Information for Investigators
in Preparation of
Human Research Protocols for IRB Review

KCOM/NRMC
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Contents

Institutional Review Board
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I. Introduction

The Institutional Review Board, established by Kirksville College of Osteopathic Medicine, serves to assure that research on human subjects is planned and carried out in accordance with certain ethical guidelines and federal regulations. Copies of the human subjects principles and policies (the Assurance of Compliance for DHHS Regulations for Protection of Human Research Subjects) and copies of relevant FDA regulations, 21 CFR Parts 50 and 56, and copies of relevant HHS regulations, 45 CFR Part 46 are available in the Dean's office or may be obtained from the Institutional Review Board office. Copies of the ethical codes are included in this informational packet.

In order to assist investigators in deciding whether a planned activity constitutes research, the following definition of research is provided: Research is any activity which has the intent of securing information from humans for the purpose of advancing generalizable knowledge. Such activity may or may not differ in a significant way from customary practice.

A research project generally is described in a protocol that sets forth explicit objectives and formal procedures designed to reach those objectives. The protocol may include therapeutic and other activities intended to benefit the subjects, as well as procedures to evaluate such activities. Research objectives range from understanding normal and abnormal physiological, psychological, or social phenomena, to evaluating diagnostic, therapeutic or preventive interventions and variations in services and practices. The activities or procedures involved in research may be invasive or noninvasive and may include surgical interventions, removal of body tissues or fluids, administration or application of chemical substances, modification of diet or daily routine, strenuous physical exertion, alteration of environment, observation, administration of questionnaires or tests, randomization of subjects, review of records, etc.

In assuring compliance with the KCOM Assurances to DHHS and FDA regulations, the College requires that, prior to initiation, all research projects involving humans as subjects or human material be reviewed and approved by the IRB. (Note: Subjects of research can include nurses, faculty members, physicians, staff employees, students, patients, as well as others.) This policy applies, regardless of source of funding and location of the study, to such research conducted by faculty, staff, and students of the college. Whenever an investigator is uncertain as to whether the study falls under IRB aegis, an informal letter (or telephone call) describing the proposed activities will elicit an IRB response and benefit both the investigator and KCOM. As a general principle, research which will involve human subjects shall not be initiated until the IRB review process has been completed and approval has been provided.

The Human Research Protocol for IRB Review and any appended material (and three copies) should be submitted to the IRB office. IRB meetings are scheduled on call. When holidays necessitate rescheduling deadlines or meetings, adequate notice is provided. This timing also allows for two IRB reviewers to become familiar with the project as described in the Protocol and to make recommendations to the full IRB. Protocols received after the deadline may not be reviewed at that meeting, and the investigator will be notified.

Protocols should be prepared carefully and signed by the investigator and the department chair or advisor. While preparing protocols, an investigator should read and follow the ethical codes included in this information packet, in fulfilling the responsibility to protect the human beings who will be the subjects of this research. Completed forms should include the hypotheses and aims of the study, the methodology, measurements and analysis to be carried out, a description of selection (inclusion/exclusion) criteria, procedures for contact and recruitment, an

explanation of potential benefits to subjects and/or society vs possible risks and means for minimizing the risks. and a consent form following the KCOM model and containing the elements of informed consent. Incompletely described proposals will be returned for additional information before final action can be taken by the IRB.

In approving human subjects research proposal, the IRB must determine (1) that the risks to subjects are minimized by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, (2) that the risks to the subject are outweighed by the potential benefit to the subject and by the importance of the knowledge to be gained, and (3) that the rights and welfare of the subject are adequately protected by using adequate and appropriate methods to obtain informed consent.

In order to enhance the review process, the IRB relies on all members of the College faculty with appropriate information to review proposals in assuring that experimental protocols are properly designed and in seeking advice as to whether the state of the science justifies the use of human subjects at the particular time. This occurs when expertise is known to be available with an individual, when other reviewers are unavailable or overloaded, when subcommittee members are overloaded, or for other reasons determined by the Chair of the IRB. The college extends this policy to seeking outside review by consultants when necessary. Comments or appropriate distillations of comments will be supplied to an investigator for consideration in strengthening the proposal.

If the proposal is approved, the investigator will be promptly notified by letter. If deferred or if more information or revision is needed (a contingent approval action) in order to make a decision, the investigator will be notified by a letter. A reply must be received in writing within 60 days. Otherwise, the IRB will administratively withdraw the Protocol from further consideration. If the IRB identifies and makes specific changes in a proposed protocol or consent document requiring concurrence of the investigator and retyping of the document(s), the IRB Chair or other IRB member may be designated to approve the revised document(s), and to allow the study to begin. The minutes of the next meeting of the IRB shall inform the membership of such actions. The amended documents shall be available to the IRB membership for review. When the IRB requires the clinical investigator to make substantial composed changes, the final review and approval of these changes shall be made at a convened meeting of the IRB membership. All such actions shall be informed to the investigator in writing.

II. Changes in Approved Protocols

Should there be a change in an approved protocol, it shall be brought directly, before implementation, to the attention of the IRB office. Please contact the IRB office for a Request for Project Re-Review form if a change in protocol is desired. If a change in protocol is desired, it must have final approval by the IRB prior to implementation, except where necessary to eliminate risks to research subjects.

III. Review of Approved Protocols

At the end of the IRB-approved project period (maximally one year), a progress report must be submitted for review and for continuance of approval to be provided. Research shall not go on without continued approval. Investigators will be reminded one month in advance of the required information and timing for re-review. The required information includes a brief progress report describing the number of subjects studied, a description of any untoward events, and other information as directed by the IRB at that time.

IV. Exemptions From Continued IRB Review

Under current regulations, the IRB may exempt from further review certain minimal risk research. The investigator must submit the Human Research Protocol for IRB Review by responding to the questions therein, including the Abstract of Proposal, to the IRB (after subcommittee approval, where one exists). If the IRB Chairman agrees with the exemption, the investigator will be notified by the IRB office. Otherwise, full IRB review will be necessary.

Research activities in which the only involvement of human subjects will be in one or more of the following categories may be determined to be exempt from continued review. These categories of exemption are:

1. Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as (i) research on regular and special education instruction strategies, or (ii) research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

2. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement) if information taken from these sources is recorded in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

3. Research involving survey or interview procedures, except where all of the following conditions exist:

    a. responses are recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects;

    b. the subject's responses, if they became known outside of the research, could reasonably place the subject at risk of criminal or civil liability or be damaging to the subject's financial standing or employability, insurability, reputation, or be stigmatizing in any way; and

    c. the research deals with sensitive aspects of the subject's own behavior, such as illegal conduct, drug use, sexual behavior, or use of alcohol. All research involving survey or interview procedures is exempt, without exception, when the respondents are elected or appointed public officials or candidates for public office. Research in this category which involves children is not exempt.

4. Research involving the observation (including observation by participants) of public behavior, except where all of the following exists:

    a. responses are recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subject;

    b. the subject's responses, if they became known outside the research, could reasonably place the subject at risk of criminal or civil liability or be damaging to other subject's financial standing or employability; and

c. the research deals with sensitive aspects of the subject's own behavior, such as illegal conduct, drug use, sexual behavior, or use of alcohol.

5. Research involving the collection or 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 subjects cannot be identified, directly or through identifiers linked to the subjects.

6. Emergency use of any test article regulated by the FDA, provided that such emergency use is reported to the IRB within 5 working days; any subsequent use of such test article at the institution is subject to IRB review.

7. Taste and food quality evaluations 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 contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

8. Unless specifically required by statute (and except to the extent specified in paragraph (i)), research and demonstration projects which are conducted by or subject to the approval of the Department of Health and Human Services, and which are designed to study, evaluate, or otherwise examine: (i) programs under the Social Security Act, or other public benefit or service programs; (ii) procedures for 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.

NOTE: Research which would involve vulnerable individuals such as pregnant women, the elderly, children, or prisoners may not be exempt from continued IRB review. These exempt categories are found in 45 CFR 46.101.

V. Emergency Exemption Provision

KCOM policy allows for an emergency exemption provision for one-time emergency use of an investigational drug or medical device. Emergency use of investigational new drugs or medical devices is restricted to research development, testing and evaluation, research designed to develop or contribute to generalizable knowledge, including, but not limited to formal research programs, demonstrations or several programs that may include research activities. Emergency use of investigational drugs or devices does not exempt investigators from the responsibility of reporting results of this use to the sponsor, including safety reports of any serious or unexpected adverse experiences. Written documentation by the investigator of the emergency situation must be on file in the IRB office and in the KCOM/NRMC hospitals or NRMC pharmacy. Included should be the patient's condition, therapies already tried and justification for the use of the experimental drug or device (i.e., in what kinds of conditions it has been used previously), and the expected outcome in the situation described. Any subsequent use of an investigational substance must be preceded by IRB approval of a fully developed Protocol. Please call the IRB office for additional information. Emergency use of any test article must be reported to the IRB within five (5) working days. Any subsequent use of the test article must have IRB review prior to usage. Compliance with these regulations will in no way render inapplicable pertinent Federal, State, or local laws or regulations.

