in any manner are considered research**.

If the investigator intends to use the data from such activities as the basis for a scientific contribution, or portrays the activity as "research" or "experimentation," then the activity will be considered research involving human participants and will be subject to **Departmental Review Committee** (DRC) and possibly UT Martin IRB review. If the investigator intends to use the data for purposes of a master's thesis or doctoral dissertation, then the activity will be considered research involving human participants and will be subject to DRC and possibly IRB review.

b. Classroom-Related Activities: The collection of information from respondents for the purpose of class discussion or for the purpose of training in research or research methods does not require IRB review. In this situation, instructors are responsible for the protection of human subjects.

Class-related projects that must be approved:

- ✓ All master's theses that involve human subjects.
- ✓ All projects for which findings may be published or otherwise disseminated. Since publication will require consent of the participants, it is prudent to seek IRB review of the informed consent form and other project materials in advance if there is any chance of publication later.
- ✓ Class-related projects for which data collected are archived for any purpose other than administrative evaluations.

B. **Minimal Risk** means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

C. A **Human Subject** means a living individual about whom an investigator (whether professional or student) conducting research obtains (1) data through intervention or

interaction with the individual, or (2) identifiable private information. "Intervention" includes both physical procedures by which data are gathered (e. g., venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes. "Interaction" includes communication or interpersonal contact between investigator and subject. "Private information" includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects. [Federal Policy §___.102(f)].

D. Informed Consent means that except as provided elsewhere in this policy, **no investigator may involve a human being as a subject in research covered by this policy unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative.** An investigator shall seek such consent only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence. A minor under age 18 may refuse to participate in the research even if the minor's legally-authorized representative (parent or guardian) has given permission for the minor to participate. The information that is given to the subject or the representative shall be in language understandable to the subject or the representative; in addition, minors must be informed about the research in language they can comprehend and asked if they want to participate in the research. No informed consent, whether oral or written, may include any exculpatory language through which the subject or the representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution, or its agents from liability for negligence (see Section X.C.3. in this Guide – The Basic Elements of Consent - for indepth discussion of Informed Consent.). **Appendix C** provides an example of Informed Consent.

E. Assent is a child's affirmative agreement to participate in research. Assent is an ethical concept. However, failure to object cannot be construed as assent [45 CFR, 46.402(b)]. Researchers who include children in their research should be especially mindful of the rights of children participating in their research. Even when assent is not required, researchers are asked to demonstrate a good- faith effort to enlist the cooperation of children who participate in their research **(see Appendices D and E for examples of a Minor Assent Document)**.

It is the responsibility of the IRB to decide if researchers should seek a child's assent as apart of a project's consent procedure. The determination of a child's capacity to provide assent is based on the nature of the research, and the child's age **(typically the IRB requires assent from children age 7 and older)**, maturity, and psychological state of the population of children from whom participants will be drawn. The decision to require assent depends on the capacity of the children to appreciate the nature, extent, and probably consequences of their participation in a research project.

Assent is especially important in cases where there is no direct benefit to the child – participants. When assent is required, the procedure must include an explanation of the

proposed research in language that is appropriate to the child's age and maturity. The investigator must indicate on his/her Application to the University of Tennessee, Martin Institutional Review Board for the Protection of Human Subjects in Research what the children will be told about the research and how the information will be conveyed. The investigator must discuss how the information provided might vary with the age, maturity, and level of experience of the children involved in the study. The assent process should be free from coercion and unfair inducements. All children who are capable of providing assent must be informed that they are free to withdraw from participation at any time.

F. Permission is the explicit agreement of parent(s) or guardian to the participation of their child or ward in research. Failure to object or other forms of passive permission cannot be constituted as permission [45 CFR, 46.402(c)]. Both parents must give their permission in any research that places the child-participant at greater than minimal risk [45 CFR, 46.406 and 46.607], unless one parent is deceased, unknown, incompetent, not reasonably available, or when only one parent has legal responsibility for the case and custody of the child [45 CFR, 46.408(b)]. Further, permission of one parent is sufficient for any research that places that child-participant at no more than minimal risk [45 CFR, 46.404]. When permission is required, the information contained in the permission procedure should include all the elements normally required in an informed consent (see Section X.C. in this Guide for discussion of Informed Consent).

G. Guardian is an individual who is authorized under applicable state or local law to give permission for a child [45 CFR, 46.402(3)].

