Belmont report

What was the charge of the commission? 1. Identifying the ethical principles to guide all research involving human subjects2. Developing guidelines for the conduct of ethical research involving human subjectsWhat are the two basic ideas in principle of respect for persons? 1. Individuals should be treated as autonomous agents. Prospective research participants must be given the information they need to determine whether or not they want to participate in research. There should be no pressure to participate and ample time to decide. Respect for persons demands that participants enter into the research voluntarily and with adequate information. This is called informed consent, and will be covered in detail in other sections of this training. A legally-effective, voluntary agreement that is given by a prospective research participant following comprehension and consideration of all relevant information pertinent to the decision to participate in a study. 2. Persons with diminished autonomy are entitled to additional protections. Special provisions may need to be made when an individual's comprehension is severely limited or when a class of research participants is considered incapable of informed decision making (e. g. children, people with severe developmental disorders, or individuals suffering from dementias). Even for these persons, however, respect for persons requires giving them the opportunity to choose, to the extent they are able, whether or not they wish to participate in research activities. In some cases, respect for persons may require seeking the permission of other parties, such as a parent or legal guardian. What are the challenges in applying the Belmont principle of respect for persons?* Making sure that potential participants comprehend the risks and potential benefits of participating in research* Avoiding influencing potential participants' decisions either through explicit

or implied threats (coercion) or through excessive compensation (undue influence)What is the challenge inherent in applying the Belmont principle of beneficence? It is how to determine when potential benefits outweigh considerations of risks and vice versa. What is Subpart A, also called?“ The Common Rule”, describes the required protections for all human subjects. How does subpart A define human subject? Subpart A defines a human subject as “ a living individual about whom an investigator…conducting research obtains:“ OHRP considers the term investigator to include anyone involved in conducting the research. OHRP does not consider the act of solely providing coded private information or specimens (for example, by a tissue repository) to constitute involvement in the conduct of the research. Note that if the individuals who provide coded information or specimens collaborate on other activities related to the conduct of this research with the investigators who receive such information or specimens, then OHRP would consider such additional activities to constitute involvement in the conduct of the research. Examples of such additional activities include, but are not limited to: (1) the study, interpretation, or analysis of the data resulting from the coded information or specimens; and (2) authorship of presentations or manuscripts related to the research.”

1. Data through intervention or interaction with the individual, or2. Identifiable private information.”

How does subpart A define research? Subpart A defines research as “ a systematic investigation…designed to develop or contribute to generalizable knowledge.”

This definition includes:

* Research development* Testing* Evaluation

What are considered vulnerable populations? Subparts B, C and D define the specific categories of research in which pregnant women, human fetuses and neonates, prisoners, or children respectively may be involved. The subparts describe additional requirements for informed consent, and may specify additional responsibilities for the Institutional Review Board (IRB) when reviewing research involving these populations, and list the requirements for research that need additional levels of review and approval. What are the criteria to evaluate application for research in supporting human subjects? The HHS regulations (45 CFR 46. 120) require that Federal Departments and Agencies that conduct or support human subjects research must evaluate all applications for research using the following criteria:

* Risks to the subjects* Adequacy of protection against these risks* Potential benefits of the research to the subjects and others* Importance of the knowledge gained or to be gained

What should each institution have to engage in NIH funded human subject research? Each institution that is engaged in NIH-funded human subjects research must:* Obtain or hold a current Federalwide Assurance (FWA), assuring that an institution will comply with HHS regulatory requirements for the protection of human subjects (this is obtained from the HHS Office for Human Subjects Protections (OHRP)); and* Certify to NIH that grant applications and contract proposals describing research involving human subjects has been reviewed and approved by an Institutional Review Board