Emergency Medical Care: In the event of the necessity of emergency medical care of a patient included in an IRB approved protocol, nothing in these regulations is intended to limit the authority of a physician to provide emergency medical care. Emergency medical care for patients may be provided without regard to IRB review and approval. Whenever emergency care is initiated without prior IRB review and approval, the patient may not be considered to be a research subject. Such emergency care may not be claimed as research, nor may the outcome of such care be included in any report of a research activity. Prior to initiation of research involving human subjects, IRB review and approval is required. If the emergency care involves drugs, devices, or biologics that are considered to be investigational by the Food and Drug Administration (FDA), then it may be necessary to meet FDA requirements to use the investigational article for emergency purposes as per 21 CFR Parts 50 and 56, as they are relevant.

VI. Expedited Review of Protocols

Under current regulations, 45 CFR Part 46 and 21 CFR Parts 50 and 56, certain minimal (physical and/or psycho-social) risk research which meets criteria can receive approval upon review by the IRB Chairman, but is subject to full review at the request of any IRB member. The list of research activities that may be reviewed through expedited review was amended and published in the Federal Register of November 9, 1998 (63FR60353). General areas include research on human matter which can be collected in a non-invasive manner (e.g., hair, sweat, saliva, etc.), limited blood sampling, certain dental plaque, voice recordings, exercise by healthy subjects, retrospective data and specimens, and non-deception psychological research. Such research usually is biomedical in nature.

The investigator must submit the Human Research Protocol for IRB Review, including consent forms where appropriate, to the IRB Chairman (after subcommittee approval, where one exists). If the IRB Chairman concludes that the research falls within the parameters for expedited review, other aspects of human subject protection will be reviewed, e.g. risk-benefit ratio, informed consent requirements, etc., and a determination made for approval or that action must be taken by full IRB.

General categories of expedited review include:

1. Collection of hair and nail clippings in a nondisfiguring manner, deciduous teeth, and permanent teeth if patient care indicates need for extraction.

2. Collection of excreta and external secretions including sweat, uncannulated saliva, placenta removed at delivery, and amniotic fluid at the time of rupture of the membrane prior to or during labor.

3. Recording of data from subjects 18 years of age or older using non-invasive procedures routinely employed in clinical practice. This includes the use of physical sensors that are applied either to the surface of the body or at a distance and do not involve input of matter or significant amounts of energy into the subject or an invasion of the subject's privacy. It also includes such procedures as weighing, testing sensory acuity, electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, diagnostic echography, and electroretinography. It does not include exposure to electromagnetic radiation outside the visible range (e.g., X-ray, micro-waves).

4. Collection of blood samples by venipuncture, in amounts not exceeding 450 milliliters in an eight-week period and no more often than two times per week, from subjects 18 years of age or older and who are in good health and not pregnant. For all children and all other adults, the amount drawn may NOT exceed the lesser of 50 ml or 3ml per kg in an eight-week period and collection may not occur more than two times per week.

5. Collection of both supra- and subgingival dental plaque and calculus, providing the procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished with accepted prophylactic techniques.

6. Voice recordings made for research purposes such as investigations of speech defects.

7. Moderate exercise by healthy volunteers.

8. The study of existing data, documents, records, pathological specimens, or diagnostic specimens.

9. Research on individual or group behavior or characteristics of individuals, such as studies of perception, cognition, game theory, or test development, where the investigator does not manipulate subject's behavior and the research will not involve stress to subjects.

10. Research on drugs or devices for which an investigational new drug exemption or an investigational device exemption is not required.

VII. Declaration of Helsinki

Recommendations Guiding Medical Doctors in Biomedical Research Involving Human Subjects

A. Basic Regulations

1. Biomedical research involving human subjects must conform to generally accepted scientific principles and should be based on adequately performed laboratory and animal experimentation and on a thorough knowledge of the scientific literature.

2. The design and performance of each experimental procedure involving human subjects should be clearly formulated in an experimental protocol which should be transmitted to a specially appointed independent committee for consideration, comment and guidance.

3. Biomedical research involving human subjects should be conducted only by scientifically qualified persons and under the supervision of a clinically competent medical person. The responsibility for the human subject must always rest with a medically qualified person and never rest on the subject of the research, even though the subject has given his or her consent.

4. Biomedical research involving human subjects cannot legitimately be carried out unless the importance of the objective is in proportion to the inherent risk to the subject.

5. Every biomedical research project involving human subjects should be preceded by careful assessment of predictable risks in comparison with foreseeable benefits to the subject or to others. Concern for the interests of the subject must always prevail over the interests of science and society.

6. The right of the research subject to safeguard his or her integrity must always be respected. Every precaution should be taken to respect the privacy of the subject and to minimize the impact of the study on the subject's physical and mental integrity and on the personality of the subject.

7. Doctors should abstain from engaging in research projects involving human subjects unless they are satisfied that the hazards involved are believed to be predictable. Doctors should cease any investigation if the hazards are found to outweigh the potential benefits.

8. In publication of the results of his or her research, the doctor is obliged to preserve the accuracy of the results. Reports of experimentation not in accordance with the principles laid down in this Declaration should not be accepted for publication.

9. In any research on human beings, each potential subject must be adequately informed of the aims, methods, anticipated benefits and potential hazards of the study and the discomfort it may entail. He or she should be informed that he or she is at liberty to abstain from participation in the study and that he or she is free to withdraw his or her consent to participation at any time. The doctor should then obtain the subject's given informed consent, preferably in writing.

10. When obtaining informed consent for the research project, the doctor should be particularly cautious if the subject is in a dependent relationship to him or her or may consent under duress. In that case the informed consent should be obtained by a doctor who is not engaged in the investigation and who is completely independent of this official relationship.

11. In case of legal incompetence, informed consent should be obtained from the legal guardian in accordance with national legislation. Where physical or mental incapacity makes it impossible to obtain informed consent, or when the subject is a minor, permission from the responsible relative replaces that of the subject in accordance with national legislation.

12. The research protocol should always contain a statement of the ethical considerations involved and should indicate that the principles enunciated in the present Declaration are complied with.

B. Medical Research Combined With Professional Care (Clinical Research)

1. In the treatment of the sick person, the doctor must be free to use a new diagnostic and therapeutic measure, if in his or her judgment it offers hope of saving life, reestablishing health or alleviating suffering.

2. The potential benefits, hazards and discomfort of a new method should be weighed against the advantages of the best current diagnostic and therapeutic methods.

3. In any medical study, every patient - including those of a control group, if any - should be assured of the best proven diagnostic and therapeutic methods.

4. The refusal of the patient to participate in a study must never interfere with the doctor-patient relationship.

5. If the doctor considers it essential not to obtain informed consent, the specific reasons for this proposal should be stated in the experimental protocol for transmission to the independent committee (see A.2 above).

6. The doctor can combine medical research with professional care, the objective being the acquisition of new medical knowledge, only to the extent that medical research is justified by its potential diagnostic or therapeutic value for the patient.

C. Non-Therapeutic Biomedical Research Involving Human Subjects (Non-Clinical Biomedical Research)

1. In the purely scientific application of medical research carried out on a human being, it is the duty of the doctor to remain the protector of the life and health of that person on whom biomedical research is being carried out.

2. The subjects should be volunteers - either healthy persons or patients for whom the experimental design is not related to the patient's illness.

3. The investigator or the investigating team should discontinue the research if in his/her or their judgment it may, if continued, be harmful to the individual.

4. In research on man, the interest of science and society should never take precedence over considerations related to the well-being of the subject.

VIII. The Nuremberg Code

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

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

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

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

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

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

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

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

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

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

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

IX. The Belmont Report

Ethical Principles and Guidelines for the Protection of Human Subjects of Research
The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research
Department of Health Education, and Welfare

Scientific research has produced substantial social benefits. It has also posed some troubling ethical questions. Public attention was drawn to these questions by reported abuses of human subjects in biomedical experiments, especially during the Second World War. During the Nuremberg War Crime Trials, the Nuremberg code was drafted as a set of standards for judging physicians and scientists who had conducted biomedical experiments on concentration camp prisoners. This code become the prototype of many later codes intended to assure that research involving human subjects would be carried out in an ethical manner.

