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Human Subjects in Research

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Human Subjects in Research presents basic ethical issues that face researchers when doing work with human participants. Matt Ronning, Assistant Vice Chancellor for Research Administration Sponsored Programs and Regulatory Compliance, (SPARCS) is our guide for this module. In the Overview section we review chapters from two well known textbooks on Research Ethics. In the Applied Ethics section we focus on the consent form as a contract and comment upon the recurring topics of Justice and Honesty as they apply particularly to human subjects. In the Central Theme section we review institutional guidelines, both at the national and institutional level, utilizing the SPARCS training site. Our Case Study focuses on the graduate student as a research subject. The topic for the Study Question is that of vulnerable populations. We close with the Resource section where you will find a sampling of articles, books and websites.

TABLE OF CONTENTS

1) Introduction: The complexity of working with human participants, the Belmont Report as a central document. Resources: [Nuremberg Code](#), [Helsinki Declaration](#), [The Belmont Report](#)

2) Central Essay: by Matt Ronning, Assistant Vice Chancellor for Research Administration Sponsored Programs and Regulatory Compliance

Overview Readings: Resources: Chapters from 1) Research Ethics: an Introductory Text With Cases, edited by Francis L. Macrina (*Use of Humans in Biomedical Experimentation*) and 2) Responsible Conduct of Research, by Adil E. Shamoo and David B. Resnik (*The Use of Humans Subjects in Research*.)

3) Applied Ethics: The consent form as a variation on the idea of a contract. Resources: *Contract and Covenant in Curacao: Reciprocal Relationships in Scholarly Research*, by Alan F. Benjamin; *Interviewing: the unspoken compact*, by Jean Rafferty.

4) Central Theme: Institutional guidelines, nationally and institutionally. Resources: [ORI Introduction to the Responsible Conduct of Research](#) by Nick Steneck and the [Sponsored Programs and Regulatory Compliance \(SPARCS\)](#) homepage at NC State University.

5) Case Study: [An Impoverished Student](#) from [Association for Practical and Professional Ethics \(APPE\)](#),

6) Study Question: Vulnerable Populations. Resource: Jeffrey P. Kahn, Anna C. Mastroianni and Jeremy Sugarman, *Changing Claims About Justice in Research: an Introduction and Overview* and Jonathan D. Moreno, *Convenient and Captive Populations*.

7) Resources: a sampling of articles, books and websites

1) Introduction

The dilemmas that accompany research with human beings are profound. Those who do this sort of work feel a strong sense of duty, both to the individuals working with them on the protocol and to the general public who will benefit from the research. Dealing with ethical concerns such as justice, beneficence and professional responsibility have particular intensity as we interact with the human participants in our research protocols.

Hierarchies of Obligation

In Module I, *Research Ethics: An Introduction*, Tom Regan talks about three different types of duties. He describes discretionary duties as what we owe to everyone by virtue of being a member of society. In addition, many of us feel a responsibility to help others in particular situations, e.g. those in severe poverty, or victims of a natural disaster. This sense of obligation is what Regan calls non-discretionary duties. Special duties are what we owe to family, friends and colleagues. In this fashion, we can see that we all decide on a particular hierarchy of obligation.

How might we relate this hierarchy to working with human participants? Are the research subjects in the discretionary or non-discretionary group? Or do they belong in the category of "special duties" along with family, friends and colleagues? How we think about this question, what our feelings are here, can determine the sense of obligation we might feel. This will affect the sort of attention we give to our research subjects.

Even our language reflects our concern: over recent years the term "human subjects" has often been replaced with the words "human participants." What does this simple verbal shift say about issues of power and respect? Do we see ourselves as having power over our subjects, or are they partners in our work?

Given the complexity of this topic, this module will be an overview of the central issues, an introduction to your thinking, with suggestions for further reading and reflection. There are many rules and regulations in place to protect human participants; some are grounded in legal documents and others are grounded in custom, without being legally binding.

We should begin with the three documents that are basic to understanding the historical evolution of our understanding of the relationship between research and human subjects: The Declaration of Helsinki, the Nuremberg Code and the Belmont Report.

Research ethics involves every individual and unit associated with North Carolina State University, and relates directly to the caliber of research we conduct, and our ability to share the knowledge and understanding contributed by our teachers and scholars. They call for nothing less than a constant striving for the highest ethical standards, and a dedication to achieving recognition through integrity.

