

## **Risk and Harm**

### **Social and Behavioral Sciences Working Group on Human Research Protections**

*Approved January 2004*

#### **Overview**

The assessment of risk has been one of the most vexing processes for Institutional Review Boards (IRBs) and researchers to understand and apply. Careful scrutiny of terms and definitions provides insights into the meaning of this term as specified in the *Federal Policy for the Protection of Human Subjects* and how it should be used. Clarification by the Office for Human Research Protections (OHRP) of three issues would be instructive:

- A. *Probability and Magnitude of Harm*: First is the need to clarify the definition of “minimal risk.” The definition included in the federal regulations at 46.102(i) conflates two very different concepts, the “probability of harm” and the “magnitude of harm.” For minimal risk studies, this means that the worst harm that could occur in a study should not be very serious, even if many subjects experience it, and if the potential harm is serious, then the probability of a subject experiencing it should be very low. Differentiating these two concepts and providing guidance to IRBs and investigators would be helpful.
- B. *Daily Life Standard*: Second is the need to attend to the “daily life” standard in defining minimal risk. Guidance indicating that the daily life standard refers to low-level harms that are transient in nature and easily ameliorated would fill gaps in understanding and applying this concept in practice.
- C. *Expedited Review*: Third, once there is revised guidance regarding “minimal risk,” there is the need to re-visit the categories of expedited review to determine if the research it intends to capture with these categories is indeed captured and expedited. Much social and behavioral science research falls at or below the level of risk encountered in daily life or during the performance of routine physical or psychological tests, and yet there appears to be considerable variability in when these studies are considered for expedited review. Guidance in this area should assist in reducing the burden on IRBs, allowing members to concentrate on research protocols where the risk is greater.

Another issue requiring consideration by OHRP is the actual procedure and time frame of expedited review. The federal regulations anticipate an “expeditious” process; yet, here too there is wide variability in IRB practices. Investigators frequently report lengthy time spans in receiving expedited approval. It would be useful for OHRP to issue guidance and set expectations regarding best practices and the time frame for such review. With better understanding and use

of the expedited process, IRBs could devote time to full protocol review where it is most necessary.

## Background

The social and behavioral science community is concerned that the definition of minimal risk as set forth in the Code of Federal Regulations may not be sufficiently understood in practice by IRBs and researchers. In recent years, as IRBs have been under heightened scrutiny about whether they are adequately assessing risk and harm, they have too frequently operated unaware of the nature of social and behavioral science research involving human subjects, the likely risks and harms associated with such research, and the best procedures for protecting subject populations involved in such research.

Understanding the “daily life” standard for minimal risk is crucial for properly evaluating research in the social and behavioral sciences. As with any activity, there is potential for harm in the social and behavioral sciences—from inconvenience or embarrassment to stigma or legal or economic consequences. Typically, however, in these sciences, both the potential harms and the risks of them are minimal and not of the type routinely being assessed in biomedical research. Much of the risk relates to disclosure of the identity of human subjects or the information they provide; thus, considerable effort in these sciences is devoted to safeguarding subjects’ privacy and the confidentiality of the data they provide even when the information has no or minimal potential for harm.

It is in this context that this Working Group offers specific and general guidance.

Fundamental to understanding risk is to distinguish conceptually between the type of harm and the level of risk. Both ideas are present in the Federal Regulations. At 46.102(i), minimal risk is defined as:

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

On the surface, the common sense meaning of this definition is clear enough. If human subjects are exposed to a degree of harm roughly equivalent to what one would expect in the course of daily life or in the course of routine tests and examinations, then “minimal risk” applies. “Risk” is being used generally to mean some combination of the degree of harm and the probability of experiencing it. Routine tests and examinations rarely result in serious physical or psychological injury, and almost all of us encounter such risks on a routine basis. In other words, “minimal risk” means that the worst harm that could occur in a study should not be very serious—even if many subjects experience it, and, if the harm is serious, then the probability of any given subject experiencing it should be quite low.

However, IRBs and investigators seem to have difficulty applying this standard. One reason, perhaps the main reason, is that the formal definition—while fully workable—is not explicit in several respects. First, in attempting to define “risk,” it conflates the probability of harm and the magnitude of harm, and applies the word “minimal” to both. Second, it implies, but does not state that *by definition* harms “ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests” are

encountered by everyone with virtual certainty (that is, with a probability near 1.0). Finally, it does not distinguish between harm that is transient, such as an emotional but temporary reaction to survey questions, and harm that is longer lasting such as the loss of reputation following a breach of confidentiality.