The codes consist of rules, some general, others specific, that guide the investigators or the reviewers of research in their work. Such rules often are inadequate to cover complex situations; at times they come into conflict, and they are frequently difficult to interpret or apply. Broader ethical principles will provide a basis on which specific rules may be formulated, criticized and interpreted.

Three principals, or general prescriptive judgements, that are relevant to research involving human subjects are identified in this statement. Other principles may also be relevant. These three are comprehensive, however, and are stated at a level of generalization that should assist scientists, subjects, reviewers, and interested citizens to understand the ethical issues inherent in research involving human subjects. These principles cannot always be applied so as to resolve beyond dispute particular ethical problems. The objective is to provide an analytical framework that will guide the resolution of ethical problems arising from research involving human subjects.

This statement consists of a distinction between research and practice, a discussion of the three basic ethical principles, and remarks about the application of these principles.

A. Boundaries Between Practice and Research

It is important to distinguish between biomedical and behavioral research, on the one hand, and the practice of accepted therapy on the other, in order to know what activities ought to undergo review for the protection of human subjects of research. The distinction between research and practice is blurred partly because both often occur together (as in research designed to evaluate therapy) and partly because notable departures from standard practice are often called "experimental" when the terms "experimental" and "research" are not carefully defined.

For the most part, the term "practice" refers to interventions that are solely designed 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. By contrast, the term "research" designates an activity designed to test an hypothesis, permit conclusions to be drawn, and thereby to develop or contribute to generalizable knowledge (expressed, for example, in theories, principles, and statements of relationships). Research is usually described in a formal protocol that sets forth an objective and a set of procedures designed to reach that objective.

When a clinician departs in a significant way from standard or accepted practice, the innovation does not, in and of itself, constitute research. The fact that a procedure is "experimental," in the sense of new, untested, or different, does not automatically place it in the category of research. Radically new procedures of this description should, however, be made the object of formal research at an early stage in order to determine whether they are safe and effective. Thus, it is the responsibility of medical practice committees, for example, to insist that a major innovation be incorporated into a formal research project.

Research and practice may be carried on together when research is designed to evaluate the safety and efficacy of a therapy. This need not cause any confusion regarding whether or not the activity requires review; the general rule is that if there is any element of research in an activity, that activity should undergo review for the protection of human subjects.

B. Basic Ethical Principles

The expression "basic ethical principles" refers to those general judgements that serve as a basic justification for the many particular ethical prescriptions and evaluations of human actions. Three basic principles, among those generally accepted in our cultural tradition, are particularly relevant to the ethics of research involving human subjects: the principles of respect for persons, beneficence and justice.

1. Respect for Persons

Respect for persons incorporates at least two ethical convictions: first, that individuals should be treated as autonomous agents, and second, that persons with diminished autonomy are entitled to protection. The principle of respect for persons thus divides into two separate moral requirements: the requirement to acknowledge autonomy and the requirement to protect those with diminished autonomy.

An autonomous person is an individual capable of deliberation about personal goals and of acting under the direction of such deliberation. To respect autonomy is to give weight to autonomous persons' considered opinions and choices while refraining from obstructing their actions unless they are clearly detrimental to others. To show lack of respect for an autonomous agent is to repudiate that person's considered judgements, or to withhold information necessary to make a considered judgment, when there are no compelling reasons to do so.

However, not every human being is capable of self-determination. The capacity for self-determination matures during an individual's life, and some individuals lose this capacity wholly or in part because of illness, mental disability, or circumstances that severely restrict liberty. Respect for the immature and the incapacitated may require protecting them as they mature or while they are incapacitated.

Some persons are in need of extensive protection, even to the point of excluding them from activities which may harm them; other persons require little protection beyond making sure they undertake activities freely and with awareness of possible adverse consequences. The extent of protection afforded should depend upon the risk of harm and the likelihood of benefit. The judgment that any individual lacks autonomy should be periodically reevaluated and will vary in different situations.

In most cases of research involving human subjects, respect for persons demands that subjects enter into the research voluntarily and with adequate information. In some situations, however, application of the principle is not obvious. The involvement of prisoners as subjects of research provides as instructive example. On the one hand, it would seem that the principle of respect for persons requires that prisoners not be deprived of the opportunity to volunteer for research. On the other hand, under prison conditions they may be subtly coerced or unduly influenced to engage in research activities for which they would not otherwise volunteer. Respect for persons would then dictate that prisoners be protected. Whether to allow prisoners to "volunteer" or to "protect" them presents a dilemma. Respecting persons, in most hard cases, is often a matter of balancing competing claims urged by the principle of respect itself.

2. Beneficence

Persons are treated in an ethical manner not only by respecting their decisions and protecting them from harm, but also by making efforts to secure their well being. Such treatment falls under the principle of beneficence. The term "beneficence" is often understood to cover acts of kindness or charity that go beyond strict obligation. In this document, beneficence is understood in a stronger sense, as an obligation. Two general rules have been formulated as complementary expressions of beneficent actions in this sense: (1) do not harm and (2) maximize possible benefits and minimize possible harms.

The Hippocratic maxim "do no harm" has long been a fundamental principle of medical ethics. Claude Bernard extended it to the realm of research, saying that one should not injure one person regardless of the benefits that might come to others. However, even avoiding harm requires learning what is harmful; and, in the process of obtaining this information, persons may be exposed to risk of harm. Further, the Hippocratic Oath requires physicians to benefit their patients "according to their best judgment." Learning what will in fact benefit may require exposing persons to risk. The problem posed by these imperatives is to decide when it is justifiable to seek certain benefits despite the risks involved, and when the benefits should be foregone because of the risks.

The obligations of beneficence affect both individual investigators and society at large, because they extend both to particular research projects and to the entire enterprise of research. In the case of particular projects, investigators and members of their institutions are obliged to recognize the longer term benefits and risks that may result from the improvement of knowledge and from the development of novel medical, psychotherapeutic, and social procedures.

The principle of beneficence often occupies a well-defined justifying role in many areas of research involving human subjects. An example is found in research involving children. Effective ways of treating childhood diseases and fostering healthy development are benefits that serve to justify research involving children--even when individual research subjects are no direct beneficiaries. Research also makes it possible to avoid the harm that may result from the application of previously accepted routine practices that on closer investigation turn out to be dangerous. But the role of the principle beneficence is not always so unambiguous. A difficult ethical problem remains, for example, about research that presents more than minimal risk without immediate prospect of direct benefit to the children involved. Some have argued that such research is inadmissible, while others have pointed out that this limit would rule out much research promising great benefit to children in the future. Here again, as with all hard cases, the different claims covered by the principle of beneficence may come into conflict and force difficult choices.

3. Justice

Who ought to receive the benefits of research and bear its burdens? This is a question of justice, in the sense of "fairness in distribution" or "what is deserved." An injustice occurs when some benefit to which a person is entitled is denied without good reason or when some burden is imposed unduly. Another way of conceiving the principle of justice is that equals ought to be treated equally. However, this statement requires explication. Who is equal and who is unequal? What considerations justify departure from equal distribution? Almost all commentators allow that distinctions based on experience, age, deprivation, competence, merit and position do sometimes constitute criteria justifying differential treatment for certain purposes. It is necessary, then, to explain in what respects people should be treated equally. There are several widely accepted formulations of just ways to distribute burdens and benefits. Each formulation mentions some relevant property on the basis of which burdens and benefits should be distributed. These formulations are (1) to each person an equal share, (2) to each person according to individual need, (3) to each person according to individual effort, (4) to each person according to societal contribution, and (5) to each person according to merit.

Questions of justice have long been associated with social practices such as punishment, taxation and political representation. Until recently these questions have not generally been associated with scientific research. However, they are foreshadowed even in the earliest reflections on the ethics of research involving human subjects. For example, during the 19th and early 20th centuries the burdens of serving as research subjects fell largely upon poor ward patients, while the benefits of improved medical care flowed primarily to private patients. Subsequently, the exploitation of unwilling prisoners as research subjects in Nazi concentration camps was condemned as a particularly flagrant injustice. In this country, in the 1940's, the Tuskegee syphilis study used disadvantaged, rural black men to study the untreated course of a disease that is by no means confined to that population. These subjects were deprived of demonstrably effective treatment in order not to interrupt the project, long after such treatment became generally available.

Against this historical background, it can be seen how conceptions of justice are relevant to research involving human subjects. For example, the selection of research subjects needs to be scrutinized in order to determine whether some classes (e.g., welfare patients, particular racial and ethnic minorities, or persons confined to institutions) are being systematically selected simply because of their easy availability, their compromised position, or their manipulability, rather than for reasons directly related to the problem being studied. Finally, whenever research supported by public funds leads to the development of therapeutic devices and procedures, justice demands both that these not provide advantages only to those who can afford them and that such research should not unduly involve persons from groups unlikely to be among the beneficiaries of subsequent applications of the research.

