VIRGINIA COMMONWEALTH UNIVERSITY

Exempt Research Guidance

Research Involving Human Subjects That May Qualify For Exemption
From Federal Regulations Requiring IRB Review and Approval[1]

Introduction

The federal government has identified certain categories of research involving human subjects that qualify for exemption from federal regulations. Virginia Commonwealth University (VCU) is authorized by the federal government to determine whether studies thought by the principal investigator (PI) to be exempt from federal regulations -- actually qualify for exemption. Such determination is made on behalf of VCU by the IRB. Only the IRB has authority to make a determination that a study is exempt from federal regulations and from IRB review and approval. When the IRB notifies a PI that a research project is EXEMPT, it also notifies the PI that the research is approved for initiation.

In order to qualify for exemption, a research study must fall entirely within one or more of the six categories for exemption identified below, and it cannot place subjects at greater than minimal risk. If the research involves prisoners, then it does not qualify for exemption from federal regulations and IRB review.

What Exemption Means

"Exemption" as used in this document means exemption from the requirements set forth in *Regulations for the Protection of Human Subjects* (**Title 45 Part 46 of the Code of Federal Regulations**), such as the requirement for a written informed consent document. At VCU, determinations of exemption are made by the IRB.

What Exemption Does Not Mean

"Exemption" does not mean that the research activity is exempt from the laws of the Commonwealth of Virginia, and it does not mean that the research need not conform to the canons of sound research ethics.

Furthermore, even if informed consent is not required by law, it is the Policy of VCU that all research studies, including those that are exempt from federal regulations, are to be guided by sound ethics. Except in extraordinary cases, it is unethical to involve a human research subject in research unless informed consent has been obtained. In prospective studies, subjects should not be enrolled -- even though the research is exempt from federal regulations -- unless they have made an informed decision to participate. Although a **formal written consent document is not required** for exempt research studies, subjects have a right, whenever it is appropriate, to be informed about the risks and benefits (if any) associated with their participation in the research study.

PIs should keep accurate research records that show that, whenever appropriate, each subject was both informed about the risks and benefits (if any) associated with participation in the study, and that each subject freely chose to participate in the study. In some cases, informed consent is not feasible and is not required, (e.g., where the research involves only existing data, documents or specimens that cannot be linked to subjects). In research that involves survey instruments, interviews, or questionnaires, subjects must be informed that they are free to refuse to answer any or all questions without fear of penalty or reprisal.

Definitions

Research involving human subjects may not be initiated or continued without IRB review and approval unless it falls entirely into one or more of the categories identified below.

RESEARCH is defined as a systematic investigation designed to develop or contribute to generalizable knowledge (45 CFR 46.102.(d).

Example: Professor X is teaching a course on research techniques. She asks each student in her class to interview five persons about their attitudes on abortion. Students are to keep no identifiers that could link answers to the subjects who are interviewed. A summary of answers is to be provided by each student to Professor X for evaluation. Because this information is gathered for a class assignment and is not intended to contribute to generalizable knowledge, the class activity does not meet the definition of research, and therefore need not be submitted to the IRB. However, if Professor X decides to aggregate all of the data received from student assignments, and to publish the results, then Professor X is planning research designed to contribute to generalizable knowledge. Her study must be submitted to the VCU IRB. The IRB may find that the study qualifies for exemption because it contains no identifiers, but Professor X may not proceed with the study until the IRB has approved it.

HUMAN SUBJECT is defined as a living individual about whom a PI (whether a professional or a student) obtains data through intervention or interaction with the individual, or identifiable private information.

Example 1: Professor Y is doing research comparing leading causes of death in the inner city with leading causes of death in the suburbs. He searches the death certificates of all persons who died in the last five years in the City of Richmond and surrounding counties. This study does not meet the definition of research involving human subjects because the research subjects are all deceased. The study need not be submitted to the IRB. However, Professor Y may choose to submit the research to the

IRB because the research (though not subject to federal regulations) may affect survivors of the deceased persons in the study.