Matt Ronning, Central Essay, p. 1

Basic Documents

Historically, the laws governing human subjects in research were actually put in place surprisingly recently. Two historic documents stating principles to be followed when working with human beings in research, the [Nuremberg Code](#) and the [Declaration of Helsinki](#) were crafted in direct response to specific situations. In 1949, as a response to the World War II war crimes tribunals, The Nuremberg Code was established. The idea that scientists could do no wrong was proven false when the horrendous use of concentration camp prisoners for medical research was brought to light.

Over the next decades medical research increased and in 1964 at a meeting of the World Medical Assembly in Helsinki, Finland, another document was published to add weight to the principles outlined in the Nuremberg Code and to further clarify the perimeters to research using human subjects. The original 1964 statement has been amended in 1975, 1983 and 1989 and updated in 1996, 2000 and 2002. The Helsinki focused on physicians doing research, building on the original Hippocratic Oath to take in the increasing importance of medical research. A distinction was made between research for knowledge in general (pure research) and that for a specific clinical application.

The design and performance of each experimental procedure involving human subjects should be clearly formulated in an experimental protocol which should be transmitted for consideration, comment and guidance to a specially appointed committee independent of the investigator and the sponsor provided that this independent committee is in conformity with the laws and regulations of the country in which the research experiment is performed.

[Declaration of Helsinki](#)

One of the central ideas of both the Nuremberg Code and the Declaration of Helsinki is to articulate the relationship between the rights of the individual and the larger common good: "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" (Nuremberg Code). In both documents, although the need to balance medical research that will benefit society with the rights of patients is emphasized there is no question that this medical research is seen as a benefit. There are specific statements intended to protect vulnerable populations, with the idea that consent may be given on their behalf.

Throughout the Principles articulated, the critical importance of research and the scientific method is stressed. 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.

As in the Nuremberg Code, the statements are not legal and binding. The Declaration does note that any research results obtained via methods not commensurate with the principles will not be considered publishable; this is the closest to punishment so far in either the Nuremberg or the Helsinki.

[The Belmont Report](#) is a structured declaration of a set of regulations that should be followed by researchers whenever human beings are used as test subjects. The first section clarifies the difference between medical practice and research. The second section describes the three basic ethical principles that are the cornerstone for the Belmont Report: respect for persons, beneficence and justice. The third section deals with the application of these principles, via the structures of informed consent, assessment of risks and benefits and the selection of subjects. The ethical principles of the Belmont Report form the basis for the decisions that Institutional Review Boards (IRB) make when deciding whether to approve protocols using human subjects. Every research protocol undertaken at an institution must be reviewed and approved by the IRB. These guidelines are legal requirements rather than mission statements or codes of conduct as were the Nuremburg Code and the Declaration of Helsinki.

There are three central principles outlined in the Belmont Report, 1) Respect for persons; 2) Beneficence; and 3) Justice. This principle of Respect has elements of Kant's approach; individuals have autonomy and need to be treated as ends in themselves, not means to an ends. We might relate Beneficence to Virtue Ethics in that beneficence means to actively seek to increase a person's welfare. The principle of Justice relates to the issue of balancing the risks undertaken with the benefits to be gained as well as the equitable distribution of risks throughout the population. So aside from Virtue Ethics, we see the Utilitarian calculus in action as well. Underlying the Belmont Report is the overall goal of improving the quality of life for everyone in general. This is an underlying theme of all three documents, how to balance the needs of the individual with those of the larger society. The central role of the Institutional Review Board (IRB) is emphasized. Every single research protocol must be reviewed by this committee and approved before work can begin. The IRB can be seen as having a dual task, advocacy for *both researchers and subjects*.

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 give forethought to the maximization of benefits and the reduction of risk that might occur from the research investigation. In the case of scientific research in general, members of the larger society 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 Belmont Report](#), Section 2: Beneficence

2) Central Essay

Research ethics involves every individual and unit associated with North Carolina State University, and relates directly to the caliber of research we conduct, and our ability to share the knowledge and understanding contributed by our teachers and scholars. They call for nothing less than a constant striving for the highest ethical standards, and a dedication to achieving recognition through integrity. By understanding the principles and activities involved in assuring the ethical conduct of research involving human subjects, every researcher, student, and member of a research team can contribute to this objective.