In making determinations about risk and in applying the definition of minimal risk, it would be useful for IRBs to keep in mind the different dimensions of risk (the type of risk, the potential for harm, the nature of risk and harm in daily life, and lasting effects). It would also be useful for researchers to address these issues in preparing protocols for review. The following recommendations are intended to provide a means for OHRP, IRBs, and investigators to come to greater understanding and clarity with regard to these issues.

### **Recommendation 1**

OHRP should issue guidance to IRBs, to others associated with the human subjects protection system, and to the research community regarding the definition of minimal risk. The document should clarify the distinction between risk as a probability of harm and risk as a magnitude of harm. Investigators should be encouraged to clearly state the various kinds of harms that subjects might incur, the likelihood of subjects actually incurring such harm, and the available methods of ameliorating the harm. Educational materials elaborating the kinds of harms that can occur in social and behavioral research should be developed.

*Rationale: It is useful for those engaged in research and the review of human subjects protection to distinguish between the magnitude of harm and the likelihood of its occurrence. Guidance issued by OHRP would help IRBs orient their review, would help “designated” IRB persons undertaking expedited review (which can now take considerable time), and would help researchers know what needs to be addressed in research protocols to inform the review process. If investigators are asked to be explicit about the kinds of harms that might occur and the actual likelihood of harm occurring, it will be easier for IRBs to make decisions.*

### **Recommendation 2**

OHRP should reexamine the categories for *expedited review* set forth in 46.110(a) as they relate to social and behavioral sciences research (see attached). Also, as allowed for in 46.110(a) and according to the procedures set forth therein, OHRP should recommend amendments to the list that more explicitly take into account minimal risk research.

*Rationale: Better explication of the categories of social and behavioral research appropriate for expedited review will assist IRBs in making these determinations. In general, training of IRB members is encouraged as well as more placement of social and behavioral science experts on IRBs or, when that is not possible, use of consultants.*

### **Recommendation 3**

OHRP should emphasize the “daily life” standard for minimal risk. Guidance should also make clear that the “daily life” standard refers to low-level harms which are transient in nature and easily ameliorated either by the passage of time, by adequate debriefing, or both. Studies in which the level of potential harm falls at or below this standard should meet the criteria for expedited review.

*Rationale: The stress, discomfort, or embarrassment experienced in routine medical and psychological examinations are things that virtually all of us have experienced. A very low proportion of persons experience anything other than transitory effects from these examinations. There are many other aspects of daily life which might be stress producing, uncomfortable, or embarrassing, such as having an argument at work, dealing with a child's routine illness, being overheard talking about someone, or losing something important such as keys or documents, that are usually of low magnitude and have little probability of short- or long-term harmful effects. Much social and behavioral research falls at or well below this standard and thus should qualify for expedited review, where it does not already (see also Recommendation 2 above).*

#### **Recommendation 4**

OHRP should clarify that, in much social and behavioral science research, the most serious harm that could occur to subjects would result from a breach of confidentiality. Thus, OHRP should emphasize to IRBs the importance of research protocols addressing how information from human subjects will be protected from disclosure. Also, OHRP should clarify that many studies in the social and behavioral sciences do not involve sensitive information and thus the magnitude of harm needs to be considering in weighing the likelihood of any conceivable breach. Investigators nevertheless should be encouraged to be specific about methods for preserving confidentiality and, where necessary (with highly sensitive information), be provided with models for doing so. OHRP should take the lead in producing educational materials on this issue. A catalog of best practices would be useful.