H. A person **cognitively impaired** is one who has either a psychiatric disorder (*e.g.*, psychosis, neurosis, personality or behavior disorders), an organic impairment (*e.g.*, dementia), or a developmental disorder (*e.g.*, mental retardation) that affects cognitive or emotional functions to the extent that capacity for judgment and reasoning is significantly diminished. Others, including persons under the influence of or dependent on drugs or alcohol, those suffering from degenerative diseases affecting the brain, terminally ill patients, and persons with severely disabling physical handicaps, may also be compromised in their ability to make decisions in their best interests.

I. Competence is technically, a legal term, used to denote capacity to act on one's own behalf; the ability to understand information presented, to appreciate the consequences of acting (or not acting) on that information, and to make a choice. Competence may fluctuate as a function of the natural course of a mental illness, response to treatment, effects of medication, general physical health, and other factors. Therefore, mental status should be re-evaluated periodically. As a designation of legal status, competence or incompetence pertains to adjudication in court proceedings that a person's abilities are so diminished that his or her decisions or actions (*e.g.*, writing a will) should have no legal effect. Such adjudications are often determined by inability to manage business or monetary affairs and do not necessarily reflect a person's ability to function in other situations.

J. An **institution** is defined as a residential facility that provides food, shelter, and professional services (including treatment, skilled nursing, intermediate or long-term care, and custodial or residential care). Examples include general, mental, or chronic disease hospitals; inpatient community mental health centers; halfway houses and nursing homes; alcohol and drug addiction treatment centers; homes for the aged or dependent, residential

schools for the mentally or physically handicapped; and homes for dependent and neglected children.

K. **Secretary** means the Secretary of Health and Human Services and any other officer or employee of the Department of Health and Human Services to whom authority has been delegated.

L. **DHHS** means the Department of Health and Human Services.

M. **Prisoner** means any individual involuntarily confined or detained in a penal institution. The term is intended to encompass individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing.

N. **Minimal risk** is the probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons.

X. ETHICAL CONSIDERATIONS

A. Protection of Individual Rights

1. Only qualified investigators should conduct research or by others only where a close supervisory relationship exists and is maintained with qualified individuals. Should an investigator become involved in areas that extend beyond his/her level of competence, appropriate consultation must be obtained.

2. Each research project must be evaluated in terms of its potential benefit to the subject and to society as well as in terms of its potential risk to the emotional and physical welfare of the subjects. Where risk is involved, or where information obtained is of a private nature, extra protection must be afforded the subject. Every effort should be made to minimize the risks or discomfort entailed in the subject's participation.

3. The investigator assumes responsibility for the procedures used throughout the course of the investigation. **It is the investigator's responsibility to report to the IRB for project review any planned changes in format or procedures from those originally approved. A Change and/or Termination Form must be filed** (see Appendix F in this *Guide*). Should problems or harmful effects arise out of the experimental procedures, such responsibility would continue until the problem or effect is removed or until the subject is referred to an appropriate professional who has assumed responsibility for the subject.

4. The investigator must not only take any immediate steps required to undo harmful effects but must also initiate appropriate follow-up procedures to detect unpredicted harm if the study presents a potential to produce harm that may only manifest itself later.

5. The investigator must be sensitive to individual factors that may predispose certain individuals to experience enduring harmful psychological or physical consequences from participation in the study and to exclude such individuals from the research sample.

6. The investigator is **obligated** to keep the subject's data in confidence. This includes keeping the data in confidence from relatives, friends, employers, school officials, and from other professional associates of the investigator unless: (a) the subject or an authorized representative consents to disclosure, or (b) regulations of the Secretary of the Department of Health and Human Services so provide, or (c) as otherwise required by law. It is the investigator's responsibility to report to the IRB how the data will be used and any subsequent changes in use.

7. Where information about private or personal matters is obtained from the subject for scientific purposes, the subject must be properly informed of how such information will be used, who will or might have occasion to examine such information, and how it might affect his/her future, including his/her civil rights. The subject must be advised that at any point he/she may withdraw from the experiment without penalty.

8. Where feasible, any private information obtained from a subject should be obtained anonymously or, if this is not possible, it should be immediately coded with care taken to keep the code separate from the data and in a secure place.

9. At the completion of the experiment, the investigator has the **obligation** to remove any misconceptions acquired by the subject, whether deliberately created or developed as an accidental byproduct of the procedure.