True, adherence to this high standard often involves processes that at times can seem arduous to an individual investigator. It is understandable that sometimes a researcher concentrating on the goal of the project can view as tangential the effects of a project on subjects, research or even the researchers themselves (physically and otherwise). For that reason, NC State relies on a committee of faculty peers to balance individual efforts with external and internal regulations and policies that contain guidelines about the ethics of human research. Members of these committees can spend long hours and coordinate extraordinary amounts of information to make reasonable decisions. However, their collective interpretations and decisions, molded into one communal action, actually help provide a stronger foundation for the project to proceed with the highest ethical standards in place.

NC State regulatory compliance committees and boards view their responsibilities as an opportunity for life-long learning about the impacts of research projects conducted on campus. Of course, these committees can make unfavorable decisions, but they do not do so without much deliberation and input from affected constituents, including the principle investigators. In fact, the committees are sensitive to the impact of their decisions, partly because they most often are principle investigators themselves.

Investigators, co-investigators and staff are responsible for conducting their research in an ethical manner. They have many resources at hand to help them make ethical decisions about their research.

For example, researchers whose research involves animals can reference the Animal Welfare Act. They can take the initiative in using the NC State training programs, consulting regulatory compliance web pages, and directing others on the project to take advantage of the same opportunities. Similarly, investigators of research involving human subjects can become familiar with the founding principles set by the Nuremberg Code, the Belmont Report and other guidance, including the Federal codes that are available on the Regulatory Compliance web pages.

Referring to these resources is a good idea, not just to learn about ethical research, but to further broaden a researcher's knowledge base, and enhance the reputation of an institution as a society of reputable research. When researchers incorporate self-directed professional development into their own environment and couple it with the training and education offered at NC State and by external organizations, they are contributing to the continuation of NC State's reputation as a top tier research institution and working to sustain the academy.

Research projects involving human and animal subjects are not the only projects requiring ethical conduct. Financial conflicts of interest, biosafety, radiological safety, and hazardous waste disposal, among other issues, qualify for inclusion in the call for research integrity. You are invited to familiarize yourself with the guidelines for complying with standards for ethical research at NC State by visiting the [Sponsored Programs and Regulatory Compliance](#) homepage.

Matt Ronning Assistant Vice Chancellor for Research Administration
Sponsored Programs and Regulatory Compliance (SPARCS)

Overview Readings

For a topic with so many ethical questions, as well as a large number of regulations, a good overview is invaluable. Out of the numerous fine books in this area, we have selected chapters from two well known texts: 1) Research Ethics: an Introductory Text With Cases, edited by Francis L. Macrina, and 2) Responsible Conduct of Research, by Adil E. Shamoo and David B. Resnik. It is useful to read and study a wide variety of basic texts in this area, since each one will have a slightly different emphasis.

The chapter, "Use of Humans in Biomedical Experimentation" by Paul S. Swerdlow, in Research Ethics: an Introductory Text With Cases, edited by Francis L. Macrina, is a good place to start. Here you will find basic information about Institutional Review Boards and Informed Consent. The [accompanying website for this chapter](#) gives links to important websites about national regulations and additional resources.

In the quotation in the box to the right, Swerdlow makes the point that there are a wide range of studies that utilize human participants. This is an important issue in a large university since students are often asked to take part in research as part of a class or as assistance to teaching assistants.

In many institutions, students in introductory psychology classes may be asked to take part in experiments the department has undertaken: sometimes teachers will make this a course requirement. It is expected in some institutions that students in upper level biology courses will be asked to take some sort of sample-saliva, blood-from each other for practice analysis. Is this the sort of research protocol that an Institutional Review Board must approve? Do you need the consent form procedure in these cases? The answer to these questions may depend on the culture and customs of your institution. Should the accepted practice at your institution, or in your department, be that these sorts of activities are too trivial to be called "research?" Why or why not? What do the laws say?

"Human subject research includes all studies where there is an intervention or interaction with a living person that would not be happening outside of the conduct of the experimentation. Even if this is not the case, the activities may still be subject to regulations if identifiable data or information gathered during the research—or collected outside of the study in question—may be linked to human subjects. Data collected through intervention include direct methods, such as drawing venous blood, and indirect methods, such as manipulating the environment of the human subject. Federal regulations also apply to human subjects that are used to test devices, materials, or products that have been developed through research."

Swerdlow, Paul S. "Use of Humans in Biomedical Experimentation." Scientific Integrity an Introductory Text with Cases, 3rd Edition, Francis L. Macrina, Ed. ASM Press: Washington, DC, 2005. 94.

