3Determining Minimal Risk in Social and Behavioral Research

The Common Rule is frequently described as a risk-based rubric, and a central task of an institutional review board (IRB) is to determine that risks are minimized and that the risks to the subjects are reasonable in relation to the anticipated benefits (45 C.F.R. § 46.111(a)(2)). “Risk” is a word fraught with many connotations, and the way the word is used in a lay context does not necessarily equate with that used in the utilitarian cost-benefit analysis intended by the Common Rule. But there is very little in the Common Rule itself or subsequent guidance that provides help with defining or assessing risk. The only definition of risk in the human subjects protection regulations is for minimal risk (45 C.F.R. § 46.102(i)). Over the past 30 years, this definition has guided IRBs in determining the level of review required by a research protocol. At the same time, there has been widespread inconsistency in IRB application of the minimal-risk criteria, due in part to the ambiguity of regulatory language (e.g., Lidz and Garverich, 2013; Shah et al., 2004).

Laudable aims of the changes to the Common Rule proposed in the Advance Notice of Proposed Rulemaking (ANPRM; 76 Fed. Reg. 44,512) were to enhance participant protections and reduce IRB and investigator burden, delay, and ambivalence (Emanuel and Menikoff, 2011; Fisher et al., 2013). The committee strongly supports these aims.

This chapter considers critical issues related to how best to ensure (a) that the definition of “minimal risk” is appropriate for the full range of current social and behavioral science research; (b) that IRBs and investigators have adequate guidance for avoiding underestimation and overestimations of minimal risk; and (c) that categories of research that may be reviewed through an expedited review adequately reflect the broad spectrum of social and behavioral science research. The committee’s proposed approach to assessing and minimizing participant risk adheres to the Belmont Report’s principles of beneficence, respect, and justice (U.S. Department of Health and Human Services, 1979) and to established canons of scientific and professional knowledge.

In response to the ANPRM, the Society for Research in Child Development (SRCD) convened the SRCD Task Force on Proposed Changes to the Common Rule (hereafter, “SRCD Task Force”). In its published report and commentary on the ANPRM, which addresses many of the issues also addressed in this report, the SRCD Task Force viewed research as “a moral endeavor that seeks to ensure that the welfare, autonomy and privacy rights of infant, child and adolescent research participants are adequately protected and that such protections do not prevent them from equitable sharing of the burdens and benefits of research” (Fisher et al., 2013, p. 4). The committee believes its approach is consistent with this view of research, expanded to apply to all research participants.

**Defining Minimal Risk**

As defined at 45 C.F.R. § 46.102(i), “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.” The ANPRM should be applauded for asking the research community to consider whether this definition of “minimal risk” needs revision. In the past 10 years, a number of ethics committees and scholars have grappled with how minimal risk should be delineated, and some consensus has developed (Meyer, 2013; Resnik, 2005; Rid et al., 2010; Wendler et al., 2005). While it is probably impossible—and in fact may be unwise—to completely eliminate variation in interpretation of the term, the regulations and guidance should be revised to reflect the developing consensus.

Whose “Daily Life” and Which Routine Procedures

One of the most persistent conundrums has been how to compare risks of the research to the risks of daily life or of routine examinations or tests. The question immediately becomes “whose daily life?” Is it the daily life of an average person in the general population or the specific population to be enrolled in the study? Despite recommendations from the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (U.S. Department of Health and Human Services, 1979) that minimal risk refers to a uniform standard based on the daily life and routine procedures experienced by the general population, in response to public comment the U.S. Department of Health and Human Services (HHS), in the Preamble to the Final Rule, articulated a relative standard describing minimal risk as “those risks encountered in the daily lives of the subjects of the research” (U.S. Department of Health and Human Services, 1981). Unfortunately, the final regulatory definition included neither the “general population” nor the “subjects of the research” language, resulting in the ongoing confusion and wide variations in the determination of minimal risk. The 2003 National Research Council report, Protecting Participants and Facilitating Social and Behavioral Sciences Research, wrestled with this question but was unable to achieve consensus for a solution. But since then, there has been considerable study of this issue and a consensus has developed that the “special population” approach should be rejected because it can result in an unjust distribution of risks. That is, a population-specific definition unjustly permits individuals to be exposed to higher levels of risk under the minimal risk category, simply because their daily lives are filled with greater risk than healthy individuals or those living in safe environments (Briefel et al., 2002; Fisher et al., 2007; Institute of Medicine, 2004; Kopelman, 2004; Oakes, 2002; Snyder et al., 2011; Wendler et al., 2005).