(IRB) designated in the FWA, and will be subject to continuing review by an IRB. What is an IRB? IRBs are committees that consist of 5 or more members with varying expertise and diversity that are responsible for reviewing and approving human subjects research activities on behalf of institutionsWhat are the principles of respect? The principle of respect for persons can be broken down into two basic ideas: 1. Individuals should be treated as autonomous agents“ An individual capable of deliberation about personal goals and of acting under the direction of such deliberation.” 2. Persons with diminished autonomy are entitled to additional protectionsHow can IRB waive or alter some or all of the required elements of an informed consent? The HHS regulations (45 CFR 46. 116(c)) allow institutional review boards (IRBs) to waive or alter some or all of the required elements of informed consentA legally-effective, voluntary agreement that is given by a prospective research participant following comprehension and consideration of all relevant information pertinent to the decision to participate in a study. if all of the following conditions are met: 1. “ The research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine: (i) 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; (iv) possible changes in methods or levels of payments for benefits or services under those programs, and2. The research could not practicably be carried out without the waiver or alteration.” How should an individual’s consent be assessed? An individual’s capacity to consent to a particular study should be assessed

based on:“ An individual capable of deliberation about personal goals and of acting under the direction of such deliberation.”

1. The individual’s level of capacity, and2. The complexity and risks of the study, i. e., the capacity needed for an individual to be able to understand the study well enough to consent to participate

What does HHS require with studies involving pregnant women? The HHS regulations require:* Preclinical studies be completed prior to the involvement of pregnant women* A consideration of risks and potential benefits for the fetus and pregnant womanWhat do you do for informed consent with children subjects? Children may not have full capacity to make decisions in their own best interests; and therefore:“ Persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted.”* Children are considered a vulnerable population, and* Children are unable to provide “ legally effective informed consent” as required by the HHS regulations at 45 CFR 46. 116A legally-effective, voluntary agreement that is given by a prospective research participant following comprehension and consideration of all relevant information pertinent to the decision to participate in a study. Because children cannot provide informed consent, children provide assent to participate in research, to the extent that they are able, and parents/guardians give permission for a child to participate in research. What are the additional protections for prisoners involved in research and why do they need them? The HHS regulations (45 CFR 46, Subpart C) require additional protections for prisoners who are involved as participants in

research because they may “ be under constraints because of their incarceration which could affect their ability to make a truly voluntary and uncoerced decision whether or not to participate as subjects in research.” What are the requirements for consent with prisoners? The requirements specific to informed consent for prisoners are: A legally-effective, voluntary agreement that is given by a prospective research participant following comprehension and consideration of all relevant information pertinent to the decision to participate in a study.

1. “ Any possible advantages accruing to the prisoner through his or her participation in the research, when compared to the general living conditions, medical care, quality of food, amenities and opportunity for earnings in the prison are not of such a magnitude that his or her ability to weigh the risks of the research against the value of such advantages in the limited choice environment of the prison is impaired” 2. “ Adequate assurance exists that parole boards will not take into account a prisoner’s participation in the research in making decisions regarding parole, and each prisoner is clearly informed in advance that participation in the research will have no effect on his or her parole”

What is community consultation? The appropriate way to attain community consent may vary widely, but is often achieved through meetings with large groups of community representatives or community leaders. A legally-effective, voluntary agreement that is given by a prospective research participant following comprehension and consideration of all relevant information pertinent to the decision to participate in a study. Graphic of a group of people with text Community Consultation Consultation. It is also

appropriate to consult a community before conducting research when the research involves risk to discrete, identifiable populations. For example, members of a community may feel stigmatized if a number of members of that community participate in research that may reveal unpopular or dangerous traits. What are the rules with beneficient in research? Two general rules have been articulated as complementary expressions of beneficent actions:

1. Do no harm2. Maximize possible benefits and minimize possible harms

What are the categories of risk and explain each one. Most risks encountered by participants in research fall into the following categories:

A. PhysicalPhysical risks may include pain, injury, and impairment of a sense such as touch or sight. These risks may be brief or extended, temporary or permanent, occur during participation in the research or arise after.

B. PsychologicalPsychological risks can include anxiety, sadness, regret and emotional distress, among others. Psychological risks exist in many different types of research in addition to behavioral studies.

C. SocialSocial risks exist whenever there is the possibility that participating in research or the revelation of data collected by investigators in the course of the research, if disclosed to individuals or entities outside of the research, could negatively impact others' perceptions of the participant. Social risks can range from jeopardizing the individual's reputation and social standing, to placing the individual at-risk of political or social reprisals.

D. LegalLegal risks include the exposure of activities of a research subject “ that could reasonably place the subjects at risk of criminal or civil liability.”