C. Applications

Applications of the general principles to the conduct of research leads to consideration of the following requirements: informed consent, risk/benefit assessment, and the selection of subjects of research.

1. Informed Consent

Respect for persons requires that subjects, to the degree that they are capable, be given the opportunity to choose what shall or shall not happen to them. This opportunity is provided when adequate standards for informed consent are satisfied.

While the importance of informed consent is unquestioned, controversy prevails over the nature and possibility of an informed consent. Nonetheless, there is widespread agreement that the consent process can be analyzed as containing three elements: information, comprehension and voluntariness.

Information. Most codes of research establish specific items for disclosure intended to assure that subjects are given sufficient information. These items generally include: the research procedure, 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. Additional items have been proposed, including how subjects are selected, the person responsible for the research, etc.

However, a simple listing of items does not answer the question of what the standard should be for judging how much and what sort of information should be provided. One standard frequently invoked in medical practice, namely the information commonly provided by practitioners in the field or in the locale, is inadequate since research takes place precisely when a common understanding does not exist. Another standard currently popular in malpractice law, requires the practitioner to reveal the information that reasonable persons would wish to know in order to make a decision regarding their care. This, too, seems insufficient since the research subject, being in essence a volunteer, may wish to know considerably more about risks gratuitously undertaken than do patients who deliver themselves into the hand of a clinician for needed care. It may be that a standard of "the reasonable volunteer" should be proposed: 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.

A special problem of consent arises where informing subjects of some pertinent aspect of the research is likely to impair the validity of the research. In many cases, it is sufficient to indicate to subjects that they are being invited to participate in research of which some features will not be revealed until the research is concluded. In all cases of research involving incomplete disclosure, such research is justified only if it is clear that (1) incomplete disclosure is truly necessary to accomplish the goals of the research, (2) there are no undisclosed risks to subjects that are more than minimal, and (3) there is an adequate plan for debriefing subjects, when appropriate, and for dissemination of research results to them. Information about risks should never be withheld for the purpose of eliciting the cooperation of subjects, and truthful answers should always be given to direct questions about the research. Care should be taken to distinguish cases in which disclosure would destroy or invalidate the research from cases in which disclosure would simply inconvenience the investigator.

Comprehension

The manner and context in which information is conveyed is as important as the information itself. For example, presenting information in a disorganized and rapid fashion, allowing too little time for consideration or curtailing opportunities for questioning, all may adversely affect a subject's ability to make an informed choice.

Because the subject's ability to understand is a function of intelligence, rationality, maturity and language, it is necessary to adapt the presentation of the information to the subject's capacities. Investigators are responsible for ascertaining that the subject has comprehended the information. While there is always an obligation to ascertain that the information about risk to

subjects is complete and adequately comprehended, when the risks are more serious, that obligation increases. On occasion, it may be suitable to give some oral or written tests of comprehension.

Special provision may be need to be made when comprehension is severely limited--for example, by conditions of immaturity or mental disability. Each class of subjects that one might consider as incompetent (e.g., infants and young children, mentally disabled patients, the terminally ill and the comatose) should be considered on its own terms. Even for those persons, however, respect requires giving them the opportunity to choose to the extent they are able, whether or not to participate in the research. The objections of these subjects to involvement should be honored, unless the research entails providing them a therapy unavailable elsewhere. Respect for persons also requires seeking the permission of other parties in order to protect the subjects from harm. Such persons are thus respected both by acknowledging their own wishes and by the use of third parties to protect them from harm.

The third parties chosen should be those who are most likely to understand the incompetent subject's situation and to act in that person's best interest. The person authorized to act on behalf of the subject should be given an opportunity to observe the research as it proceeds in order to be able to withdraw the subject from the research, if such action appears in the subject's best interest.

Voluntariness

An agreement to participate in research constitutes a valid consent only if voluntarily given. This element of informed consent requires conditions free of coercion and undue influence. Coercion occurs when an overt threat of harm is intentionally presented by one person to another in order to obtain compliance. Undue influence, by contrast, occurs through an offer of an excessive, unwarranted, inappropriate or improper reward or other overture in order to obtain compliance. Also, inducements that would ordinarily be acceptable may become undue influences if the subject is especially vulnerable.

Unjustifiable pressures usually occur when persons in positions of authority or commanding influence--especially where possible sanctions are involved--urge a course of action for a subject. A continuum of such influencing factors exists, however, and it is impossible to state precisely where justifiable persuasion ends and undue influence begins. But undue influence would include actions such as manipulating a person's choice through the controlling influence of a close relative and threatening to withdraw health services to which an individual would otherwise be entitled.

2. Assessment of Risks and Benefits

The assessment of risks and benefits requires a careful arrayal of relevant data, including, in some cases, alternative ways of obtaining the benefits sought in the research. Thus, the assessment presents both an opportunity and a responsibility to gather systematic and comprehensive information about proposed research. For the investigator, it is a means to examine whether the proposed research is properly designed. For a review committee, it is a method for determining whether the risks that will be presented to subjects are justified. For prospective subjects, the assessment will assist the determination whether or not to participate.

The Nature and Scope of Risks and Benefits

The requirement that research be justified on the basis of a favorable risk/benefit assessment bears close relation to the principle of beneficence, just as the moral requirement that informed consent be obtained is derived primarily from the principle of respect for persons. The term "risk" refers to a possibility that harm may occur. However, when expressions such as "small risk" or "high risk" are used, they usually refer (often ambiguously) both to the chance (probability) of experiencing a harm and the severity (magnitude) of the envisioned harm.

The term "benefit" is used in the research context to refer to something of positive value related to health or welfare. Unlike "risk," "benefit" is not a term that expresses probabilities. Risk is properly contrasted to probability of benefits, and benefits are properly contrasted with harms rather than risks of harm. Accordingly, so-called risk/benefit assessments are concerned with the probabilities and magnitudes of possible harms and anticipated benefits. Many kinds of possible harms and benefits need to be taken into account. There are, for example, risks of psychological harm, physical harm and economic harm and the corresponding benefits. While the most likely types of harms to research subjects are those of psychological or physical pain or injury, other possible kinds should not be overlooked.

Risks and benefits of research may affect the individual subjects, the families of the individual subjects, and society at large (or special groups of subjects in society). Previous codes and Federal regulations have required that risks to subjects be outweighed by the sum of both the anticipated benefit to the subject, if any, and the anticipated benefit to society in the form of knowledge to be gained from the research. In balancing these different elements, the risks and benefits affecting the immediate research subject will normally carry special weight. On the other hand, interests other than those of the subject may on some occasions be sufficient by themselves to justify the risks involved in the research, so long as the subject's rights have been protected. Beneficence thus requires that we protect against risk of harm to subjects and also that we be concerned about the loss of substantial benefits that might be gained from research.

The Systematic Assessment of Risks and Benefits

It is commonly said that benefits and risks must be "balanced" and shown to be "in a favorable ratio." The metaphorical character of these terms draws attention to the difficulty of making precise judgments. Only on rare occasions will quantitative techniques be available for the scrutiny of research protocols. However, the idea of systematic, non-arbitrary analysis of risks and benefits should be emulated insofar as possible. This ideal requires those making decisions about the justifiability of research to be thorough in the accumulation and assessment of information about all aspects of the research, and to consider alternatives systematically. This procedure renders the assessment of research more rigorous and precise, while making communication between review board members and investigators less subject to misinterpretation, misinformation and conflicting judgments. Thus, there should first be a determination of the validity of the presuppositions of the research; then the nature, probability and magnitude of risk should be distinguished with as much clarity as possible. The method of ascertaining risks should be explicit, especially where there is no alternative to the use of such vague categories as small or slight risk. It should also be determined whether an investigator's estimates of the probability of harm or benefits are reasonable, as judged by known facts or other available studies.

Finally, assessment of the justifiability of research should reflect at least the following considerations: (i) Brutal or inhumane treatment of human subjects is never morally justified. (ii) Risks should be reduced to those necessary to achieve the research objective. It should be determined whether it is in fact necessary to use human subjects at all. Risk can perhaps never be entirely eliminated, but it can often be reduced by careful attention to alternative procedures. (iii) When research involves significant risk of serious impairment, review committees should be extraordinarily insistent on the justification of the risk (looking usually to the likelihood of benefit to the subject--or, in some rare cases, to the manifest voluntariness of the participation). (iv) When vulnerable populations are involved in research, the appropriateness of involving them should itself be demonstrated. A number of variables go into such judgments, including the nature and degree of risk, the condition of the particular population involved, and the nature and level of the anticipated benefits. (v) Relevant risks and benefits must be thoroughly arrayed in documents and procedures used in the informed consent process.