Defining the General Population Standard

Drawing on recommendations from the Belmont Report and more recent federal committees and independent reviews (Institute of Medicine, 2004; National Human Research Protections Advisory Committee, 2001; Secretary's Advisory Committee on Human Research Protections, 2005, 2008; U.S. Department of Health and Human Services, 2011), the Secretary's Advisory Committee on Human Research Protections (SACHRP) has noted that the definition of minimal risk based on the risks faced in daily life should “reflect ‘background risks’ that are familiar and part of the routine experience of life for ‘the average person’ in the ‘general population.”’ Although the definition of “general population” requires additional discussion, one starting point is to harmonize the Common Rule minimal risk definition with the “healthy persons” standard for minimal risk required for Subpart C, Additional Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners (45 C.F.R. § 46.303(d)).

While the healthy persons standard is a good start for grounding a general population definition, it may not sufficiently protect from unjust exposure to research harms healthy individuals living in unsafe environments in which violence and trauma produced by human or natural causes characterize experiences of daily life. Thus, regulators should consider whether the concept of safe
environments should be considered along with that of healthy persons in creating a uniform minimal risk definition.

An important caveat is that any modification to the definition of minimal risk may have substantial implications for the conduct of social and behavioral science research involving children (as well as for biomedical and educational research involving children) because Subpart D, Additional Protections for Children Involved as Subjects in Research, refers to the Common Rule's minimal risk definition as an anchor for regulations evaluating acceptable research procedures and required human subjects protections (Fisher et al., 2013). For example, the Common Rule minimal risk definition informs the conditions, stated in Subpart D (45 C.F.R. § 46.404 and § 46.405), under which an IRB can approve research that has no prospect of direct benefit to child participants. It also anchors IRB approval of a subset of waivers for parental permission and child assent (45 C.F.R. § 46.408). (Informed consent for research with child participants is addressed in detail below, in Chapter 4.)

As long as the Common Rule minimal risk definition remains the default criterion for risk categorization of research involving children, the Office for Human Research Protections (OHRP) must ensure that the application of the recommended general population standard does not result in the inadvertent application of an adult minimal risk standard to child participants. To address this concern, the committee recommends below that OHRP issue guidance on applying age-indexed criteria for application of the minimal risk criteria to risks in daily life and routine examinations (Fisher et al., 2007; Institute of Medicine, 2004; National Human Research Protections Advisory Committee, 2001; Secretary's Advisory Committee on Human Research Protections, 2005).

**Which Tests and Which Routine Procedures**

Any modifications to the definition of minimal risk also need to recognize that social and behavioral research is often conducted in or for educational institutions. Although much educational research involving normal educational practices conducted in educational settings is appropriately exempt from 45 C.F.R § 46, as currently stated under Exemption Category (1), other social and behavioral research conducted outside of educational settings may also include traditional tests of reading, mathematical abilities, problem solving, and other academic skills. For such research, the reference in the current minimal risk definition to routine medical or psychological examinations or tests is insufficient; the definition should be expanded to explicitly include educational examinations or tests. Additionally, the committee believes that restricting the definition of routine “examinations or tests” has caused confusion in IRB evaluation of prevention and intervention research in both biomedical and social and behavioral research contexts. Such research may include both routine medical and psychological examinations and routine medical and mental health procedures. For example, a community-based translational study examining the efficacy of two standard grief counseling techniques for elderly widows and widowers may pose no greater risks than procedures currently available to this population and should be classified as minimal risk. Similarly, a school-based prevention program to reduce interpersonal conflicts among students may use routine conflict-resolution psycho-educational procedures. To appropriately classify minimal prevention and intervention studies, a revised Common Rule could adopt the definition in **Recommendation 3.1** below, which includes “procedures” in its definition of minimal risk.

**Calculating the Probability and Magnitude of Harm**

An objective assessment of minimal research risk is a calculus involving both the magnitude of a potential harmful outcome and the likelihood that the outcome will occur. In particular, just because a risk of high magnitude is possible does not make it probable. The definition of minimal risk
incorporated into the original 1981 federal regulations was designed to reflect the Belmont Report’s recommendations on the importance of appropriately weighing probability against magnitude of harm. Although identifying the probability and magnitude of harm may have been more objective when research sponsored by the National Institutes of Health (NIH) was focused on a narrower range of biomedical disorders, over time the expansion of areas covered by both biomedical and behavioral research has left a vacuum in guidance on the knowledge base from which such estimates may be drawn. Consequently, IRBs often evaluate research as greater than minimal risk if there is a very small probability that the research may produce harm of high magnitude or if there is a high probability that research may produce harms or discomfort of small magnitude. The frequency of such misjudgments has heightened the need for guidance specific to research domains on the most appropriate knowledge bases for determining probability of a harm occurring and the magnitude of the harm if it occurs.