"The Use of Human Subjects in Research," a chapter from the text by Shamoo and Resnik, contains an excellent review of the history of human subjects research.

It is important to understand this history for several reasons. Firstly, many of the examples of treatment of research subjects that we might be shocked at today were considered normal and acceptable at the time: this can serve as a warning in that what we might consider standard practice might very well be a practice worth questioning. Secondly, there is a very troubling history of selecting research subjects from populations historically at risk: the poor, the mentally handicapped, the lower classes in a society as research subjects. Thus, people from these populations are understandably concerned, even suspicious of medical research. We now have laws in place to protect such populations and have increased our sensitivity to such problems. Understanding this history helps us to appreciate why there might be a variety of personal responses to the idea of human participation in research.

Shamoo and Resnik have an extensive discussion of what they see as ethical themes central to the topic of human subjects. These include "The Good of the Individual versus the Good of Society," "Weighing Risks and Benefits," and "Just Distribution of Benefits and Harm." This brings out a theme that we thought about in Module 3, *The Mentoring of Graduate Students*, that of "right balance." Clearly there may be a difference, in research, as to what benefits the individual human subject and what benefits society at large. What this "right balance" might be and who should decide this is clearly a critical question.

This is one of the major tasks of the Institutional Review Boards, to act as a go between, examining the proposed contract between the researcher and subject to be sure that while the greater good is kept in mind, the individual is not at undue risk.

In many ways, human experimentation raises a classic ethical dilemma addressed by moral philosophers since antiquity—the good of the individual versus the good of society. According to all of the moral theories...human beings have moral worth and we should respect and promote the rights and welfare of individual human beings. On the other hand, most theories also stress the importance of promoting social welfare. Scientific and medical research can promote many important goals that enhance social welfare, such as human health, education, control of the environment, agriculture and so on. It is important to use human subjects in research in order to gain scientific and medical knowledge but this also places people at risk and may violate their dignity or rights. Thus, a central ethical question in all human subject research is how to protect the rights and welfare of human subjects without compromising the scientific validity or social value of the research.

Shamoo and Resnik, *The Use of Human Subjects in Research*, p. 192

3) Applied Ethics: The consent form as a variation on the idea of a contract. Informed Consent as a Contract Between Equals

The cornerstone of research ethics when working with human participants is the idea of informed consent. It is a legal requirement that every person taking part in research as a subject, of any kind, must be given complete information about the research and then they must sign a consent form. Shall we think of this consent form as a regulatory requirement or as a contract between people in a relationship? This question was central to a conference held in November, 1995 at the University of North Carolina, Chapel Hill. The conference, "From 'Regs' to Relationships: Reexamining Research Ethics" focused on the complexity of relationships between researchers and their human subjects across a wide variety of disciplinary work.

"The reason why informed consent is an ethical requirement even when the proposed research carries a very low or virtually nonexistent risk of harm, as is true of some social or behavioral investigations, is that people can be wronged even when they are not harmed. To carry out perfectly benign studies on human beings without their knowledge or consent thus wrongs them because their right to self-determination is violated. In the absence of granting voluntary, informed consent, research subjects are being treated as mere means to the ends of others, as objects or instruments rather than as persons worthy of respect."

Ruth Macklin, *Is Ethics Universal?* P. 26

We can see that the consent form is the ethical principle of respect made tangible. It is also our societal value of Justice made tangible: treating other people as means to an end is unfair, thus, when doing research, our unspoken contract, to treat each other as autonomous beings, is made tangible in the consent process.

Gaining consent from a human participant is an ongoing process. The roles and responsibilities of both the participant and the researchers must be discussed before and during the research project. A consent form should describe the study in detail, and include all the risks and possible benefits expected from the research. In this manner, important information about the study is documented for both the participant and the researcher.

For the purpose of the study, the researcher asks an individual for permission to "use you as an object." The individual, in turn, agrees to "be used as an object" even if in so doing they gain no personal benefit. The goal is the greater societal good that derives from the research. The researcher will usually also benefit. In most cases, there is the goal that the research subject benefit as well. So we see that the consent form is also an articulation of the principle of Beneficence, or, at the very least, Non-Maleficence since a major goal of the consent process is to assure the subject that they will be free from harm during the research process. And yet,

realistically given that research involves the unknown, is “completely risk-free” a reasonable expectation?