E. EconomicEconomic risks may exist if knowledge of one’s participation in research, for example, could make it difficult for a research participant to retain a job or to find a job, or if insurance premiums increase or loss of insurance is a result of the disclosure of research data.

What is the protection of physical risk? In many situations, physical risks in research can be minimized by carefully and skillfully following protocols, by having trained individuals conduct research procedures, through careful monitoring of research participants’ health status, by recruiting appropriate populations, and by providing clinical care when needed. What is the protection of psychological risk? Possible ways to protect against psychological risks include reminding participants of their right to withdraw from research or limit their participation if they become uncomfortable, providing counseling or psychological support for participants who experience distress, or thoroughly debriefing research participants after research sessions are completed. What is the protection of social risk? Often, minimizing social risks to participants involves protecting confidential data, including not only the data collected, but the fact of participation in the research project itself. D. LegalWhat is the proctection with legal risk? Protections against legal risks often involve protecting the confidentiality of research data. For studies conducted in the United States, investigators can apply for Certificates of Confidentiality, which are intended to prevent investigators from being forced to disclose data that can be linked to identifiable research participants in legal proceedings. What is the protection

of economic risk? Protecting confidentiality of data is one method for protecting against economic risks, such as those to employability and insurability. Investigators may elect to keep research data separate from medical records in order to prevent employers and insurance companies from obtaining information that could put the participants at risk. What are the regulated Protections against risks? Where appropriate, investigators must describe procedures for minimizing potential risks, including risks to confidentiality, plans for ensuring any necessary medical or professional intervention, plans for data and safety monitoring for clinical trials, etc. What are the regulated potential benefits to individual participants? The proposed research has a favorable ratio of potential benefit to risk. This balancing act is often called a risk-benefit analysis. What is the importance of the knowledge to be gained? Investigators reasonably anticipate that the research will contribute to generalizable knowledge. This generalizable knowledge is considered a benefit to others, and risks to research participants must be reasonable in relation to the importance of the knowledge that reasonably may be expected to resultWhat are undue inducements? Undue inducements are troublesome because: 1. offers that are too attractive may blind prospective subjects to the risks or impair their ability to exercise proper judgment; and2. they may prompt subjects to lie or conceal information that, if known, would disqualify them from enrolling — or continuing — as participants in a research project. What is therapeutic misconception? Therapeutic misconception is the tendency for research participants to:

“… downplay or ignore the risks posed to their own well-being by participation … [due to] the participants’ deeply held and nearly unshakeable conviction that every aspect of their participation in research has been designed for their own individual benefit.”

What are the principle of beneficence factors that investigators consider? The principle of beneficence requires that investigators consider a number of factors including:* EquipoiseSubstantial scientific uncertainty about which treatments will benefit subjects most, or a lack of consensus in the field that one intervention is superior to another.* Protecting the privacy of research participants and the confidentiality of research data* Establishing oversight mechanisms to protect the rights and welfare of research participants and to determine the significance of the dataWhat is equipose? Equipoise is essential for obtaining generalizable knowledge. If a clear and agreed-upon answer exists, asking research participants to assume the risks of research that will provide the same information is not acceptable; no new knowledge will be gained from the study. What is the general criteria IRB needs from researchers?* Risks to human subjects are minimized* Risks to human subjects are reasonable in relation to anticipated benefits, if any, to human subjects and the importance of the knowledge that may reasonably be expected to result from the research* Selection of human subjects is equitable* Informed consent will be sought from each prospective research participant or the prospective research participant’s legally authorized representative in accordance with and to the extent required by the HHS regulations (45 CFR 46. 116)A legally-effective, voluntary agreement that is given by a prospective research participant following comprehension and