Recommendation 3.1: HHS should adopt the following definition of minimal risk under the Common Rule: “Minimal risk means that the probability and magnitude of physical or psychological harm does not exceed that which is ordinarily encountered in daily life or in the routine medical, psychological, or educational examinations, tests, or procedures of the general population.”

Guidance Recommended: OHRP guidance should be issued in the following areas to assist in operationalizing the definition of minimal risk in Recommendation 3.1:

- Clarify that estimates of risk should be uniformly applied across the general population and should not be indexed to the experience of the study population alone, in order to be certain that the benefits and burdens of research are distributed evenly across populations and to avoid an unjust distribution of risks.
- Define the general population standard in terms of healthy persons living in safe environments.
- Apply age-indexed criteria for determining the probability and magnitude of harms or discomfort in the daily life of, and in routine medical, psychological, or educational examinations, tests, or procedures of, infants, children, and adolescents (if the Common Rule minimal risk definition remains the default criterion for risk categorization of research involving children).
- Clarify how to calculate appropriately both the probability and magnitude of harm and discomfort, when determining whether research meets minimal risk criteria that include examples from domain-specific areas of research.

Procedural Improvements Needed: To avoid subjectivity and enhance continuity within and across institutions, IRBs could draw on established scientific and professional knowledge in their determination of the probability and magnitude of research harms in daily life and in routine medical, psychological, or educational examinations, tests, or procedures of the general population. However, care is needed to avoid confusing evidence-based probability estimates with the subjective possibility that harms and discomforts of high magnitude are likely to be produced by the research. For example, IRBs could consider adopting procedures that appropriately balance the probability and magnitude of research harms, in order to avoid subjectively judging research as having a greater than minimal risk in cases where there is a very small probability that the research may produce harm of high magnitude or where there is a high probability that research may produce harms or discomfort of small magnitude.

Research Needed: To build a stronger evidence base, research is needed for identifying the probability and magnitude of harms and discomfort in daily life and the nature of age-indexed, routine medical, psychological, or educational examinations, tests, or procedures of the general population. In addition research is needed to examine appropriate algorithms for determining
whether the calculus of probability and magnitude of harms and discomfort meets minimal-risk criteria.

**AVOIDING OVERESTIMATION AND UNDERESTIMATION OF HARM**

The definition of minimal risk in the Common Rule has confounded the research community since the human subjects protection regulations were first promulgated. The first comments warned that the vagueness of the definition would cause variability and confusion, and this outcome has certainly come to pass (Ceci and Bruck, 2009; Fisher et al., 2007; Wendler et al., 2005; Westra et al., 2011). And there is evidence that it leads to both overestimation and underestimation of risk (Wendler et al., 2005). This vagueness has been especially problematic for the conduct of research in the social and behavioral sciences, due in large part to (1) the lack of specificity in examples provided for minimal risk under the expedited risk category, (2) difficulty distinguishing research risks from participant vulnerabilities, and (3) the tendency of some IRBs to apply subjective overestimations of the level of harms that may be incurred through social and behavioral science research methods (Green et al., 2006).

Moreover, there may be little awareness by IRBs and investigators of the growing body of published empirical evidence describing participant perspectives on research risks and benefits of social and behavioral research, as well as biomedical research (Fendrich et al., 2007; Fisher et al., 2008; Langhinrichsen-Rohling et al., 2006; Lazovski et al., 2009; Leykin et al., 2011; McDonald et al., 2008; Pearlman et al., 2013). This increase is due in part to several NIH-sponsored funding initiatives supporting research on the responsible conduct of research (e.g., the NIH-wide Program Announcement, Research on Ethical Issues in Biomedical, Social and Behavioral Research) and to the growth of journals in the field, including the *Journal of Empirical Research on Research Ethics, Ethics & Behavior*, and the *American Journal of Bioethics: Primary Research, and Narrative Inquiry in Bioethics*.