Mindful of the fact that research is a multidisciplinary activity, we will ground our discussion in two articles from two non-medical fields, journalism and anthropology.

A key point in a contract is honest disclosure. Without this, it is questionable whether an agreement is binding. Risks need to be clearly spelled out and if researchers are uncertain about all the risks, short term or long term, they need to be rigorously honest about this as well. Just as false reporting of data hurts all concerned, incomplete information about a protocol can result in harm to the subject and quite possibly invalidate the contract.

We quote Deb Paxton, Regulatory Compliance Office, North Carolina State University, in the box to the right.

“To adhere to the principle of honesty, the researcher must make subjects aware of what they are agreeing to. Subjects have the right to make their own decisions about whether or not the research adds to the common good, and whether or not they wish to participate. This means that the subject has the right to know the purpose of the research, how it will be done, and what the expected benefits (both to society and to him/herself) might be. The subject must also be fully informed about potential risks from the study, so that s/he can weigh the risks and benefits during decision-making.” (Deb Paxton, NC State University)

We might not consider investigative journalism as research, but it is. The journalist gathers information that is intended for the public good, either to increase understanding, or to add to the dissemination of knowledge. Just as data points are needed for scientific research, personal interviews are needed for journalistic inquiry. One of the cornerstones of journalism is protection of resources, thus the value of privacy (a variation on respect for persons, as well as non-maleficence) is part of the tradition here. Newspapers and magazines see themselves as working in the public interest, exposing injustice and righting wrongs. Thus, investigative journalism fulfills the Belmont exhortation for Respect for Persons, Beneficence and Justice.

Jean Rafferty describes her many ethical concerns when conducting personal interviews, noting that one of the challenges is respecting the privacy of the interview and yet retaining the freedom to write as she sees fit, saying that her “primary obligation is to the story” (Rafferty, 126). Again, we see the theme of “right balance,” in that Rafferty’s job involves balancing her obligation to her sources as well.

“They depend on the journalist to disseminate the story on their behalf, just as the journalist depends on the interviewee for raw material. This mutual dependence leads to an implicit contract between the interviewer and interviewee. In return for telling the journalist intimate details of their life, the journalist pledges to bear witness to them in as truthful a manner as possible. ...The parallel between journalism and research here is with the independence of researchers, or academic freedom. (Jean Rafferty, *Interviewing: the unspoken compact*, in *Researchers and Their Subjects*, Marie Smyth and Emma Williamson, Eds. The Policy Press, 2004. 124, 131.

In another chapters of the book resulting from the Chapel Hill conference mentioned earlier, Alan F. Benjamin describes his research on ethnic identity, a study of a Jewish congregation in the Caribbean. This group is one of the most ancient Jewish communities in the Western Hemisphere and thus is of interest to historians, sociologists, anthropologists and students of religion. Prior to beginning his study, Benjamin met with the Congregation's Board of Directors: the Board presented the researcher with a contract. The people being studied wanted more than to sign a consent form, they wanted to have some measure of control over what was written about them. They wanted to be active participants rather than passive subjects. Benjamin agreed to this.

One of the interesting items in this book is the chapter by Sue E. Estroff about her response to Benjamin's situation. Benjamin was her graduate student and Estroff discusses and organizes a list of the variety of obligations that she, as faculty advisor, felt incumbent to fulfill. For example, she lists her obligations toward her student: "advise, support, protect and represent/advocate, train, monitor, evaluate, inform/disclose" and to the congregation she notes her obligation to "implement and enforce the contract" (Estroff, 76).

"My fieldwork experience indicates that the practice of research involves more than the neutral acquisition of knowledge. Scholarly research implicates power relations; it is not an innocent practice...Therefore, the central contention of this paper is for broader recognition among scholars that research occurs within contexts of social relations, and the central call of this paper is not to privilege the practice of research over the concerns of those studied...I immediately agreed to the idea of a contract because I believed that people being studied should have some control over representations of their lives. Complete absence of control on their part would constitute exploitation of them on my part – it would be using their lives to advance my research and career without considering their wishes. Justice would seem to require that they have the opportunity to attempt to protect themselves from harm."