consideration of all relevant information pertinent to the decision to participate in a study.“ An individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject” s participation in the procedure(s) involved in the research.”* Informed consent will be appropriately documented in accordance with and to the extent required by the HHS regulations (45 CFR 46. 117)* When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of the human subjects, and when appropriate there are adequate provisions to protect the privacy of human subjects and to maintain the confidentiality of dataWhat is an expedited review from the IRB? Investigators should understand that expedited review is conducted by fewer individuals, but is no less stringent and not necessarily faster than a full IRB review. If any individual reviewer who conducts an expedited review is unable to approve a proposed study, the study must be discussed by the full IRB. What are data and safety monitoring plans? Data and Safety Monitoring Plans describe protections for research participants and data integrity, and oversight for clinical trials at a level that is commensurate with the risks of participating in the clinical trial. That is, the method and frequency of monitoring is directly related to the possible harms to research participants in the clinical trial. What is justice? The definition of justice has two parts:* Fair procedures and outcomes are used to select research participants, and* There is a fair distribution of benefits and burdens to populations who participate in research. What is individual justice? Individual justice requires that investigators “ should not offer potentially beneficial research only to some patients who are in their favor or select only ‘ undesirable’ persons for risky research. What is social justice?

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.” What does it mean with Equity vs. Equality in Human Subjects Research? To treat “ equitably” means to treat fairly; To treat “ equally” means to treat in exactly the same way.

Research should strive for equitable distribution of the risks and potential benefits of the research. This means that investigators are treating the groups involved in the research fairly and justly. It does not necessarily mean that all groups are equally represented, but that their representation is fair and just based on the risks and potential benefits associated with the research.

What is equitable distribution? In order to achieve an equitable distribution of the risks and potential benefits of the research, investigators must determine the distribution of different groups (men and women, racial or ethnic groups, adults and children, age, etc.) in the populations that: 1. May be affected by the disease or condition under study, and2. That are anticipated to benefit from the knowledge gained through the researchWhy is it important to have NIH Inclusion Policies: Women and Minorities? Because knowledge gained from clinical research may define health policy and shape standards of care for all patients, it is important to consider whether the intervention or therapy under scrutiny “ affects women or men or members of minority groups and their subpopulations differently.” How does a researcher justify the use of placebos? Examples of justifications for

the use of placebos include: An inactive intervention designed to resemble, as much as possible, its active counterpart in clinical research. 1. When there are no approved, effective treatments for the condition, or2. If there is disagreement about whether standard treatment is better than placebo, or3. When the additional risk posed by the use of placebo is minor and withholding the current standard therapy would not lead to serious or permanent harm, or4. If the study is anticipated to result in widespread or major benefits and the receipt of placebo by individuals poses minimal risk. What does “ practice” refer to? Interventions that enhance the well-being of an individual client and the expectation of success. What does “ research” refer to? Designates an activity designed to test a hypothesis to be drawn, and to develop or contribute to generalizable examples in theories, principles, and statements in the relationships described in a formal protocol that has objectives and a plan to reach that objective. How is experimental and research different? 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. What are the three basic ethical principles? 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 of persons, beneficence and justice. What are 3 examples to show lack of respect? 1. to repudiate that person’s considered judgments, 2. to deny an individual the freedom to act on those considered judgments, 3. to withhold information necessary to make a considered judgment, when there are nocompelling reasons to do so. Why does the

selection of research subjects need 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 because of easy availability, their compromised position, or manipulation rather than for reasons directly related to the problem being studied. 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. What is the question that remains regarding informed consent? What the standard should be for judging how much and what sort of information should be provided. What are the 3 criteria to be met when incomplete disclosure is used? 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. What does practice refer to?...the term “ practice” refers to interventions that are designed solely to enhance the well-being of an individual patient or client and that have a reasonable expectation of success. What does research refer to?...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. How is experiental and research different? 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. What the three basic ethical principles? the principles of respect of persons, beneficence and justice. What are 2 basic convictions related to respect of persons? 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. What are 3 examples to show lack of respect? 1. 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 an instructive example. 2. 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. 3. 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 consequence. 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. What are two general rules of beneficence? 1. Do no harm2. Maximize possible benefits and minimize possible harmsWhat is the principle of justice? It requires that individuals and groups be treated fairly and equitably in terms of bearing the burdens and receiving the benefits of research. The principle of justice may arise in decisions about inclusion and exclusion criteria for participation in research and requires investigators to question whether groups are considered for inclusion simply because of their availability, their compromised position, or their vulnerability — rather than for reasons directly related to the problem being studied. What are 5 formulations of the principle of justice?(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. Why does the selection of research subjects need to be scrutinized? 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. What is informed consent? Informed consent is designed to inform research subjects about the purpose, risks, potential benefits and alternatives to the research that allows people to make a decision about whether or not to participate based on their own goals and values. This exchange of such information should occur at enrollment and throughout the study. 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. What question remains regarding informed consent? a simple listing of items does not It does not answer the question of what the standard should be for judging how much and what sort of information should be provided. What 3 criteria needs to be met when incomplete disclosure is used? 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. How does comprehension impact informed consent? he 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. under what conditions do you need to adapt presentation of informed consent? Special provision may 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 disable patients, the terminally ill and the comatose) should be considered on its own terms. What criteria used to select third party for informed consent? Even for these persons, however, respect requires giving them the opportunity to choose to the extent they are able, whether or not to participate in 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.