In addition, there is evidence that many IRBs, regardless of whether their purview is mostly biomedical or social and behavioral science, tend to focus more on the magnitude of a harmful outcome, should it occur, and not on the likelihood that it will occur (National Research Council, 2003). This can result in what has been called concern for “the eggshell participant”: an IRB may come to focus on any conceivable risk for any conceivable participant and proceed “as if the risk faced by this ‘eggshell’ participant were the risk faced by all (or even the modal) prospective participant” (Meyer, 2013, p. 39).

This tendency to overestimation of risk has important and widespread consequences. It means that much research that currently fits within the current exempt category is subjected to expedited review, while minimal-risk research appropriate for expedited review is sometimes inappropriately viewed by an IRB as requiring full board review (Freundschuh, 2012; Petersen et al., 2012). At a minimum, overestimation of social and behavioral science research risk has slowed the review process. But more critically it has also resulted in IRBs requiring changes to minimize remote risks—changes that can compromise the scientific validity of the research or pose insurmountable barriers to studies essential for understanding social, behavioral, cognitive, and emotional influences affecting public health and well-being. If not adequately addressed through regulation or OHRP guidance, this problem may persist and extend to IRB evaluation of the ANPRM’s newly proposed “excused” category (76 Fed. Reg. 44,518-44,520). Indeed, mission creep has persisted in IRB review despite statements throughout the *Final Regulations Amending Basic HHS Policy for the Protection of Human Research Subjects* that the exempt and expedited categories were
specifically included to help reduce IRB burden in reviewing social science research that poses no risk, low risk, or minimal risk (U.S. Department of Health and Human Services, 1981).

Distinguishing Research Vulnerability from Social Vulnerability

One reason for the overestimation of harm in social and behavioral research, as well as in biomedical research, is the vague regulatory requirement to provide special protections for “vulnerable” populations under 45 C.F.R. § 46.111(b):

When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects.

The current wording of § 46.111(b), while well intentioned, is too broad to provide a useful metric for determining when and under what circumstances research would pose greater than minimal risk for any specific population. At the same time, this wording inadvertently encourages IRBs to apply subjective estimations of the nature, magnitude, and probability of the research harms faced by any population assumed to be vulnerable. In the absence of guidance to distinguish social vulnerability from research vulnerability, this wording appears to have inadvertently led IRBs to overestimate research risks for these populations, a particular problem for social and behavioral research studies. For example, there is an abundance of investigator reports of survey studies for research on sexuality, drug use, and other health-relevant behaviors in which IRBs have created barriers to research implementation based on the empirically unsupported claim that surveys or interviews on such topics may harm participants by encouraging them to engage in the behaviors being studied (Fendrich et al., 2007; Fisher, 2002, 2003; Fisher et al., 2013, p. 5; Langhinrichsen-Rohling et al., 2006; Mustanski, 2011).

Many social and behavioral science studies are designed to observe, survey, assess, or evaluate prevention or intervention programs designed to address vulnerabilities and protective factors associated with health disparities among socially vulnerable populations: for example, individuals with learning problems, substance abuse disorders, sexual and other health compromising behaviors, or a history of interpersonal violence or racial or sexual discrimination. However, just because the life histories of these individuals are characterized by higher levels of psychological and other harms than the general population does not mean that they are more susceptible to research risks (DuBois et al., 2012). As proposed in her model of Goodness-of-Fit Ethics, Fisher has argued that research vulnerability should be defined not by participant characteristics but as the joint product of the fit between participant characteristics and the specific research context (Fisher, 2002; Fisher and Goodman, 2009; Fisher and Ragsdale, 2006; Masty and Fisher, 2008). Thus, in assessing risk, it is crucial to distinguish between harm that may be caused by the research participation itself and harms that may be caused by the life situation or characteristics of the research participants. The latter harms, while real, are not caused by the research. For example, members of historically oppressed racial/ethnic minority groups in the United States may be subject to higher levels of psychological stress associated with explicit and implicit social, economic, and other forms of discrimination. But that fact alone does not raise to above minimal risk levels of psychological harm their participation in a survey study on frequency of, and their emotional responses to, everyday discrimination.