10. Whenever possible, subjects should receive something of value for their participation. This benefit may be material (e. g., money, gifts, etc.) or educational (e. g., information, self-knowledge, etc.).

11. When the methodological requirements of research lead some subjects to experience failure or require the withholding of a potentially beneficial program or treatment from control subjects, the investigator must, insofar as possible, provide these subjects with a beneficial experience when the experiment is concluded.

12. It is unacceptable to intentionally cause a research subject to suffer embarrassment, fear, anxiety, or loss of self-esteem. Such research may be justified only when (a) the research objectives can be realized in no other way, and (b) the suffering of the research subject is limited in degree and duration to that minimum required to accomplish the research objectives.

13. An individual has the right to control any use of his/her person. Where a condition or circumstance exists which interferes with the right to freely control the use of his/her person, special precautions must be instituted to safeguard his/her rights and welfare.

14. It is incumbent upon the investigator to make sure that all subjects are treated with respect and dignity, and that the subjects are not imposed upon for the convenience of the researcher.

15. Rather than adopting an ethical code, the University encourages researchers to follow the ethical codes established by their disciplines. Ethical codes or statements of principles established by the American Psychological Association, American Dental Association, American Sociological Association, and the World Medical Association will be referred to when appropriate to the conduct of the research.

B. Participant Data and Identity Confidentiality Considerations

Whenever researchers promise participants that their responses and data will be maintained in confidence, all research project members (investigators, directors, transcribers, students, and staff) are **required** to prevent accidental and intentional breaches of confidentiality. In most cases, confidentiality can be assured by following simple practices (e. g., substituting codes for identifiers, removing survey cover sheets that contain names and addresses, limiting access to identified data, and/or storing research records in a locked cabinet). However, all measures used to assure confidentiality of data need to be understood by all research staff before research is initiated, and followed once research is initiated. Confidentiality procedures **must be described** in research applications that come before the UT Martin IRB.

Researchers should recognize that the assurance of confidentiality includes keeping the identity of participants confidential. Researchers proposing projects that will address sensitive, stigmatizing, or illegal subjects must explicitly outline the steps they will take to assure any information linking participants to the study is maintained in confidence. The requirement of signed consent forms is often waived in sensitive studies, if the consent document is the only written record linking participants to the project **and** a breach of confidentiality presents the principal risk of harm anticipated in that research.

If there is any chance that data or participants' identities might be sought by law enforcement agencies or subpoenaed by a court, a **grant of confidentiality** should be obtained. Under federal law (Public Health Act § 301(d)), researchers, prior to the initiation of the research project, may request grants of confidentiality to protect against forced data and participant identity disclosures. These grants provide protection for specific research projects where protection is judged necessary to achieve the research objectives.

To take advantage of § 301(d), the investigator must request a grant of confidentiality from the appropriate official. Protection for research on mental disorder or the use and effect of alcohol and other psychoactive drugs can be obtained from the National Institute on Alcohol Abuse and Alcoholism (NIAAA), the National Institute on Drug Abuse (MIDA), or the National Institute of Mental Health (NIMH). Certificates for confidentiality for biomedical, behavioral, clinical, or other research that does not fall into these categories are issued by the Assistant Secretary of Health. A more complete discussion of § 301(d) can be found at the OHRP website (www.hhs.gov/ohrp/humansubjects/guidance).

C. Informed Consent

A subject's participation in research should at all times be voluntary on the basis of informed consent. It is incumbent upon the investigator to provide the subject with all information about the study that is likely to bear upon the subject's willingness to participate.

No informed consent, whether oral or written, may include any exculpatory language through which the subject is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution, or its agents from liability for negligence. --- 45 CFR 46.116

Examples of Exculpatory Language:

- By agreeing to this use, you should understand that you will give up all claims to personal benefit from commercial or other use of these substances.
- I voluntarily and freely donate any and all blood, urine, and tissue samples to the U.S. Government and hereby relinquish all right, title, and interest to said items.
- By consent to participate in this research, I give up any property rights I may have in bodily fluids or tissue samples obtained in the course of the research.
- I waive any possibility of compensation for injuries that I may receive as a result of participation in this research.

Examples of Acceptable Language

- Tissue obtained from you in this research may be used to establish a cell line that could be patented and licensed. There are no plans to provide financial compensation to you should this occur.
- By consenting to participate, you authorize the use of your bodily fluids and tissue samples for the research described above.
- This hospital is not able to offer financial compensation nor to absorb the costs of medical treatment should you be injured as a result of participating in this research.
- This hospital makes no commitment to provide free medical care or payment for any unfavorable outcomes resulting from participation in this research. Medical services will be offered at the usual charge.