Benjamin, Alan F. "***Contract and Covenant in Curacao Reciprocal Relationships in Scholarly Research.***" *Beyond Regulations: ethics in human subjects research*, Nancy M. P. King, et al., Eds. The University of North Carolina Press, 1999. 50, 55

4) Central Theme: Institutional Guidelines at the national and institutional level at North Carolina State University

Sometimes researchers feel that the many guidelines, rules and committees get in the way of doing research, but actually both scientists and subjects on are in the same side. As we noted in Module V, *Professional Responsibility and Codes of Conduct*, guidelines are the values of society made tangible. Rules safeguard the researcher as well as the subject, giving perimeters for working on the frontiers of knowledge.

To familiarize yourself with the complex set of regulations for working with human participants begin with the chapter, [The Protection of Human Subjects](#), in the online book, [ORI Introduction to the Responsible Conduct of Research](#) by Nick Steneck. This is a basic text, commissioned by the Office of Research Integrity for its Responsible Conduct of Research (RCR) training program. You will find it readable and well organized. In the box we quote Steneck's information about Institutional Review Boards. Even in the composition of IRBs we can see several ethical principles at work, e.g. the idea of peer review as well as the effort to avoid conflict of interest.

Under the Common Rule, IRBs must have at least five members and include at least one scientist, one non-scientist, and "one member who is not otherwise affiliated with the institution and who is not part of the immediate family of a person who is affiliated with the institution"(§ 46.107(d)). IRBs have authority to approve, require modification of (in order to secure approval), and disapprove all research activities covered by the Common Rule. They also are responsible for conducting continuing review of research at least once per year and for ensuring that proposed changes in approved research are not initiated without IRB review and approval, except when necessary to eliminate apparent immediate hazards to the subject. [The Protection of Human Subjects](#)

As a land grant state university, North Carolina State University follows federally mandated guidelines. In addition to the ORI material that is available, The United States Department of Human Health and Services has published an online module, [Protecting Human Subjects Training](#). You will find information about the federal regulations at this same site, [The Office for Human Research Protections \(OHRP\)](#) As well as additional educational materials. Check with the head of your department or study project to see which of these informational sites you should study the most.

In addition, the regulations from the sponsoring agency for your particular grant, often the [National Science Foundation \(NSF\)](#) or the [National Institutes of Health \(NIH\)](#) have their own rules. Many researchers at NCSU use the NIH guidelines as part of their standard operating procedure.

NC State University Guidelines and Training

In his essay in this module, Matt Ronning emphasizes self-study and training for those working with human participants. The SPARCS website is set up to facilitate this. Click on the [Sponsored Programs and Regulatory Compliance](#) homepage and review the available material. Select the online tutorial [Basic Training for Personnel Involved in Human Research](#). In the box at the right we have quoted a statement about informed consent from the tutorial. You can think of informed consent as a sub-theme for this module, it is indeed a central focus for research ethics when working with human participants.

This site, along with the ORI handbook, is an excellent place to begin your self training and education in Responsible Conduct of Research (RCR) as it relates to human subjects. You will find information about national regulations and Institutional Review Boards (IRBs), vulnerable population, risk reduction, and details about informed consent. As you work through the tutorial you will be able to check yourself with quizzes on the material.

Informed consent is a basic principle of ethical research with human subjects. A potential subject must be made aware of the purpose of the study, potential risks and benefits from the study, and that they may withdraw from a study at any time. An important part of informed consent is making sure that subjects have ample opportunities to ask questions, and that those questions are adequately answered. While informed consent often takes the form of a written document signed by each subject, it is actually an entire process that begins with advertisements about the study and spans the length of the study. Investigators may be obligated to give subjects important information concerning the study and their participation in it long after the study is completed and/or published.

[Basic Training for Personnel Involved in Human Research](#)

Institutional Guidelines and “Right Balance”

How do the various guidelines set out the boundaries of “right balance” for both researchers and subjects? If we can think about guidelines as the values of a society made tangible then possibly we can think about these regulations for human participation in research as a means by which society tries to set a balance between the rights of the individual and the needs of society at large. To give you grist for the mill to think about this question, access the Office for Human Research Protections pamphlet, [Becoming a Research Volunteer](#). Does this pamphlet address the issue of “right balance” adequately? Why or why not?”

5) Case Study

This case study is from the collection published by the [Association for Practical and Professional Ethics \(APPE\)](#), posted by the [Online Ethics Center hosted by the National Academy of Engineering](#). The case, [An Impoverished student](#), tells the story of a graduate student who volunteers for clinical trials.