Failure to distinguish between vulnerabilities in participants' lives and their vulnerability to research risks can also lead to erroneous greater-than-minimal-risk classifications in IRB evaluations of prevention programs based on social and behavioral research results. Take, for example, a study...
designed to use a peer-education model to increase participants' knowledge about, and motivation to
get tested at, local clinics for HIV, in which the participants are economically disenfranchised
persons who inject drugs. The outcome measures include pre- and post-intervention surveys and
individual interviews on drug use, HIV risk behavior, frequency of HIV testing, and, with written
permission of participants, access to clinic information on their HIV testing. Although there are
health risks of potentially high magnitude associated with injection drug use, HIV risk behaviors,
and reactions to HIV testing, these risks are not produced by the educational prevention format; the
survey and interview questions; or the adequacy of HIV testing, counseling, and treatment provided
by local clinics. No evidence-based rationale exists for assuming the study procedures themselves
exacerbate or create the risks faced by the study population.

In addition, since Subparts B, C, and D of Part 46 are specifically designed to provide adequate
additional protections for pregnant women, prisoners, and children, respectively, asking IRBs to
consider these populations at risk not covered by these subparts places an undue barrier to research
critical in enhancing understanding and promotion of health and well-being in these populations.
The committee believes the regulatory language of § 46.111 should be eliminated and replaced by
guidance (discussed in greater detail below) on (a) distinguishing between vulnerabilities in
participants' lives and their vulnerability to research risks and (b) procedures for assessing the extent
to which the fit between participant characteristics and research procedures adequately minimizes
research harms and discomforts.

With respect to a related issue, even though considering the long-range effects of applying
knowledge gained in research is currently outside an IRB's purview (45 C.F.R. § 46.111(a)(2)),
some IRBs have included in their evaluation of social harm the consequences for the entire group of
conducting social and behavioral research studies involving members of populations suffering from
current and historical discrimination, if the study includes collection of data on socially stigmatizing
topics such as substance abuse or antisocial behavior. The ethical relevance of considering group
consequences will differ depending on the extent to which an individual person or a community is
the focus of research. Risks to groups in community-engaged research may arise from transferring,
for example, disease study results for an individual to a group, or stigma from a group causing harm
to an individual (Anderson et al., 2012). For example, in some instances the needs of the
community may not coincide with the needs of less powerful individuals who are the focus of an
investigation (Fisher et al., 2002). Investigator and IRB decision making regarding research
involving individual members of social minorities' communities and that involving the community
itself will benefit from identifying and communicating with the stakeholders to whom human
subjects protections are directly applicable (DuBois et al., 2012).

The committee believes that Subpart D of Part 46 already includes sufficient provisions for
protecting the rights and welfare of child populations, and we endorse the recommendation of the
SRCD Task Force that OHRP provide explicit guidance indicating that research involving children
as a class should not by default be required to undergo full board review (Fisher et al., 2013, p. 4).

Consideration of Steps Taken to Reduce Risk in the Assessment of Minimal Risk

Under current OHRP guidance, research posing what in the current ANPRM is labeled
“informational risk” can be considered minimal-risk research if reasonable and appropriate
protections are implemented so that disclosure risks are no greater than minimal.4

The expedited review procedure may not be used where identification of the subjects and/or their
responses would reasonably place them at risk of criminal or civil liability or be damaging to the
subjects' financial standing, employability, insurability, reputation, or be stigmatizing, unless
reasonable and appropriate protections will be implemented so that risks related to invasion of 
privacy and breach of confidentiality are no greater than minimal.

In its response to the ANPRM, SACHRP noted that an IRB's evaluation of whether the harms and 
discomforts of research subject to expedited review meet minimal risk standards should take into 
account steps taken to minimize risk. The committee agrees with this SACHRP recommendation 
that regulations harmonize criteria for evaluating the level of risk for informational and other types 
of research harms by requiring consideration of the adequacy of steps taken to minimize risk in the 
calibration of magnitude and probability of harm. In Recommendation 3.3, below, we recommend 
that any changes to regulations expand this statement beyond informational risks to require IRBs to 
consider appropriate procedures for minimizing all categories of risk.

Drawing on the National Bioethics Advisory Commission's report on Ethical and Policy Issues in 
Research Involving Human Participants, a 2003 National Research Council report described the 
types of harms that may occur to subjects in social and behavioral science studies: namely, physical, 
psychological, social, economic, legal, and dignitary harms (National Research Council, 2003, pp. 
46-47). (Dignitary harms were an added category that was absent in the Advisory Commission's 
analysis.) These categories continue to be useful ways to discuss potential harm, but only if they are 
embedded within a framework more conducive to assessing minimal risk within the context of risk-
minimizing procedures and distinguishing between the harms produced by the experimental 
methods and informational risk. The next sections of this chapter discuss traditional categories of 
harm within an experimental method/participant protections framework, with special emphasis on 
both ensuring adequate protections against greater than minimal risk and reducing overestimation of 
harm for social and behavioral research.