3. Selection of Subjects

Just as the principle of respect for persons finds expression in the requirements for consent, and the principle of beneficence in risk/benefit assessment, the principle of justice gives rise to moral requirements that there be fair procedures and outcomes in the selection of research subjects.

Justice is relevant to the selection of subjects of research at two levels: the social and the individual. Individual justice in the selection of subjects would require that researchers exhibit fairness: thus, they should not offer potentially beneficial research only to some patients who are in their favor or select only "undesirable" persons for risky research. Social justice requires that distinction be drawn between classes of subjects that ought, and ought not, to participate in any particular kind of research, based on the ability of members of that class to bear burdens and on the appropriateness of placing further burdens on already burdened persons. Thus, it can be considered a matter of social justice that there is 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.

Injustice may appear in the selection of subjects, even if individual subjects are selected fairly by investigators and treated fairly in the course of research. This injustice arises from social, sexual, and cultural biases institutionalized in society. Thus, even if individual researchers are treating their research subjects fairly, and even if IRBs are taking care to assure that subjects are selected fairly within a particular institution, unjust social patterns may nevertheless appear in the overall distribution of the burdens and benefits of research. Although individual institutions or investigators may not be able to resolve a problem that is pervasive in their social setting, they can consider distributive justice in selecting research subjects.

Some populations, especially institutionalized ones, are already burdened in many ways by their infirmities and environments. When research is proposed that involves risks and does not include a therapeutic component, other less burdened classes of persons should be called upon first to accept these risks of research, except where the research is directly related to the specific conditions of the class involved. Also, even though public funds for research may often flow in the same directions as public funds for health care, it seems unfair that populations dependent on public health care constitute a pool of preferred research subjects if more advantaged populations are likely to be the recipients of the benefits.

One special instance of injustice results from the involvement of vulnerable subjects. Certain groups, such as racial minorities, the economically disadvantaged, the very sick, and the institutionalized may continually be sought as research subjects, owing to their ready availability in settings where research is conducted. Given their dependent status and their frequently compromised capacity for free consent, they should be protected against the danger of being involved in research solely for administrative convenience, or because they are easy to manipulate as a result of their illness or socioeconomic condition.

X. The Ethical Principles of the American Psychological Association

The decision to undertake research rests upon a considered judgment by the individual psychologist about how best to contribute to psychological science and to human welfare. Having made the decision to conduct research, the psychologist considers alternative directions in which research energies and resources might be invested. On the basis of this consideration, the psychologist carries out the investigation with respect and concern for the dignity and welfare of the people who participate and with cognizance of research with human participants.

A. In planning a study, the investigator has the responsibility to make a careful evaluation of its ethical acceptability. To the extent that the weighing of scientific and human values suggests a compromise of any principle, the investigator incurs a correspondingly serious obligation to seek ethical advice and to observe stringent safeguards to protect the rights of the human participants.

B. Considering whether a participant in a planned study will be a "subject at risk" or a "subject at minimal risk," according to recognized standards, is of primary ethical concern to the investigator.

C. The investigator always retains the responsibility for ensuring ethical practice in research. The investigator is also responsible for the ethical treatment of research participants by collaborators, assistants, students, and employees, all of whom, however, incur parallel obligation.

D. Except in minimal-risk research, the investigator establishes a clear and fair agreement with research participants, prior to their participation, that clarifies the obligations and responsibilities of each. The investigator has the obligation to honor all promises and commitments included in that agreement. The investigator informs the participants of all aspects of the research that might reasonably be expected to influence willingness to participate and explains all other aspects of the research about which the participants inquire. Failure to make full disclosure prior to obtaining informed consent requires additional safeguards to protect the welfare and dignity of the research participants. Research with children or with participants who have impairments that would limit understanding and/or communication requires special safeguarding procedures.

E. Methodological requirements of a study may make the use of concealment or deception necessary. Before conducting such a study, the investigator has a special responsibility to (1) determine whether the use of such techniques is justified by the study's prospective scientific, educational, or applied value; (2) determine whether alternative procedures are available that do not use concealment or deception; and (3) ensure that the participants are provided with sufficient explanation as soon as possible.

F. The investigator respects the individual's freedom to decline to participate in research in or to withdraw from the research at any time. The obligation to protect this freedom requires careful thought and consideration when the investigator is in a position of authority or influence over the participant. Such positions of authority include, but are not limited to, situations in which research participation is required as part of employment or in which the participant is a student, client, or employee of the investigator.

G. The investigator protects the participant from physical and mental discomfort, harm, and danger that may arise from research procedures. If risks of such consequences exist, the investigator informs the participant of the fact. Research procedures likely to cause serious or lasting harm to a participant are not used unless the failure to use these procedures might expose the participant to risk of greater harm or unless the research has great potential benefit and fully informed and voluntary consent is obtained from each participant. The participant should be informed of procedures for contacting the investigator within a reasonable time period following participation should stress, potential harm, or related questions or concerns arise.

H. After the data is collected, the investigator provides the participant with information about the nature of the study and attempts to remove any misconceptions that may have arisen. Where scientific or humane values justify delaying or withholding this information, the investigator incurs a special responsibility to monitor the research and to ensure that there are no damaging consequences for the participant.

I. Where research procedures result in undesirable consequences for the individual participant, the investigator has the responsibility to detect and remove or correct these consequences, including long-term effects.

J. Information obtained about a research participant during the course of an investigation is confidential unless otherwise agreed upon in advance. When the possibility exists that others may obtain access to information, this possibility, together with the plans for protecting confidentiality, is explained to the participants as part of the procedure for obtaining informed consent.

XI. Human Research Protocol for IRB Review

(Copies of this protocol form are available in the IRB office)

Principal Investigator: _____

Title of Investigator: _____

Department: _____

Address: _____

_____

Telephone Number(s): _____

TITLE OF PROJECT

_____

_____

Funding Source:

Number Assigned: _____

Signatures of _____

Principal Investigator	Department Chairman	Advisor
_____	_____	_____
Date	Date	Date
_____	_____	_____

It should be noted that if a research project is performed by someone in a training status (e.g., Medical Student, Intern, Resident), the Department Chairperson and the Project Advisor are responsible for daily oversight of the project. In this instance both the Chairman and the Advisor must sign the application. Reports must be made to the IRB on a quarterly basis to assure proper oversight. Forms for this report are found later in this document.

The policies of KCOM and the assurances provided by the College to the DHHS require the Institutional Review Board to review all research proposals involving human subjects. No research involving humans can be initiated prior to approval from the IRB. In order to comply with these regulations, the IRB requests that you provide the information requested on this page and in the following questions.

ABSTRACT OF PROTOCOL

Within the above space, give a brief synopsis of the research project, describing (1) the purposes and hypotheses, (2) where the research is to be done, (3) the types of subjects involved and how they will be recruited, (4) the role of the subjects (clinical trials, questionnaires, interviews, observation, use of tissues or body fluids, etc.), (5) the parameters to be investigated, (6) the risks and benefits to the subject and society, and (7) how confidentiality will be maintained or anonymity assured.

Names of Other Investigators	Affiliation

Indicate expected sites of investigation

If the investigation is to be conducted at multiple sites, enter the names of each:

Institution Name

Letters confirming cooperation from the appropriate official of each outside institution must be appended

1. Does the research involve using an investigational drug or medical device?
   ____**NO**
   ____**YES** If so, enter the:
   Name of the Drug/Device: _____
   FDA Study Phase of Drug: _____
   IND/IDE Number of Drug/Device: _____

2. Does the research involve using an FDA approved drug or medical device in an unapproved capacity?
   ____**NO**
   ____**YES** If so, enter the:
   Name of the Drug Device: _____
   IND/IDE Number for this use: _____

3. Does the research involve use of radioactive materials in normal subjects, or use in patients in an uncommon way?
   ____**NO**
   ____**YES** If so, a copy of the Letter of Approval from the Radioactive Drug Research Committee must be appended.

4. Does the research involve using a new medical or surgical procedure?
   ____**NO**
   ____**YES** If so, enter the:
   Name of Procedure: _____

5. Does the research involve using an accepted medical or surgical procedure in a new capacity?
   ____**NO**
   ____**YES** If so, enter the:
   Name of Procedure: _____

6. Might the research involve subjects from any of the special groups listed below?
   ____**NO**
   ____**YES** If so, check the appropriate categories.