What is voluntariness? An agreement to participate in research constitutes a valid consent only if voluntarily given. What are the 2 components of voluntary consent? his 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. What is meant by the nature and scope of risks and benefits? The requirement that research be justified on the basis of a favorable risk/benefit assessment bears a 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. What is meant by risk? 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. What is meant by benefits? The term “ benefit” is used in the research context to refer to something of positive value related to health or welfare. What types of harm should be considered? Many kinds of possible harms and benefits need to be taken into account. There are, for example, risks of psychological harm, physical harm, legal harm, social harm and economic harm and the corresponding benefits. How does the principle of bene apply to risk of harm? 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 subjects' 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 the substantial benefits that might be gained from research. Whats meant by systematic assess of risks and benefits? 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. What are 5 considerations of justify of research?(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. How does the principle of justice impact the selection of 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. What sources of injustice are there? Thus injustice arises from social, racial, 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. Whats the definition of vulnerable subject? 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. WHats the Nuremborg code? This means that the person involved should have legal capacity to give consent; should be so situated as to be able to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress, over-reaching, or other ulterior form of constraint or coercion; and should have sufficient knowledge and comprehension of the elements of the subject matter involved as to enable him to make an understanding and enlightened decision. This latter element requires that before the acceptance of an affirmative decision by the experimental subject there should be made known to him the nature, duration, and purpose of the experiment; the method and means by which it is to be conducted; all inconveniences and hazards reasonable to be expected; and the effects upon his health or person which may possibly come from his participation in the experiment.

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

designed and based on the results of animal experimentation and a knowledge of the natural history of the disease or other problem under study that the anticipated results will justify the performance of the experiment. The experiment should be so conducted as to avoid all unnecessary physical and mental suffering and injury. No experiment should be conducted where there is an a priori reason to believe that death or disabling injury will occur; except, perhaps, in those experiments where the experimental physicians also serve as subjects. The degree of risk to be taken should never exceed that determined by the humanitarian importance of the problem to be solved by the experiment. Proper preparations should be made and adequate facilities provided to protect the experimental subject against even remote possibilities of injury, disability, or death. 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. During the course of the experiment the human subject should be at liberty to bring the experiment to an end if he has reached the physical or mental state where continuation of the experiment seems to him to be impossible. During the course of the experiment the scientist in charge must be prepared to terminate the experiment at any stage, if he has probable cause to believe, in the exercise of the good faith, superior skill and careful judgment required of him that a continuation of the experiment is likely to result in injury, disability, or death to the experimental subject.

What contributions of the Declaration of Helsinki? 1. The World Medical Association (WMA) has developed the Declaration of Helsinki as a statement

of ethical principles for medical research involving human subjects, including research on identifiable human material and data.

The Declaration is intended to be read as a whole and each of its constituent paragraphs should not be applied without consideration of all other relevant paragraphs.

2. Although the Declaration is addressed primarily to physicians, the WMA encourages other participants in medical research involving human subjects to adopt these principles.

3. It is the duty of the physician to promote and safeguard the health of patients, including those who are involved in medical research. The physician’s knowledge and conscience are dedicated to the fulfilment of this duty.

4. The Declaration of Geneva of the WMA binds the physician with the words, “ The health of my patient will be my first consideration,” and the International Code of Medical Ethics declares that, “ A physician shall act in the patient’s best interest when providing medical care.”