Example 2: Professor Z wishes to gather data on blood units donated, but not used for transfusion by the Virginia Blood Donor system. The Virginia Blood Donor system removes all identifiers from the blood units prior to turning them over to Professor Z for research. Because Professor Z cannot link the blood samples to identifiable living individuals, he is not conducting research involving human subjects. Professor Z need not submit his research to the IRB. See Exemption (4) below.

EXEMPT CATEGORIES: Research activities involving human subjects that may qualify for exemption from Federal Regulations for the Protection of Human Subjects (45 CFR 46). The regulations include six broad categories of research that may be exempt at VCU; the determination that research study qualifies for exemption is made by the VCU IRB.

INSTITUTIONAL REVIEW BOARD (IRBs): Each institution that conducts research subject to Federal Regulations for the Protection of Human Subjects is required to establish a Board to review and approve research prior to its initiation and at appropriate intervals thereafter. A research study must be reviewed no less than once per year. The IRB's primary obligation is to exercise oversight of research to protect the rights and the well-being of research subjects. The IRB is charged to: protect the autonomy of subjects; to minimize risks to subjects and maximize benefits to the subjects and/or to society as a whole; and to assure that the risks and benefits of research are equitably distributed across all segments of society. The IRB has additional responsibilities to protect vulnerable populations including human fetuses, prisoners, children, and the cognitively impaired. The IRB has responsibility to minimize physical, psychological or social risks to subjects, and to maximize benefits to the subjects and to society.

INTERVENTION OR INTERACTION WITH SUBJECTS: Interaction includes interpersonal communication between investigators and subjects through surveys, interviews, administration of educational or diagnostic tests (e.g. x-rays, spinal taps, blood samples etc.) etc. Intervention includes physical procedures (e.g. taking blood samples, spinal taps, or x-rays). Intervention also includes manipulation of the environment.

EXISTING DATA, DOCUMENTS OR SPECIMENS: Existing data is constitutive of retrospective research. An item is considered to be existing if it was previously collected for another purpose. Information is considered to be existing if it is already contained in a system of files or records, or a data bank at the time that the research is submitted to the IRB. Data is not existing, (for regulatory purposes), if it is to be collected

during the course of the research study.

PUBLICLY AVAILABLE: Information is publicly available if any adult member of society can legally access it. For example: if the information can be found in a newspaper or magazine, in a public library, in publicly accessible data banks, in city directories or telephone books, on the internet (unless access is restricted), or in information published by federal agencies such as the Bureau of the Census or the National Center for Health Statistics. Information is not publicly available if access to it is restricted to certain individuals. Examples of information that is not public, include: college registration records, education transcripts, medical records, personal files, individuals' credit card debts, private correspondence, personnel files, etc. Please note that if information like credit card debts is not very secure, it is, nevertheless not intended to be available to any member of the public.

LINKED TO A SUBJECT: This phrase refers to any information that can identify a subject who participates in research. Information that can be directly linked to a subject includes: a person's name, address, social security number, medical record number, or e-mail address. An indirect link is information that can be combined with other sources of information such as file codes, birth dates, zip codes, height, weight, and physical characteristics. These Items of information can provide clues as to the identity of subjects. Indirect links might include: date of surgery, residence in a small town, (e.g. the subject is identified as a student at VCU who resides in Paw Paw, W.VA.) Birth, graduation, and marriage dates, can often be combined with other data to identify a person. For example, if information is filed in a database that includes 30 persons, and 5 of 30 are African Americans, one of the five is a woman. Any reference to an African American woman in the study could be easily linked to the single African American woman in the study.

Categories of Research that may be exempt (See 45 CFR 46 101.(b) (1) --(6).

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

Comment: This category allows exemption for research studies that involve evaluation of normal educational practices conducted in commonly accepted educational settings. Minors or children, as well as adults, may be subjects of such studies. Commonly accepted settings are not limited to schools. A car may be a commonly accepted setting for a driver education program. A kitchen may be a commonly accepted setting for a

chefs education program. A repair shop may be a commonly accepted setting for a mechanics education program. PIs who seek exemption for research in this category should provide evidence that the educational practices to be studied are frequently used educational practices carried out in a place where such practices are commonly accepted.