1. Recommendations for Researchers. Researchers are accountable for the quality of the informed consent protocol and for assessing comprehension of information for an informed consent. Accountability should take two forms: (a) researchers should incorporate empirically-based strategies that have been shown to increase comprehension and (b) researchers should assess research subjects' level of comprehension of information for an informed consent prior to admitting them into a study. If comprehension is inadequate, the researcher should make an effort to enhance the research subject's comprehension based on empirically effective strategies or, if impossible to attain adequate comprehension, the researcher should exclude the subject from the study (or obtain a proxy).

The IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth above, or waive the requirement to obtain informed consent provided that the IRB finds and documents that various conditions under the federal common rule regulations are met.

2. Researchers should consider the following:

1. present an amount of information for an informed consent that research subjects perceive to be the right amount for them;

2. present information clearly;

3. present any necessary anxiety-producing information (e.g., risks, complications, side effects) in as non-threatening a manner as possible;

4. present information simply -- ensure that level of difficulty of information in consent forms does not exceed research subjects' preferences or capabilities;

5. have the investigator, a nurse, or a health care team present (or follow up) information for an informed consent;

6. if possible, leave the informed consent form with research subjects so that they have adequate time to reflect upon it;

7. possibly use an audiovisual format to present information for an informed consent; and

8. actively involve research subjects in the processing of information for an informed consent.

3. The Basic Elements of Informed Consent*:*

a. a statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental;

b. a description of any reasonably foreseeable risks or discomforts to the subject;

c. a description of any benefits to the subject or to others which may reasonably be expected from the research;

d. a disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;

e. a statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained;

f. for research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained;

g. an explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research related injury to the subject; and

h. a statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

4. Additional Elements of Informed Consent. When appropriate, one or more of the following elements of information shall also be provided to each subject:

a. a statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable;

b. anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent;

c. any additional costs to the subject that may result from participation in the research;

d. the consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject;

e. a statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject; and

f. the approximate number of subjects involved in the study.

5. Appropriate Methods for Obtaining Consent

a. Conducting the proposed research in violation of this principle of informed consent may be justified only when all of the following conditions are met:

1. the risk to any subject is minimal;
2. the rights and welfare of any subject will not be adversely affected;
3. the research objectives cannot be realized without concealment;
4. any reasonable alternative means for attaining those objectives would be less advantageous to the subjects;
5. there is sufficient reason for concealment so that when the subject is later informed, he/she can be expected to find the concealment reasonable and suffer no serious loss of confidence in the integrity of the investigator or others involved in the situation;
6. the subject is allowed to withdraw his/her data from the study if he/she so wishes when the concealment is revealed to him/her before publication and/or publicity of data; and
7. the investigator takes full responsibility for detecting and removing stressful aftereffects and, insofar as possible, for providing the subject with positive gain from the research experience.

b. In recruiting subjects for research and obtaining their informed consent, the investigator must give potential subjects an honest description of the study without misrepresenting the purposes, procedures, benefits, or sponsorship of the research. Potential subjects should also be informed of the investment being asked of them (e.g., amount of time involved). Violations of this principle can be justified only under the conditions noted under C.4. above.

c. Where private information is sought or where risk may be involved, the subject should be fully informed regarding the nature of the information he/she will be asked to divulge and/or the possible risks, discomforts, or harm that he/she may undergo as a result of participating.

d. Where minors are used as the subjects for research outside of a school system or institution, **only** the parent or guardian shall give informed consent. In addition to this consent, children must have the research and informed consent information discussed with them so that they can understand these items and must be asked if they will participate in the research, thus providing their assent to participate in the research. Conditions noted under C.4.1 and C.4.2. above also apply. Contact the UT Martin Office of Research, Grants, and Contracts for information on obtaining implicit consent from the parent or guardian if signing the consent form presents difficulties. (e. g., some researchers send letters home to the parents/guardians asking them to contact the school if they do not want their child[ren] to participate in the described research; if the parents/guardians do not contact the school, they are told that they have given their implicit consent for the child[ren] to participate in the research.)