We will present a summary of the Case Study here in the box to the right, but reading the original Case Study, Discussion Questions and Commentaries will enable you to go more deeply into the issues. You will find that with this case, as well as with most case study scenarios, there are two levels of questions and/or concerns; firstly there will be the specific dilemmas in terms of human subjects in this particular situation and then secondly, the deeper, more complex societal implications to ponder.

Gary is a graduate student who has finished his coursework, exams and research and is finishing up his thesis. Unfortunately, his university has not renewed his ongoing teaching assistant position so he finds himself with financial problems right at the end of his university program. What should he do? Anthony, a friend of Gary's, tells him about volunteer opportunities at pharmaceutical companies. Thinking his problems to be over, Gary signs up for two studies, planning to use the \$3500 he earns to finance his last semester. However, due to drug interactions, he becomes ill, is hospitalized, and thus, is unable to finish his thesis in time to graduate.

This case brings up several key points we need to consider when thinking about human participation in research protocols. What is the real meaning of consent in this case? What information did Gary hold back, not intending to be dishonest, but not considering it relevant? Is the researcher responsible for Gary's lack of information or not? What about the issue of the financial need of the participant – was Gary under pressure to get into the study? With this sort of financial pressure, is this really free consent?

There are also the deeper issues to consider, e.g. should a graduate institution have the right to withdraw funding as a student is just finishing up their program? What is the responsibility of the department to its graduate students? What about Gary's committee chair: what are his responsibilities to Gary. In terms of the pharmaceutical trial, what might be a result in terms of data when a student, needing money, signs up for a drug trial? Is advertising for volunteers a good approach when looking for a random sampling? How should pharmaceutical volunteers for clinical trials be chosen?

Suggested Methodology:

Access the original Case Study, [An Impoverished Student](#), read it thoroughly, including the Discussion Questions. As we have done in the other modules in this series, review [Tom Regan's Check List](#) from page 4 of Module 1. Doing this will enable you to see the inter-relationship of research ethics in general to the context specific concerns of human participants in research.

For example, the "*responsibility for and leadership of the performance of the study*" – how does that link to Regan's point 8: "*Are any duties of justice involved? If so, who has what rights? Against whom?*"

Clearly a university department and faculty have a responsibility to their students, but does this include financial support? If Gary neglected to inform the pharmaceutical trial interviewer about his other medications, both the herbal one and the one from another study, is the pharmaceutical team responsible? How could the ending of this case study – hospitalization with failure to finish the thesis – be prevented? How vulnerable are students in these situations? Cast a wide net in your thinking in terms of Regan's *Morally Relevant Questions*.

Again, as in previous Case Studies,
 What seems to you to be *resolved* in your own mind?
 What seems to you to be *unresolved* in your own mind?
 What do you find challenging to *articulate*?

Now review the [Commentary by Brian Schrag](#) that accompanies this case. Reading his ideas when you have already struggled with this case will add to your ability to become articulate with the ethical issues and help you work on areas you are still unresolved and will help you articulate the deeper issues of this case. One of the realities of both case studies and real life situations that involve moral dilemmas is that you might have decided on how to go forward, and yet still feel the pull of the dilemma or find that there are still areas that feel unresolved to you.

What would you have done in Gary's situation? What can be done about the very real financial pressures and burdens that graduate students face in today's society? Is the PhD process similar in any way to that of being a research participant? If so, do you think we need to have an "informed consent" procedure for PhD students?

6) Study Question: Vulnerable Populations

By now, you have read something of the history of human subjects research and it is clear that certain populations are vulnerable because they are not in a position of power in our society in general. These populations (the poor, minorities, the mentally handicapped, prisoners, the elderly, the mentally ill) are often called “populations at risk” because of this. Over the last decade two other groups have been added to the list: students and those in the military.

When we think about our ethical theme of “right balance” we can see that this takes on tremendous importance when selecting people to take part in clinical trials. Legally, drugs cannot go on the market unless they have gone through the clinical trial stage with human beings. Animals are not enough. If we are attempting to balance the rights of the individual with the benefits to the larger society, how shall we select our volunteers?

One of the most critically debated challenges in research ethics in terms of human participants is how to deal with the concept of informed consent when the study population is taken from a group at risk. If we think about asking a prison population for volunteers, we immediately see that there are problems. Is the consent freely given, or is there the implication of early parole, special treatment or other favors earned from participation? Many say, even many prisoners themselves, that to participate in research is a way to repay the debt to society, to actually be part of society again.