Exemption Category 2: Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless: (I) information obtained is recorded in such a manner that human subjects can be identified, directly or indirectly through identifiers linked to the subjects; *and* (ii) any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability, or be damaging to the subjects' financial standing, employability, or reputation. This category does not apply to research involving children if the research involves survey procedures, interview procedures, or observation of public behavior where the investigator participates in the activities being observed.

Comment 1: Exemption Category 2 includes research studies that collect research data by means of educational tests, survey or interview techniques, and observation of public behavior. Research may be exempt if data are recorded in such a way that no information can be linked to subjects, or, if information can be linked to subjects, such data could not reasonably place the subjects at significant risk. Research involving observation of public behavior is exempt unless the investigator participates in the public behavior, or manipulates the environment in order to elicit certain kinds of public behavior.

Comment 2: If the information gathered cannot be linked to a subject directly (by name, code, or social security number), or indirectly (by including information that contains clues to subjects' identity), the research will qualify for exemption. Even if information can be linked to the subjects, the study may qualify for exemption if the study data does not include sensitive information that could reasonably place the subjects at risk if it were revealed.

Example 1: Dr. Goodfellow is conducting a study of nutrition. He is comparing and contrasting the height and weight of 50 five-year-old children who live in a middle-class suburb, with the height and weight of 50 five-year-old children who live in the inner city. Dr. Goodfellow records no names. He has no code linking the children to a master list of participants. He records birth dates, zip codes, and racial characteristics of subjects. Dr. Goodfellow's research data could be linked to some subjects by cross-checking the information with public record systems such as city directories, and birth records. His research does not qualify for exemption

on grounds that it contains no identifiers. However, data concerning the height, weight and racial characteristics of five-year-olds cannot reasonably place the children at a significant level of risk even if it were to be disclosed outside the research. Therefore, the IRB may find that Dr. Goodfellow's research qualifies for exemption. Nevertheless, Dr. Goodfellow may not proceed with the study without obtaining permission from at least one parent of each child.

Example 2: Smartmoney, a business school student, wants to conduct a survey of individuals selected at random from an employment roster. The survey will ask employee-subjects to evaluate the managerial skills of their supervisors. Neither subjects nor supervisors will be identified. However, the investigator plans to place a tiny code on the back of each questionnaire so that he can tell which employees failed to respond. After a three week period he will send a second questionnaire to those who failed to respond to his first request. Smartmoney's study does not qualify for exemption because he is using a code that could be used to identify subjects, and because the information, if it became known outside the context of the research, could affect the subjects' financial standing or employability.

Comment 3: This category allows for exemption of research that involves the observation of the behavior of subjects if the behavior is public, and the investigator does not participate in or manipulate the activities being observed.

Example 3: Smartgrad is a social psychology doctoral student writing a thesis on the behavior of teenagers. One of his planned studies will include observation of high school students at basketball games. Smartgrad is a good friend of the person who makes loudspeaker announcements at basketball games of Greatjocks high school. He plans to have his friend announce the wrong score at the beginning of the second half of a critical basketball game. Smartgrad wants to study how the spectators and the players will react to false information. He plans to have his announcer friend correct the information after five minutes. He applies to the IRB for exemption under this category. The IRB finds that Smartgrad's research does not qualify for exemption because he is manipulating the environment in which he will observe the behavior of the subjects.

Exemption Category 3: Research involving the use of education tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under Exemption category (2) (above) of this section if : (I) The human subjects are elected or appointed public officials or candidates for public office; or (ii) federal statutes require, without exception, that the

confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.

Comment 1: If the research involves only education tests, or survey, interview or observation of public behavior of public officials, then the research may qualify for exemption -- despite the fact that it may involve significant risks for subjects -- because public officials are not entitled to the same degree of privacy that applies to private individuals.

Example: Buddingpol is a graduate student in the Department of Political Science. He designs a questionnaire to send to all presidential candidates in the year 2000. The questionnaire includes questions concerning possible marital infidelity, use of illicit drugs, any history of psychiatric treatment, serious health conditions that candidates may have faced, and the financial net worth of all candidates. Buddingpol's study is found by the IRB to qualify for exemption because it deals only with public officeholders or candidates for public office.