*Rationale: There are at least two areas in which investigators could use guidance on this topic. Investigators who collect survey data on sensitive topics need instruction on how to properly safeguard raw data and computerized files. Investigators who gather ethnographic data need guidance on how to report results in such a way as to conceal the identity of organizations, groups, or individual subjects where appropriate. Also, certain subject populations may be more vulnerable to harm from even a minimal risk of being identified or having information they provided be linked to them (e.g., undercover law enforcement officials, HIV-positive employees, illegal immigrants, professionals engaged in white collar crime, victims of spouse abuse). Under such circumstances, procedures for ensuring privacy (e.g., no signed consent forms or recording of identifiers) and the confidentiality of the data need to be fully and completely addressed.*

**Table A: Summary of Harms and Ameliorative Measures\***

Kind of Harm	Minimal	Minor Increase over Minimal	Major	Ways to Ameliorate
Inconvenience	Boring, interruption	Unexpected major involvement		Adequate informed consent
	Most vulnerable are those with complicated lives or time constraints.			
Physical Harm	Transitory or very minor injury	First aid may be indicated	Violent assault, life threatening**	Appropriate safety considerations
	Most vulnerable: Those in contexts in which there are safety issues.			
Psychological Harm				
Worry (warranted or otherwise)	All of these psychological harms are highly idiosyncratic in occurrence and degree of harm, and difficult to predict. Sensitively administered informed consent can give persons an opportunity to decline if feeling particularly fragile and vulnerable. Post-research procedures (debriefing and desensitizing, offering counseling, making referrals) can ameliorate or prevent harms and turn unpleasant experiences into lasting benefits. These are excellent opportunities for subjects to learn and grow from the experience; debriefing should be educational and nurture personal insight and wisdom. Reiteration of confidentiality measures taken to prevent disclosure may be useful after participation in some research. Deception and concealment, especially with powerful induction to involve self in upsetting or reprehensible acts is ameliorated by initial consent to concealment with promise of total debriefing. An alternative, when studying aggressive or other reprehensible behavior is to study response to heavily induced desirable behavior (e.g., disobedience to authority).			
Upset, depression				
Embarrassment				
Shame or Guilt				
Loss of Self-Confidence				
Disrespectful Treatment of Subjects	This is an attribute of the researcher or the research treatment that may cause any of the other above forms of psychological harm. Effective respectful congruent communication (not a consent form) is essential.			
	Most vulnerable: those who are immature or emotionally fragile.			
Social Harm	Transitory embarrassment	Short-term minor stigma, conflict	Long-term stigma or scapegoating	Confidentiality & privacy protected
	Most vulnerable: those with something to hide.			
Economic Harm	Loss of a few \$\$s	Short-term loss of financial opportunity	Loss of credit, insurance, job, loss of lawsuit	Compensate minor harm, assure privacy & confidentiality
	Most vulnerable: those in need of relevant forms of financial security			
Legal Harm	Involvement with law enforcement	Misdemeanor conviction	Subpoena of damaging data, felony conviction	Certificate of Confidentiality, anonymity
	Most vulnerable: those involved in studies of illegal behavior and those currently involved in legal action relating to the research (whose data might be subpoenaed by the prosecution or opposing party).			

\*Table prepared for the Social and Behavioral Sciences Working Group on Human Research Protections by Joan E. Sieber, Working Group member (January 2004).

\*\*Major harms of this nature are secondary.

## **Categories of Research That May Be Reviewed by the Institutional Review Board (IRB) through an Expedited Review Procedure**

### Research Categories

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

(a) Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required. (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.)

(b) Research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

(2) Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:

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

(b) from other adults and children<sup>2</sup>, 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.

(3) Prospective collection of biological specimens for research purposes by noninvasive means.

Examples: (a) hair and nail clippings in a nondisfiguring manner; (b) deciduous teeth at time of exfoliation or if routine patient care indicates a need

for extraction; (c) permanent teeth if routine patient care indicates a need for extraction; (d) excreta and external secretions (including sweat); (e) uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue; (f) placenta removed at delivery; (g) amniotic fluid obtained at the time of rupture of the membrane prior to or during labor; (h) supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques; (i) mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings; (j) sputum collected after saline mist nebulization.

(4) Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. 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, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography; (e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

(5) Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for nonresearch 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. [45 CFR 46.101\(b\)\(4\)](#). This listing refers only to research that is not exempt.)



(6) Collection of data from voice, video, digital, or image recordings made for research purposes.

(7) Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, 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 from the HHS regulations for the protection of human subjects. [45 CFR 46.101\(b\)\(2\)](#) and [\(b\)\(3\)](#). This listing refers only to research that is not exempt.)

(8) Continuing review of research previously approved by the convened IRB as follows:

(a) where (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of subjects; or

(b) where no subjects have been enrolled and no additional risks have been identified; or

(c) where the remaining research activities are limited to data analysis.

(9) Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where categories two (2) through eight (8) do not apply but 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.