e. In the circumstances that the research is conducted in an institutional setting, such as a school or hospital, where minors or committed patients are used as the subjects for research, informed consent should be secured both from the appropriate official and from the parent or guardian if any, as well as assent from the children or patients. Conditions noted under C.4.1. and C.4.2. above also apply.

f. In the circumstance of captives and/or dependents as found in institutions, prisons, hospitals, schools, etc., and relationships such as employer/employee, teacher/student, etc., where control is inherent in the circumstance, particular care is necessary to obtain informed consent using procedures that maximize the freedom of the subject to refuse participation. In the case of prisoners, UT Martin will follow the Department of Health and Human Services regulations. Any value offered as a participation reward should not take advantage of any subject's deprived state. Conditions noted under C.4.1. and C.4.2. above also apply.

g. Care must be taken that the subject's decision concerning participation is truly free and voluntary. To be avoided are:

1. being required to participate in research as a course requirement where no course-related pedagogical benefit can be justified;

2. direct or implicit suggestions that needed services (such as counseling, employment, housing) may be withheld or reduced if the subject refuses to

participate in the research it is the responsibility of the investigator to make clear to the subject that such services are not contingent upon participation;

3. pressure to participate because the subject's relationship to the investigator creates a situation where it is difficult to refuse (e.g., teacher/student, superior/subordinate relationships); and

4. pressure to participate put on subjects by arousing anxieties concerning personal shortcomings (e.g., cowardice, defensiveness) or by the use of undue social influence or moral appeals.

h. Once involved in the study, the subject should still have the prerogative, at any time, to refuse to participate or to withdraw from an experiment, regardless of the reasons. Should he/she choose to exercise this prerogative, this right must be respected without obstruction or coercion by the investigator. An opportunity to discuss the reasons for withdrawal may be offered to the subject for the purpose of clarifying misunderstandings or reducing anxiety or other discomfort that may have been aroused by participation as a subject.

C. Risks versus Benefits

1. All guidelines in **PART X.A**. apply here.

2. Each research project must be evaluated in terms of the potential benefits to new knowledge, to society, and to the research subject as against the potential risks to the individuals involved. Where a proposed project involves substantial potential risks to subjects, the investigator:

   a. has the responsibility to justify the possible benefits of the project, and

   b. must be cognizant of previous research, both animal and human, done in the subject area.

3. Any project in which there exists a possibility of alteration or impairment of physical or psychological functions; of acute discomfort; or of emotional, social, or other harm constitutes a risk. Such projects require special precautions and must follow approved procedures as set forth in **Section XII**, below, to obtain approval. Furthermore, any project which solicits private or confidential information as defined by the subject or qualified person (or if this is not possible, by a parent, guardian, or other designated authority) must also be reviewed according to approved procedures under **PART X.A**.

XI. TYPES OF RESEARCH REVIEW

A. Exempt refers to various types of research (including some survey and ongoing educational research projects) that do not require continued monitoring by the IRB. Guided by the federal regulations, the Office of Research, Grants, and Contracts determines which projects fall into the Exempt classification.

An exemption may be used for studies in which children are participants only if the research is limited to observation of public behavior. The use of surveys or interviews, review of any records, and direct or indirect interaction by the researcher, or any adjustment

of the setting in which the observations take place does not qualify as an observation of public behavior. Research activities exempt from formal review must present no greater than minimal risk to participants **and** meet the definition of one or more of the six (6) categories listed below.

According to 45 CFR, 46.101(b), research activities in which the only involvement of human participants will be in one or more of the following categories are exempt form IRB review:

1. **Category A** [45 CFR, 46.101(b)1]: Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as: (i) research on regular and special education instructional strategies, or (ii) research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

   Limitations to Category A – Confidentiality of identifiable information must be maintained without the express permission of the participants to do otherwise.

2. **Category B** [45 CFR, 46.101(b)2]: Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior.

   Limitations to Category B – This exemption does not apply if (a) the information obtained is recorded in such a manner that participants can be identified, directly or through identifiers linked to the participants; and (b) any disclosure of the human participants' responses outside the research could reasonably place the participants at risk of criminal or civil liability or be damaging to the participants' financial standing, employability, or reputation. The exemption does not apply to observation of public behavior if the investigator interacts with participants or manipulates the setting in which the observations take place.

3. **Category C** [45 CFR, 46101(b)3]**:** Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under paragraph (2) above, if: (i) the participants are elected or appointed public officials or candidates for public office; or (ii) Federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.