5. Medical progress is based on research that ultimately must include studies involving human subjects. Populations that are underrepresented in medical research should be provided appropriate access to participation in research.

6. In medical research involving human subjects, the well-being of the individual research subject must take precedence over all other interests.

7. The primary purpose of medical research involving human subjects is to understand the causes, development and effects of diseases and improve preventive, diagnostic and therapeutic interventions (methods, procedures and treatments). Even the best current interventions must be evaluated continually through research for their safety, effectiveness, efficiency, accessibility and quality.

8. In medical practice and in medical research, most interventions involve risks and burdens.

9. Medical research is subject to ethical standards that promote respect for all human subjects and protect their health and rights. Some research populations are particularly vulnerable and need special protection. These include those who cannot give or refuse consent for themselves and those who may be vulnerable to coercion or undue influence.

10. Physicians should consider the ethical, legal and regulatory norms and standards for research involving human subjects in their own countries as well as applicable international norms and standards. No national or international ethical, legal or regulatory requirement should reduce or eliminate any of the protections for research subjects set forth in this Declaration.

What is minimal risk? Minimal risk is defined in the Common Rule to be “ that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.” Whats the common rule? For all

participating departments and agencies the Common Rule outlines the basic provisions for IRBs, informed consent, and Assurances of Compliance. Human subject research conducted or supported by each federal department/agency is governed by the regulations of that department/agency. The head of that department/agency retains final judgment as to whether a particular activity it conducts or supports is covered by the Common Rule. If an institution seeks guidance on implementation of the Common Rule and other applicable federal regulations, the institution should contact the department/agency conducting or supporting the research. What are the 3 basic principles in the Belmont Report? hree 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 of persons, beneficence and justice. What are the responsibilities of the IRB? afeguard the rights, safety, and well-being of all trial subjects. Special attention should be paid to trials that may include vulnerable subjects, such as pregnant women, children, prisoners, the elderly, or persons with diminished comprehension. The primary ethical principles in human subjects review are outlined in the Belmont Report, and include “ respect for persons”, “ beneficence,” and “ justice.” The IRB may only approve research for which there is a bona fide informed consent process for participants, for which the risks to subjects are balanced by potential benefits to society, and for which the selection of subjects presents a fair or just distribution of risks and benefits to eligible participants. What are requirements for IRB composition? The composition of an IRB for the FDA’s requirements is set in 21 CFR 56. 107.(a)1 The IRB must have at least five members.[3](a)2 The members must have enough

experience, expertise, and diversity to make an informed decision on whether the research is ethical, informed consent is sufficient, and appropriate safeguards have been put in place.(a)3 If the IRB works with studies that include vulnerable populations, the IRB should have members who are familiar with these groups. It is common for an IRB to include an advocate for prisoners when considering research that involves them.(b)1 The IRB should include both men and women, as long as they aren't chosen specifically for their gender.(b)2 The members of the IRB must not be all of the same profession.(c) The IRB must include at least one scientist and at least one non-scientist. These terms are not defined in the regulations.(d) The IRB must include at least one person who is not affiliated with the institution or in the immediate family of a person affiliated with the institution. These are commonly called " Community Members."(e) IRB members may not vote on their own projects.(f) The IRB may include consultants in their discussions to meet requirements for expertise or diversity, but only actual IRB members may vote. What is an exempt review? Generally, research involving surveys or interviews, the use of existing data, and educational research in the classroom falls within the exempt category. This does not mean, however, that the research is exempt from the requirement to submit an application or follow federal guidelines. It means that the application involves less than minimal risk to subjects and that it is exempt from full review, but the IRB must still review the application to determine that this is the appropriate level of review (and may require modification to ensure that the research proposed poses only this minimal amount of risk). The purpose of the application for exempt IRB review is to provide concurrence that the research application does fall into the exempt

research category and furnish documentation that the application has been examined.

One difference between an exempt review and other forms (expedited and full review), is that exempt research will not be monitored by the IRB on an ongoing basis. Thus, there are no reporting or record-keeping requirements with the IRB after the original report has been accepted.