   ___ Children (subjects of less than legal age)
   ___ Children who are wards of the state, or any other entity
   ___ Adults who are wards of the state, or any other entity
   ___ Pregnant subjects
   ___ Fetuses in utero
   ___ Fetuses ex utero, viable or non-viable
   ___ Prisoners
   ___ Terminally-ill patients
   ___ Handicapped or mentally disabled persons
   ___ Economically or educationally disadvantaged persons

7. Does the research involve more *frequent or greater* risks to the subject than the risks ordinarily encountered in daily life or during the performance of routine physical or psychological examination or tests?
   ____**NO**
   ____**YES**

8. Will research data from any surveys, interviews, and/or observations:
    a. Allow subject identification directly or through identifiers
    AND
    b. Have the potential of placing the subject at risk of criminal or civil liability or of damaging the subject's financial standing, employability, insurability, reputation, or be stigmatizing in any way,
    AND
    c. Have the potential of revealing sensitive aspects of the subject's behavior, such as illegal conduct, drug use, sexual behavior, or use of alcohol?

    ___**NO**
    ___**YES** (Do not answer YES unless *all* above answers (a, b, and c) are "yes.")

9. Will identifiers be maintained, directly or indirectly, on data to be collected?
    ___**NO**
    ___**YES**

If you have answered NO to all the above nine questions or if you have answered YES to questions 6 and/or 9 only, and if your answers are satisfactorily substantiated in the *Abstract of Protocol*, your proposal may be found exempt from continued IRB review. If you are requesting exemption from continued review, complete the appropriate sections below and submit the first 5 pages of this Protocol and Appendix C (and other appended material as appropriate) to the IRB.

If you are not requesting exemption from continued IRB review, complete the Protocol by answering questions 10 through 30. If you answered YES to questions 6, and/or 8, and/or 9, you may request an expedited review by so signifying below, but questions 10 through 30 must be answered and submitted with material requested as *Appendices*.

EXEMPTION REQUESTED **EXPEDITED REVIEW REQUESTED**

_____ _____
Signature of Investigator Signature of Investigator

FOR DEPARTMENTAL IRB SUBCOMMITTEES

The IRB Subcommittee has reviewed the above responses, the details of the proposal, and any appended materials. We recommend to the IRB that (check one):

___ The proposal is exempt from continued IRB review.
___ The proposal may be reviewed expeditiously, but requires continued review.
___ The proposal requires full IRB review

_____ _____
Date Signature of Subcommittee Chairman

_____ _____
Date Signature of IRB Chairman

To complete the Protocol for IRB Review, please supply on additional pages the information requested below. Prepare the information using the same number for each division and subdivision and the same capitalized key words of each as the division and subdivision titles. All categories of information requested must be supplied and submitted with material requested as *Appendices*.

INTRODUCTION

10. Describe the GENERAL PURPOSE of the study.

11. Describe the BACKGROUND RATIONALE for the study. (If a new drug or medical device is being used, describe any results from previous animal or human studies, including the risks and benefits observed. If therapy will be modified, explain standard therapy. If a questionnaire is being used, include information supporting its validity and reliability.)

12. List the SPECIFIC AIMS AND HYPOTHESES.

13. Describe the PREVIOUS EXPERIENCE of each investigator(s) in this study and the responsibilities of each investigator in this study.

METHODOLOGY

14. Describe the EXPECTED GROUPS(S) (control, experimental, etc.) which will comprise the study.

15. Give the NUMBER OF SUBJECTS anticipated for each of the above groups.

16. Outline the INCLUSION CRITERIA for subjects into each group. (Justify the involvement of any of the special groups of citizens cited in question 6.)

17. Outline the EXCLUSION CRITERIA for subjects from each group.

18. Describe the method(s) of SUBJECT RECRUITMENT (media ads, posters, mailing list, classroom announcements, clinic or hospital surveillance, etc.).

19. Describe the method of SUBJECT ASSIGNMENT to each group (randomization technique, sequential assignment, double-blind, etc.).

20. Describe in detail the ROLE OF SUBJECTS in the investigation (drug trials, medical device studies, follow-up visits or tests, questionnaires, use of body fluids, observation, etc.).

21. Describe the PARAMETERS TO BE MEASURED, and how and when these measurements will be made.

22. Describe the EXPECTED DURATION of the total study, and the duration of each subject's participation.

23. Describe how DATA ANALYSIS will be accomplished (statistical tests, consultation with statisticians, etc.) and indicate the smallest unit or group for which separate reporting will occur.

RISK/BENEFIT ASSESSMENT

24. Describe any foreseeable RISKS TO THE SUBJECT which might arise from participation in this study, including the risks which might result from loss of confidentiality. Include an assessment of each risk and cost of participation, and indicate the steps you have taken to minimize each risk. Describe subject costs and reimbursements.

    A. PHYSICAL RISKS
    B. PSYCHOLOGICAL RISKS
    C. SOCIAL RISKS
    D. ECONOMIC RISKS
    E. LEGAL RISKS
    F. OTHER RISKS

Investigators may be required to provide a subject/patient input of subjective assessment to the IRB.

25. Describe the POSSIBLE BENEFITS TO SUBJECT.

26. Describe the POSSIBLE BENEFITS TO SOCIETY.

27. Describe any accepted ALTERNATIVE PROCEDURES OR THERAPIES which are available to the subject, including the alternative of non-participation.

SUBJECT CONSENT

28. Describe how INFORMED CONSENT will be obtained. Indicate who will discuss risks, benefits, and alternatives with the subject; where and when this discussion will occur; and measures taken to assure the subject's understanding of the study.

29. Describe how SUBJECT CONFIDENTIALITY will be maintained. Indicate the measures employed to protect the identity of the subject, how records will be protected, and who will have access to the confidential information.

30. Append a copy of the CONSENT FORM. Use the attached Model Consent Form in developing the consent form. Follow the directions stated at the top and throughout the Model. Enough information about the purpose and procedures must be provided in every day language so that the subject will have an adequate comprehension of the hazards and benefits of participation. Statements of rights and alternatives assure the voluntariness of consent and participation. If there will be no consent form or if not all elements of informed consent are to be addressed, please justify. A copy of the Informed Consent Form (ICB) will be provided to the IRB for formal review.

APPENDICES

A. Copy of the Consent Form, prepared in accordance with "30" above.
B. Copies of full proposal/protocol prepared by you (or your sponsor) for other purposes.
C. Copies of any research instruments (questionnaires, letters to institutions and prospective subjects, material to be read or seen by subjects, investigator's brochure, etc.).
D. Bibliography, if not provided in (B).
E. Copies of pertinent literature.
F. Copies of letters of cooperation from outside institutions.
G. Copy of the Letter of Approval from the Biohazards Committee.

XII. Elements of Informed Consent

The Food and Drug Administration has issued regulations pertaining to the elements required in an informed consent. All informed consents must comply with these regulations. To ensure compliance, the informed consent itemization listed below is provided to guide the investigator in drafting an acceptable informed consent. Please include any statement that is relevant to your project. However, you do not have to include the language example listed below.

1. A statement that the study involves research, an explanation of the purposes of the research, the expected duration of the your participation, a description of the procedures to be followed, and identification of any procedures which are experimental.

2. A description of any reasonably foreseeable risks or discomfort to you.

3. A description of any benefits to you or to others which may reasonably be expected from the research.

4. A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to you.

5. A statement of whom to contact for answers to pertinent questions about the research, and whom to contact in the event of a research-related injury to you, that person is the IRB Chairperson, currently R.J. Theobald, Jr., Ph.D. (660-626-2316).

6. A statement that participation is voluntary, that refusal to participate will involve no penalty or loss of benefits to which you are otherwise entitled, and that you may discontinue participation at any time without penalty or loss of benefits to which you are otherwise entitled.

7. A statement regarding confidentiality of records including references to:

   a. Confidential follow-up form filed at KCOM IRB
   b. KCOM IRB personnel reviewing pertinent medical records associated with the study
   c. The possibility that FDA staff may review pertinent medical records associated with the study

8. As required under new Federal law, the Health Insurance Portability and Accountability Act (HIPAA), the Notice of Privacy Practice has been explained to me, I was permitted to ask questions about HIPAA and which, in summary, included the following information:

   The commitment to privacy and a contact person to whom I can direct questions.

   An explanation of how my information may be used and disclosure of which individually identifiable health information (Information) may be used.

   How my information may be used and disclosed in certain special circumstances.

   My rights regarding my Information.

The HIPAA Privacy Rule protects the privacy of personal health information contained in your medical records (defined as "protected health information" (PHI) by HIPAA). The University has to obtain this Authorization from you so it can use your personal health information for the medical research described in this Consent Form. This Authorization gives you information about:

how your health information may be used as part of the research,
how your health information may be disclosed to others as part of the research,
who may disclose and receive your health information.

By signing this document, you agree to the release of certain personally identifiable health information from your medical record by (person or entity releasing information) to (the Principal Investigator, Researcher, and other members of the research team) or others as listed: for the research purposes described in this Consent Form and to the research sponsor and government agencies as required to monitor the research.