   Limitations to Category C – Confidentiality of identifiable information must be maintained without express permission of the participants to do otherwise.

4. **Category D** [45 CFR, 46.101(b)4]: Research involving the collection of study of existing data, documents, records, pathological specimens or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that participants cannot be identified, directly or through identifiers linked to the participants.

Limitations to Category D – The requirement for consent of the participants is waived if the data, documents, records, or specimens are publicly available. The authorization of the custodian of the data or document can serve in lieu of specific participant consent for access to the data, if the data or records are not publicly available. However, the investigator and the UT Martin IRB must be satisfied that the custodian is authorized to release the data for research purposes.

Note: The researcher must be sure to have legal access to the materials in question, even if the data is recorded without identifiers. Some records are by nature confidential (e. g., school records) and others are property of clients only held in trust by an institution (e. g., patient records). These records **do not** qualify for exemption. However, they may fall under a classification for **expedited review**.

5. **Category E** [45 CFR, 46.101(b) 5]: Research and demonstration projects which are conducted by or subject to the approval of Federal Department or Agency heads, and which are designed to study, evaluate, or otherwise examine: (i) Public benefit or service programs; (ii) procedures of obtaining benefits or services under those programs; (iii) possible changes in or alternatives to those programs or procedures; or (iv) possible changes in methods or levels of payment for benefits or services under those programs.

Limitations to Category E - The UT Martin requirements for informed consent may be waived if the research cannot be carried out practicably without the waiver.

6. **Category F** [45 CFR, 46.101(b) 6]: Taste and food quality evaluation and consumer acceptance studies, if wholesome foods **without** additives are consumed or if a food is consumed that contains a food ingredient **at or below the level and for a use found to be safe**, or agricultural chemical or environmental contaminants **at or below the level found to by safe**, by the Food and Drug Administration (FDA) or approved by the Environmental Protection Agency (EPA) or the Food Safety and Inspection Service (FSIS) of the U.S. Department of Agriculture (USDA).

B. **Expedited** review procedure consists of a review of research involving human subjects by the UT Martin IRB Expedited board consisting of the chair and the secretary of the university board in accordance with the requirements set forth in 45 CFR, 46.110. Research activities may be eligible for **expedited review** if they present no more than minimal risk to human subjects **and** involve only procedures listed in one or more of the nine categories listed below. The nine categories activities listed should not be considered to be of minimal risk simply because they are listed. Inclusion on this list means that the activity is eligible for review through the expedited review procedure when the specific circumstances of the proposed research involve no more than minimal risk to human subjects

1. **Category G:** Clinical studies of drugs and medical devices only when condition (a) or (b) is met.

   a. Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required. (Note: Research on marketed drugs that significantly

increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.)

b. Research on medical devices for which (1) an investigational device exemption application (21 CFR Part 812) is not required; or (2) the medical device is cleared/approved for marketing

2. **Category H:** Collection of blood samples by finger stick, heel stick, ear stick, or venipucture as follows:

a. From healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amount drawn may not exceed 550 ml in an 8-week period and collection may not occur more frequently than 2 times per week; or

b. From other adults and children considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8-week period and collection may not occur more frequently than 2 times per week.

NOTE: Children are defined in the HHS regulations as "persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted." 45 CFR 46.402 (a).

3. **Category I:** Prospective collection of biological specimens for research purposes by noninvasive means.

4. **Category J:** Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwave. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.)

Examples:

(a) applying physical sensors either to the surface of the body or at a distance and not involving input of significant amounts of energy into the subject or an invasion of the subject's privacy;

(b) weighing or testing sensory acuity;

(c) magnetic resonance imaging;

(d) electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, Doppler blood flow, and echocardiography; or

(e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

5. **Category K:** Research involving materials (data, documents, records, or specimens) that have been collected or will be collected solely for non-research purposes (such as medical treatment or diagnosis).

Note: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45CFR 46.101 (b)(4). This listing refers only to research that is not exempt.

6. **Category L:** Collection of data from voice, video, digital, or image recordings made for research purposes.

7. **Category M:** Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identify, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.

Note: Some research in this category may be exempt for the HHS regulations for the protection of human subjects 45 CFR 46.101 (b)(2) and (b)(3). This listing refers only to research that is not exempt.