What are the requirements to be exempt? Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as (a) research on regular and special education instructional strategies or (b) 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), survey procedures, interview procedures or observation of public behavior, unless: a. information obtained is recorded in such a manner that subjects can be identified, directly orthrough identifiers linked to the subjects and b. any disclosure of the human subjects' responses outside the research could reasonably place thesubjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability or reputation. 3. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior that is not exempt under paragraph # 2 (above) if: a. the human subjects are elected or appointed public officials or candidates for public office, orb. federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the

research and thereafter. 4. Research involving the collection or study of existing data, documents, records, pathological specimens or diagnostic specimens, if these sources are publicly available or the information is recorded by the investigator in such a manner that the subjects cannot be identified directly or through identifiers linked to the subjects. 5. Research and demonstration projects which are conducted by or subject to the approval of (federal) department or agency heads and which are designed to study, evaluate or otherwise examine: (a) public benefit or service programs, (b) procedures for obtaining benefits or services under those programs, (c) possible changes in or alternatives to those programs or procedures or (d) possible changes in methods or levels of payment for benefits or services under those programs. 6. Taste and food quality evaluation and consumer acceptance studies, if: a. wholesome foods without additives are consumed or b. 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. What is an expedited reveiw? What are the requirements and who conducts an expedited review? An expedited review procedure consists of a review of research involving human subjects by the IRB chairperson or by one or more experienced reviewers designated by the chairperson from among members of the IRB in accordance with the requirements set forth in 45 CFR 46. 110. Expedited Research CategoriesResearch categories that may be reviewed using expedited review procedures by the University of Tennessee at Martin Institutional Review Board (IRB) match federal

guidelines and include:●●Category G: Clinical studies of drugs and medical devices only when condition (a) or (b) are met.❍ (a) Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required. (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.)❍ (b) Research on medical devices for which (1) an investigational device exemption application (21 CFR Part 812) is not required; or (2) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling. Category H: Collection of blood samples by finger stick, heel stick, ear stick, or venipucture as follows: ❍ (a) From healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amount drawn may notexceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or❍ (b) From other adults and children2 considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week. 2Childern are defined in the HHS regulations as “ persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted.” 45 CFR 46. 402 (a).● Category I: Prospective collection of biological specimens for research purposes by noninvasive means.● Category J: Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical

practice, excluding procedures involving x-rays or microwave. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.)Examples:(a) Physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy;(b) weighing or testing sensory acuity;(c) magnetic resonance imaging;(d) electrocardiography, electrencephalography, themography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, Doppler blood flow, and echocardiography; or(e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.● Category K: Research involving materials (data, documents, records, or specimens) that have been collected or will be collected solely for non-research purposes (such as medical treatment or diagnosis). Note: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45CFR 46. 101 (b)(4). This listing refers only to research that is not exempt.● Category L: Collection of data from voice, video, digital, or image recordings made for research purposes.● Category M: Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identify, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.

Note: Some research in this category may be exempt for the HHS regulations for the protection of human subjects 45 CFR 46. 101 (b)(2) and (b)(3). This listing refers only to research that is not exempt.● Category N: Continuing review of research previously approved by the convened IRB as follows: Wherefile:///C|/Web Site/irb-expedited. html (1 of 3) [9/9/2002 3: 01: 18 PM]Expedited(a) the research is permanently closed to the enrollment of new subjects; (b) all subjects have completed all research-related interventions; and (c) the research remains active only for long-term follow-up of subjects; or (d) no subjects have been enrolled and no additional risks have been identified; or (e) the remaining research activities are limited to data analysis.● Category O: Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where the following conditions apply:(a) Categories two (2) through eight (8) do not apply; and(b) The IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified. What is research? 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. What is a human subject? 45 CFR 102(f) defines a human subject as an individual about whom an investigator conducting research obtains data through intervention or interaction with individual or identifiable private information. What is meant by non-engagement in research? Institutions would be considered not engaged in an

HHS-conducted or -supported non-exempt human subjects research project (and, therefore, would not need to hold an OHRP-approved FWA or certify IRB review and approval to HHS) if the involvement of their employees or agents in that project is limited to one or more of the following. The following are scenarios describing the types of institutional involvement that would make an institution not engaged in human subjects research; there may be additional such scenarios:

Institutions whose employees or agents perform commercial or other services for investigators provided that all of the following conditions also are met: the services performed do not merit professional recognition or publication privileges; the services performed are typically performed by those institutions for non-research purposes; andthe institution’s employees or agents do not administer any study intervention being tested or evaluated under the protocol.