In the well known book, *Beyond Consent Seeking Justice in Research*, the authors of the series of edited articles ponder the many challenges of vulnerable populations as research subjects.

“Clinical research is a complex, expensive and valued social activity. One of the conditions that makes clinical research possible is a subject population that is convenient, both in terms of availability...and monitoring through the course of the study...The paradigm case of a captive population is those who are imprisoned. Other populations seem to occupy a middle ground between short –term hospitalized patients and long-term prisoners, including students, institutionalized persons and military personnel. Among the ways that these populations differ from others is their degree of availability, the greater likelihood that those who are captive can be coerced or manipulated into participation by virtue of their dependent status, and that captive populations are more likely than others to be readily available for research activities for extended periods, enhancing their attractiveness to the research enterprise.”

Jonathan D. Moreno, *Convenient and Captive Populations*, p. 111 in *Beyond Consent Seeking Justice in Research*, Jeffrey P. Kahn et al. Ed. Oxford University Press, 1998.

Another area of intense scrutiny is that of clinical trials in the less industrialized nations. This became an obvious ethical issue in terms of HIV drug research. The very population that was useful for clinical trials was unable to afford to continue treatment if it proved successful: they were unable to have access to the drugs unless they were in a clinical study. These studies also brought out the inherent ethical conflict with giving people placebos; yet, for rigorous studies, a control group was necessary.

This ongoing dilemma, trying to balance the needs of the individual and the common good, is, as Resnik pointed out, one of the major themes of ethics in general. If you study the Belmont Report you can see that this challenge is at the heart of the document: society needs to do research and the individuals who make up society will benefit from the research. Somehow, the research subjects need to benefit as well.

“Thus, although the principle of justice has long been an important part of research ethics, its interpretation and accompanying application seems to be changing. Specifically, there seems to be a new interest in access to research, both at the individual and societal level. This new calculus seems to go beyond obtaining consent to endure the risk and burdens of this research towards an appeal concerning fairness in the distribution of the benefits of research. In addition, this shift demands thinking differently about subject populations than has historically been the case. It may, for instance, mean creating opportunities for fair access to research and its potential benefits, while simultaneously developing mechanisms of protecting subjects from exploitation. This balancing is a critical challenge for research ethics.”

Jeffrey P. Kahn, Anna C. Mastroianni and Jeremy Sugarman, *Changing Claims About Justice in Research: an Introduction and Overview*, p. 2, in **Beyond Consent Seeking Justice in Research**, Jeffrey P. Kahn et al. Ed. Oxford University Press, 1998.

7) Resources

Articles

Beech, Mary Catherine, et al. [What Does 'Respect' Mean? Exploring the Moral Obligation of Health Professionals to Respect Patients.](#) *JGIM: Journal of General Internal Medicine*, 22.5, 2007. 692-695, 4p.

Fisher, Celia et al., *Marginalized Populations and Drug Addiction Research: Realism, Mistrust, and Misconceptions*, publication from [the Hastings Center](#): free registration required to view this article.

Peterson, R.A., [On the Use of College Students in Social Science Research: Insights from a Second-Order Meta-analysis](#), *Journal of Consumer Research*, 28.3, 2001. 450-461,

Pimple, Ken [The Least You Need to Know about the Rules Governing Human Subjects Research at IU](#)

Books

Kahn, Jeffrey P., Anna C. Mastroianni, & Jeremy Sugarman. [Beyond Consent: Seeking Justice in Research.](#) Oxford University Press, 1998

King, Nancy M.P. (ED) and Jane Stein (ED), [Beyond Regulations: Ethics in Human Subjects Research.](#) The University of North Carolina Press, January 1999, from the Series: Studies in Social Medicine. (Includes case studies)

Smyth, Marie and Emma Williamson, Ed. *Researchers and Their 'Subjects' Ethics, power, knowledge and consent.* The Policy Press, 2004.

Websites

[Bioethics Resources on the Web: Human Subjects Research](#)

The Office of Research Integrity (ORI) program on Responsible Conduct of Research (RCR) educational resources has an excellent set of materials on [Human Subject Research](#). There are direct links to educational materials produced especially for the RCR program and a list of articles.

Ken Pimple and Julie A. Pedroni (The Poynter Center), [The Least of My Brothers](#), is about the Tuskegee Study. See also their: [A Brief Introduction to Informed Consent in Research with Human Subjects](#)

Goldman, Edward, [Vulnerable Populations](#), a web based outline of information and resources.