8. **Category N:** Continuing review of research previously approved by the convened IRB as follows:

Where

a. the research is permanently closed to the enrollment of new subjects;

b. all subjects have completed all research-related interventions; and

c. the research remains active only for long-term follow-up of subjects; or

d. no subjects have been enrolled and no additional risks have been identified; or

e. the remaining research activities are limited to data analysis.

9. **Category O:** Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where the following conditions apply:

a. Categories two (2) through eight (8) do not apply; and

Chart 1: Is an Activity Research Involving Human Subjects Covered by 45 CFR part 46?

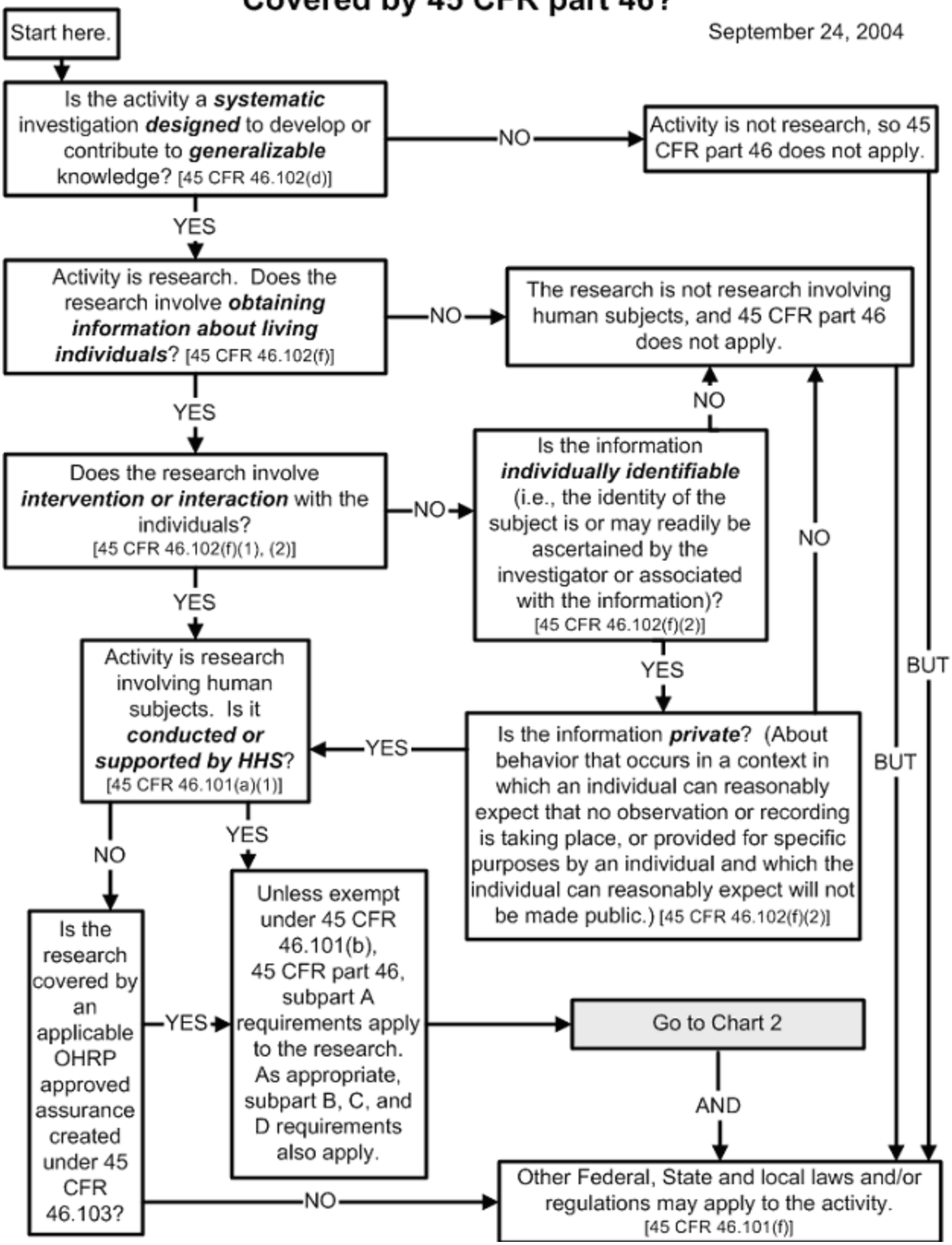

Chart 2: Is the Research Involving Human Subjects Eligible for Exemption Under 45 CFR 46.101(b)?