The following are some examples, assuming the services described would not merit professional recognition or publication privileges: an appropriately qualified laboratory whose employees perform routine serum chemistry analyses of blood samples for investigators as a commercial service. a transcription company whose employees transcribes research study interviews as a commercial service. a hospital whose employees obtain blood through a blood draw or collect urine and provide such specimens to investigators as a service. a radiology clinic whose employees perform chest x-rays and send the results to investigators as a service. Institutions (including private practices) not selected as a research site whose employees or agents provide clinical trial-related medical services that are

dictated by the protocol and would typically be performed as part of routine clinical monitoring and/or follow-up of subjects enrolled at a study site by clinical trial investigators (e. g., medical history, physical examination, assessment of adverse events, blood test, chest X-ray, or CT scan) provided that all of the following conditions also are met: the institution’s employees or agents do not administer the study interventions being tested or evaluated under the protocol; the clinical trial-related medical services are typically provided by the institution for clinical purposes; the institution’s employees or agents do not enroll subjects or obtain the informed consent of any subject for participation in the research; andwhen appropriate, investigators from an institution engaged in the research retain responsibility for: overseeing protocol-related activities; andensuring appropriate arrangements are made for reporting protocol-related data to investigators at an engaged institution, including the reporting of safety monitoring data and adverse events as required under the IRB-approved protocol.

Note that institutions (including private practices) not initially selected as research sites whose employees or agents administer the interventions being tested or evaluated in the study—such as administering either of two chemotherapy regimens as part of an oncology clinical trial evaluating the safety and effectiveness of the two regimens—generally would be engaged in human subjects research (see scenario B.(3) below for a limited exception). If such an institution does not have an FWA, its employees or agents may be covered by the FWA of another institution that is engaged in the research through an Individual Investigator Agreement. See http://www. hhs. gov/ohrp/policy/guidanceonalternativetofwa. pdf. Institutions (including

private practices) not initially selected as a research site whose employees or agents administer the study interventions being tested or evaluated under the protocol limited to a one-time or short-term basis (e. g., an oncologist at the institution administers chemotherapy to a research subject as part of a clinical trial because the subject unexpectedly goes out of town, or is unexpectedly hospitalized), provided that all of the following conditions also are met: an investigator from an institution engaged in the research determines that it would be in the subject's best interest to receive the study interventions being tested or evaluated under the protocol; the institution's employees or agents do not enroll subjects or obtain the informed consent of any subject for participation in the research; investigators from the institution engaged in the research retain responsibility for: overseeing protocol-related activities; ensuring the study interventions are administered in accordance with the IRB-approved protocol; andensuring appropriate arrangements are made for reporting protocol-related data to investigators at the engaged institution, including the reporting of safety monitoring data and adverse events as required under the IRB-approved protocol; andan IRB designated on the engaged institution's FWA is informed that study interventions being tested or evaluated under the protocol have been administered at an institution not selected as a research site. Institutions whose employees or agents: inform prospective subjects about the availability of the research; provide prospective subjects with information about the research (which may include a copy of the relevant informed consent document and other IRB approved materials) but do not obtain subjects' consent for the research or act as representatives of the investigators; provide prospective subjects with information about contacting

investigators for information or enrollment; and/orseek or obtain the prospective subjects’ permission for investigators to contact them.

An example of this would be a clinician who provides patients with literature about a research study at another institution, including a copy of the informed consent document, and obtains permission from the patient to provide the patient’s name and telephone number to investigators. Institutions (e. g., schools, nursing homes, businesses) that permit use of their facilities for intervention or interaction with subjects by investigators from another institution.

Examples would be a school that permits investigators from another institution to conduct or distribute a research survey in the classroom; or a business that permits investigators from another institution to recruit research subjects or to draw a blood sample at the work site for research purposes. Institutions whose employees or agents release to investigators at another institution identifiable private information or identifiable biological specimens pertaining