SPECIFIC AUTHORIZATIONS

The following information will not be released unless you specifically authorize its disclosure by initialing the relevant line(s) below:

_____ I specifically authorize the release of information pertaining to drug and alcohol abuse diagnosis or treatment (42 C.F.R. §§2.34 and 2.35).

_____ I specifically authorize the release of information pertaining to mental health diagnosis or treatment as follows:_____

_____ I specifically authorize the release of HIV/AIDS testing information.

_____ I specifically authorize the release of genetic testing information.

The Investigator must circle one of the following two options:

This Authorization will expire at the end of the research study;

OR

This Authorization has no expiration date.

REVOKING AUTHORIZATION

You can cancel this Authorization to allow release of your personally identifiable health information from your medical record at any time. To cancel this Authorization: write to the principal investigator identified in this Consent Form, or ask a member of the research team to give you a form to revoke this Authorization.

If you cancel this Authorization, you will not be able to continue to participate in the research. The cancellation could affect your current research related treatment. You may want to discuss with your research team any impact on your treatment of revoking this Authorization. If you cancel this Authorization, the principal investigator and the research team may continue to use information about you that has already been collected.

POSSIBLE DISCLOSURES

Once your health information is disclosed to the research team it is not protected under HIPAA. The information may be redisclosed to others and the HIPAA Privacy Rule would not apply in those circumstances. Nevertheless the research team will continue to protect your personally identifiable health information as described in this Consent Form and the Notice of Privacy Practice. The research team and the University will comply with the requirements of all applicable laws that protect the confidentiality of your health information.

_____ _____
Signature of Subject Date

(If subject is between 12 and 18 years of age, provide a space for the child's signature, assenting to participation. Also provide a separate space for the parent or guardian's signature.)

_____

_____ _____
Print Name of Subject Date

_____ _____
Signature of Witness Date
(If required by the sponsor or funding agency or if the particular nature of the subject, investigation, or consent process suggest the need for a witness. There is no general legal requirement for a witness.

9. "I certify that I have explained to the above individual the nature and purpose, the potential benefits and possible risks associated with participation in this research study, have answered any questions that have been raised, and have witnessed the above signature."

10. "These elements of Informed Consent conform to the assurance given by the University to the DHHS to protect the rights of human subjects."

11. "I have provided the subject/patient a copy of this signed consent document."

_____ _____
Signature of Investigator Date

(Each consent form must be signed by the investigator at the time consent is obtained.)

12. A statement of compensation and medical treatment available if injury occurs. The following may be incorporated:

> "If during the course of this study any injury shall occur to you as a direct result of the administration of study drug therapy,_____ agrees to pay all medical expenses necessary to treat such injury (1) to the extent you are not otherwise reimbursed by medical insurance and (2)

provided you have followed the directions of the investigator.

If you desire, you may arrange to have such treatment performed by a licensed physician selected by you; however, upon your request_____ will arrange to have such treatment provided by the investigator or some other licensed physician.

_____makes no commitment to provide compensation beyond that specified. However, should you require further information, you should contact _____, or IRB Chairman, Dr. Robert J. Theobald, 800 W. Jefferson, Kirksville, MO 63501 (660) 626-2316.

13. *A statement of any additional costs to you that may result from participation.

14. *The consequence of your decision to withdraw and procedures for orderly termination of participation.

15. *A statement that significant new findings will be conveyed to you in writing.

16. *A statement that certain risks may be currently unforeseeable.

17. *A statement that individual participation may be terminated by the investigator with or without your consent.

18. *A statement of the approximate number of patients in the study.

19. A copy of the consent form given to the patient.

20. A statement of consent, e.g., "I agree to participate....."

21. A place for signature and date of signature for the patient or patient and parent (or legally authorized representative).

22. Each page of the Informed Consent must have a place for the patient's initials.

23. The IRB phone number should be included in the Informed Consent.

* When appropriate, one or more of these additional elements should also be included.

Please submit all material in original, plus three copies.

XIII. Model Consent Form

Read and address each numbered element of this model form in developing a consent form for the proposed human research study. The items numbered and in quotations are to be included in the consent form. The consent form must be written in lay language. When the subject is a child or ward, substitute "my ward" when appropriate. Add additional statements as directed and/or when appropriate. Copies of this Model Consent Form are available in the IRB office.

KIRKSVILLE COLLEGE OF OSTEOPATHIC MEDICINE
(Also list other facilities where the research will be conducted.)

CONSENT FOR PARTICIPATION IN RESEARCH ACTIVITIES
List all investigators on the protocol who may request subject participation and list their academic titles.

1. You agree to participate in a research study at this institution. The title of the research is *title of research.*

2. "You understand that the purpose of the research is to . . . ."
   Also, briefly describe the pertinent background information justifying the research, so that the subject can understand why the research is important.

If appropriate:
Indicate the number of subjects to be involved in the study.
If the study is also being performed at other institutions, indicate the number of institutions and total number of subjects. This information should be included if it may have a bearing on the subject's decision to participate.

3. "Your participation will involve . . . "
   Describe the subject's participation and identify those aspects of participation which are experimental or which would not be used otherwise. Indicate the expected duration of the subject's participation.

4. "You understand there are possible risks to you if you agree to participate in the study. They are." Any foreseeable risks or discomforts, including the consequences of ineffective treatment shall be explained. Breach of confidentiality, embarrassment, loss of privacy, etc., should also be considered as risks.

   "You understand that if side effects or discomforts do occur, *name of investigator* will try to minimize and treat these by. . . ." **If appropriate, add the following statements:**

Patient's Initials_____

"You understand that the treatment or procedure described may involve risks to you which are currently unforeseeable."

"You understand that the researcher may terminate your participation without regard to your consent under certain circumstances or when, in the investigator's judgement, it is in your interest to do so."

5. "You understand that the results of the research study may be published but that your name or identity will not be revealed and that your records will remain confidential. In order that confidentiality can be maintained, *name of investigator* will . . ."

Describe the specific procedure for maintaining the subject's confidentiality. Indicate specifically how the investigator will keep the names of subjects confidential, the use of subject identifiers (codes), how this information will be secured, and who will have access to the confidential information. "Confidentiality will be maintained" is not acceptable.

If appropriate, include the statements:

"You understand that your records from this study may be reviewed by the FDA and/or *the sponso*r.

6. "You understand that the possible benefits of your participation in the research study are . . . " Describe the benefits of participation, or lack of benefits, to the individual subject as well as to society.

If appropriate, include the statements:

"You understand that your participation in this study will not benefit you."

7. "You understand that there are alternatives to this procedure." If the only alternative is non-participation, state, "I understand that the alternative is non-participation." If there are other alternatives that either are procedural or therapeutic, these should be stated in language the subject can understand. Explain the risks and benefits of the alternatives.

8. "You also understand that your participation is voluntary and that refusal to participate will involve no penalty to you or loss of benefits to which you are otherwise entitled. You also understand that you may withdraw from the research study at any time without penalty or prejudice."

If appropriate, include the statements:

"You understand that if you do withdraw from the research there may be possible risks to your health. They are. . . ."

"If you withdraw from the study, you will notify *name of investigator*, who will try to minimize the risks of withdrawing by . . . ."

Patient's Initials _____

"You will be informed of any significant (major) new findings developed during the course of your participation in this research which may have a bearing on my willingness to continue in the study."

"As a voluntary participant in this research study, you understand that you will be charged (or not be charged) for . . . "

(consider the cost of drugs, devices, procedures, treatment of side effects, follow-up tests, etc.)

9. "You will be paid $_____ for participation in the research study. If you should decide to terminate your participation prior to completion, you will be paid $_____.

10. "You understand that there may be harm to an embryo or fetus if you should become pregnant. To the best of your knowledge, you am not pregnant, and if you do become pregnant, you will notify the researcher of my pregnancy.

11. "To the best of my knowledge, you are not participating in any other medical research study".

Add the above element if the study is medical research. If potential subjects are or may be involved in other medical research studies, contact the IRB office for further instructions.

12. "Any questions that you may have concerning your participation in the research study will be answered by *name of individual*, who can be reached at (telephone number).

13. "You understand that the *name of individual* will evaluate and refer you for treatment in the event that an injury results because of your participation in this project. The College has not set aside funds to provide financial compensation. The College assumes no liability for any injury that results from your participation in this project.

This element must be included in all research where the risks are judged to be more than minimal, and in all investigational clinical studies.

14. "If you have any questions about your rights as a research subject or in the event your believe you have suffered any injury as a result of participation in the research project, you may contact, Robert Theobald, Ph.D., the Chairman of KCOM Institutional Review Board (660-626-2316), who will discuss your questions or will be able to refer you to the individual who will review the matter with you, identify other resources that may be available, and provide further information as to how to proceed."