Comment 2: If the research is intended to include educational tests, surveys, interviews or observation of public behavior carried out under specific federal programs supported by the Department of Justice or the National Center for Education Statistics of the U.S. Dept. Of Education, then it may qualify for exemption. This exception is allowed because information in these programs falls under tight security required by federal law. PIs who conduct studies that derive data from, or add data to federal data bases operated by the agencies identified above, should check with the agency to determine whether their research qualifies for exemption. This information should be communicated to the IRB.

Exemption Category 4: Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

Comment 1: To qualify for this exemption, the data, documents, records or specimens used in research must be in existence at the time of review by the IRB. Data must be recorded in such a manner that subjects cannot be identified directly or indirectly.

Example 1: Dr. Curious operates a pathology laboratory in the basement of one of the MCV hospitals. He makes an arrangement with Dr. Stitch, a thoracic surgeon, to save small samples of tissue from each of Dr. Stitch's lung surgery patients. The tissue, if it is not turned over to Dr. Curious, will be discarded. The tissue samples contain no identifiers other than the gender and age of the unwitting tissue donors. Dr. Curious is anxious to

compare diseased tissue in young adults, middle-aged persons, and elderly persons to determine whether there is a correlation between the virulence of lung cancer and age. Dr. Curious' study does not qualify for exemption because he is not using specimens that already existed at the time the research project was submitted for review. He should prepare a consent document to obtain informed consent from each surgical patient whose tissue is to be used in his study.

Example 2: Dr. Epi is a dermatologist. For 20 years he has treated advanced basal cell carcinoma by surgery. In recent years he has tried repeated quickfreezing of basal cell lesions with some success. He has decided to review and compare results of both techniques in all of his basal cell carcinoma patients. He designs his research in such a way that he reviews the records of all basal cell carcinoma patients and extracts data from them. He also retrieves specimens of the same patients from the MCV path laboratory. He matches the names and pertinent information of the specimen donors to his patient records. He records the information without identifiers or clues to the identity of the subjects. He submits his study to the IRB for review. His study qualifies for exemption, because Dr. Epi plans to use existing data and specimens for his research, and because he will record the data with no identifiers that can be linked to human subjects.

Exemption Category 5: Research and demonstration projects which are conducted by or subject to approval of [federal] department or agency heads, and which are designed to study, evaluate, or otherwise examine (I) public benefit or service programs; (ii) procedures for obtaining benefits or services under these programs; (iii) possible changes or alternatives to those programs or procedures; or (iv) possible changes in methods or levels of payments for benefits or services under those programs.

Comment: This exemption grew out of the need to evaluate alternative methods of administering certain federal programs. If the proposed research is intended to evaluate methods for administration of federal programs authorized under the Social Security Act, Medicare, Medicaid or other public benefit programs, then it may qualify for exemption. The IRB will check such studies with OHRP to make certain that the proposed study qualifies for exemption.

Exemption Category 6: Tests and food qua lity evaluation and consumer studies, (I) if wholesome food without additives is consumed, or (ii) 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 (FDA) or approved by the Environmental Protection Agency (EPA) or the Food Safety and Inspection Service of the U.S. Department of

Agriculture (USDA).

Comment: This exemption pertains to food testing.

Example: Dr. Eatwell obtains a contract from Grapefruit Juice Unlimited to test the taste of pure grapefruit juice against grapefruit juice that is sweetened and contains preservatives. He plans to have each of 20 subjects test both pure and treated grapefruit juice to evaluate which is more likely to increase sales, and which, if either, may cause indigestion. This study qualifies for exemption only if the additives in the sweetened grapefruit juice fall within "safe" limits established by FDA, EPA, or USDA. It is Dr. Eatwell's responsibility to check the policies on safe levels of additives in the three agencies and to document the fact that the levels of additives will fall within those limits. If he does so, and submits the protocol to the IRB, the study will qualify for exemption.