Patient's Initials_____

15. "I have read the above statement and have been able to ask questions and express concerns, which have been satisfactorily responded to by the investigator. I believe I understand the purpose of the study as well as the potential benefits and risks that are involved. I hereby give my informed and free consent to be a participant in this study."

Date _____ Signature of Subject _____

(If subject is between 12 and 18 years of age, provide a space for the child's signature, assenting to participation. Also provide a separate space for the parent or guardian's signature.)

Print Name of Subject _____

Signature of Witness _____

(If required by the sponsor or funding agency or if the particular nature of the subject, investigation, or consent process suggest the need for a witness. There is no general legal requirement for a witness.

16. "I certify that I have explained to the above individual the nature and purpose, the potential benefits and possible risks associated with participation in this research study, have answered any questions that have been raised, and have witnessed the above signature."

17. "These elements of Informed Consent conform to the assurance given by KCOM to the DHHS to protect the rights of human subjects."

18. "I have provided the subject/patient a copy of this signed consent document."

Date _____ Signature of Investigator _____

(Each consent form must be signed by the investigator at the time consent is obtained.)

Please submit all material in original, plus three copies.

XIV. Model Advisor Report Form

Read and address each numbered question below (for the reporting period only) and submit this form every three (3) calendars months that this project is active. The frequency of these reports may be increased by the IRB if it is deemed necessary by the IRB. If you have questions, please contact Robert Theobald, Ph.D., the Chairman of KCOM Institutional Review Board (660-626-2320) (rtheobald@atsu.edu).

Title of Project: _____

Advisor: _____ _____

Name Title

Reporting Period: Start _____ End _____

1. How many potential subjects have been interviewed for this project? _____

2. How many subjects were enrolled in the project? _____

3. How many subjects were assigned to the
   control group? _____ treatment group? _____

4. How many subjects are still enrolled? _____

5. Have there been any adverse events in any subject? Y ____ N _____
   If Yes, please describe including number of subjects, type of adverse event, severity, and if the research protocol contributed to the adverse event.

   What was the resolution of the adverse event?

6. Open Comment:

Advisor's Signature: _____ Date: _____

XV. REVIEWER'S CHECKLISTS

To Reviewers: _____ Date: _____
Investigator: _____ IRB #: _____

In the enclosed HUMAN RESEARCH PROTOCOL FOR IRB REVIEW, the investigator should have addressed each of the categories numbered below. Indicate YES on the checklist if the information is adequate and meets the guidelines for IRB approval. Indicate NO if the information is inadequate and/or does not meet guidelines for approval. Organize your written objections/suggestions on additional pages using the same numbers as used for each category below. After you have completed the review, please return this page and any written suggestions/objections to the IRB office.

APPROVAL		PROTOCOL CATEGORY
YES	**NO**	
___	___	1. Investigator's assessment of status of a new drug/device
___	___	2. Investigator's assessment of use of an approved drug/device
___	___	3. Investigator's assessment of use of radioactive materials
___	___	4. Investigator's assessment of new medical/surgical procedures
___	___	5. Investigator's assessment of use of approved procedures
___	___	6. Investigator's assessment of subjects' being in special groups
___	___	7. Investigator's assessment of minimal risks
___	___	8. Investigator's assessment of risks if confidentiality is broken
___	___	9. Investigator's assessment of anonymity
___	___	10. General purpose of the investigation
___	___	11. Background rationale and previous human/animal studies
___	___	12. Specific aims and hypotheses
___	___	13. Previous experience of investigator(s)
___	___	14. Expected groups in investigation
___	___	15. Number of subjects
___	___	16. Inclusion criteria
___	___	17. Exclusion criteria
___	___	18. Subject recruitment
___	___	19. Subject assignment to groups
___	___	20. Role of subject in study
___	___	21. Parameters measured
___	___	22. Duration of study
___	___	23. Data analysis
___	___	24. Risks to subject, and minimization of risks
___	___	25. Benefit to subject
___	___	26. Benefit to society
___	___	27. Alternatives procedures or therapies
___	___	28. Method of obtaining consent
___	___	29. Subject confidentiality, and maintenance of confidentiality
___	___	30. Consent form - see next page

Use the following checklist while reviewing each element of the consent form. Check YES if the element is satisfactory. NO if not satisfactory, or NA if the element is not required. Organize any written objections/suggestions on additional pages using the same numbers as used for each element below.

APPROVAL			**CONSENT FORM ELEMENT**
YES	**NO**	**NA**	
___	___	___	30.01 Investigator's title and research title
___	___	___	30.02 Explanation of purpose and justification of research
___	___	___	30.03 Description of subject's participation
___	___	___	30.04 Description of risks, and minimization of risks
___	___	___	Description of investigator's aid in case of side effects
___	___	___	30.05 Declaration and explanation of confidentiality
___	___	___	30.06 Description of benefits to subject/society
___	___	___	30.07 Description of alternative procedures
___	___	___	30.08 Explanation of voluntary participation
___	___	___	30.09 Statement of pregnancy status
___	___	___	30.10 Statement of non-participation in other medical research
___	___	___	30.11 Statement naming investigator who will answer questions
___	___	___	30.12 Statement of KCOM liability in cause of injury
___	___	___	30.13 Statement of referring subject to IRB in case of injury
___	___	___	30.14 Statement that subject has read and understands consent
___	___	___	30.15 Statement that investigator has explained the research
___	___	___	30.16 Statement that consent elements conform to regulations
___	___	___	30.17 Statement that subject is given copy of consent form

Is the consent form clearly written and in lay language?
Do the benefits of the research outweigh the risks?

Comments:

I have reviewed the enclosed Protocol and recommend:

___ Full approval ___ Deferral

___ Contingent approval ___ Disapproval

___ Suggestions/contingencies/objections attached

_____ _____

Signature of Reviewer Date

XVI. REQUEST FOR PROJECT RE-REVIEW
Kirksville College of Osteopathic Medicine
Institutional Review Board

REQUEST FOR PROJECT RE-REVIEW

Reason for Re-Review (check 1)

Periodic Review___ Change in Protocol___

Report of Untoward Event___ Project Ended___
(must be reported immediately)

Expedited: Yes____ No____

Principal Investigator:_____Date:_____

Department: _____

Home Address:_____

Title of Project:_____

IRB #:_____Date of Last IRB Approval:_____

Please check appropriate items and attach pertinent information

__1. The study is in progress as last approved by the IRB and a (not more than 200 word) summary of findings within that period is attached. Attached is a copy of the consent form which is being used at present.

__2. The study is in progress; attached is the description of a change in protocol, including the reasons for the change. (If due to untoward event, include date event occurred and date of initial notification of IRB.)

__3. The study has been discontinued for the following reason:

__4. The study was never begun for the following reason:

__5. The study has been completed and a brief (two-three paragraph) summary is attached.

__6. A legal _____, medical _____, or other _____ problem has developed; attached is a description of the situation. (Include date problem was first noted and date of initial notification of the IRB.)

__7.The problem has been resolved, as the attachment describes.

Principal Investigator:_____ (signature)

Advisor or
Dept. Chairman:_____ (signature)

This form and attachments should be submitted as noted in your last approval letter or as appropriate, ten (10) days before a scheduled IRB meeting.

Send this form and its attachments to the Coordinator, Institutional Review Board, KCOM. For further information, contact the Coordinator at 660-626-2316.

XVII. Institutional Review Board Membership
A. T. Still University - KCOM IRB #1

Name	Sex	Date of Appt.	Background (profession, or capacity)	Institution Affiliation (College, Hospital, Government, Agency, etc.)
Theobald, Robert	M	01/01/85	Ph.D., Pharmacology Department Chairman	KCOM
Nancy L. Rourke	F	07/29/14	Risk Manager/ Facility Compliance Officer N.E. Reg. Medical Center	NRMC
Matt Eichor	M	12-04-80	Retired	Community
Stuart, Melissa	F	08-21-00	Ph.D., Microbiology	KCOM
Evans, Maria	F	08-21-00	M.D., Pathology	Community
Snider, Karen	F	08-21-00	D.O., OMM	KCOM
Grider, John	M	07-29-14	D.O., Internal Medicine	KCOM
Goldman, David	M	01-29-09	JD, DO, FCLM	KCOM
Deborah Clay	F	08-23-12	Sponsored Research and Program Development	KCOM
Jane Johnson	F	07-02-14	Sponsored Research and Program Development	KCOM
Tim Geisbuhler	M	07-02-14	Ph.D., Physiology	KCOM

Name: A.T. Still University – KCOM IRB #1
Assurance No.: FWA00001046
IRB No.: IRB00000557