Avoiding Overestimations of Psychological Harm in Social and Behavioral Research

Traditionally, psychological harm has been viewed as the most probable (although still unlikely) 
type of harm to result from social and behavioral research. It may include negative self-perception, 
stress, anxiety, or an exacerbation of psychiatric symptoms. It may be momentary and of very 
limited impact, or it can be long-lasting and intense. Subjective evaluations and overestimation of 
psychological harm are seen by many social and behavioral researchers as a significant and unfair 
barrier to the conduct of their research (Fisher et al., 2013; Klitzman, 2011; Mustanski, 2011; 
Pritchard, 2011). One source of this overestimation of risk may be the diffuse nature of 
psychological reactions. Biomedical procedures pose specific risks of harms or discomfort, the 
probability and magnitude of which can be easily circumscribed. For example, under the current 
expedited research category 2, federal regulations specifically identify venipuncture as a minimal 
risk. In healthy participant populations, venipuncture poses a high probability of pain of minor 
magnitude and brief duration and, in less probable cases, of excessive bleeding. For some 
participants, it may cause dizziness of moderate magnitude, which can be rapidly reversed. For 
participant populations with hemophilia or other such disorders, there is sufficient scientific data on 
the increased probability and magnitude of the same harms to allow IRBs to determine whether 
sufficient participant protections are in place to minimize risk. IRBs are also unlikely to 
overestimate the risk of venipunctures. For example, although a serious infection can result any 
time skin is broken, the probability is rare; following the HHS list of procedures, an IRB would 
typically classify venipuncture as a minimal risk.

By contrast, participants can have a wide range of psychological reactions to any research method, 
whether the method is in the social, behavioral, or biomedical disciplines. Reactions can be positive 
(for example, feelings of altruism in contributing to scientific knowledge, pleasure in solving math
or verbal problems, appreciation of the knowledge gained from surveys or interviews on health topics) or negative (for instance, anxiety in anticipation of having a blood draw or answering survey questions about sexual behavior, frustration in response to participating in a difficult or boring task, anger at learning one has been deceived, emotional discomfort describing family conflict or peer bullying). Such reactions are probable but of small magnitude, short duration, transient, and reversible; in the majority of cases, the probability and magnitude of these reactions is not intrinsically different from similar reactions experienced in daily life or during the performance of routine physical or psychological examination or tests.

Dignitary harm may be considered within the class of psychological harms. It can result when research procedures create a violation of privacy or do not provide individuals with the opportunity to make an informed and voluntary choice to participate in research. Difficulties in distinguishing between public and private behaviors often create dilemmas for determining appropriate human subjects protections. For example, drawing on public death notices to contact surviving relatives to participate in a suicide autopsy study may be experienced as an invasion of privacy by those contacted, despite the fact that the information is public. Invasion of privacy may also be experienced by participants if informed consent procedures do not adequately describe the nature of survey or interview questions that would be included in the study. However, as detailed in the discussion of informed consent in Chapter 4, any such potential harms can be mitigated through appropriate risk-minimizing recruitment and informed consent procedures. Dignitary harms may also emerge in studies using deception, as there is some likelihood that some participants could be highly embarrassed or deeply insulted by the deception. However, the committee asserts that these reactions are rare, and deception per se should not be regarded as involving more than minimal risk.

Avoiding Overestimations of Physical Harm in Social and Behavioral Research

Misconceptions regarding physical harms have also created barriers to appropriate estimation of minimal risk levels for social and behavioral research designed to inform interventions and policies directed toward improving health and reducing health disparities. Human subjects protections for physical harm caused directly by research methods, while appropriate for the regulation of invasive biomedical research, rarely apply to social and behavioral research. In the rare situations that physical harm may be associated with research procedures in the social and behavioral sciences, the risk of harm is usually not a direct result of the experimental procedures. For example, in highly circumscribed situations physical harm may be an indirect risk of participating in behavioral intervention studies on mental disorders associated with self-harm. However, potential harms may be reduced to minimal levels if appropriate risk-minimizing procedures are integrated into the research design. Such procedures could involve trained personnel who would (a) conduct continual assessment and monitoring of self-harm ideation and behaviors and (b) implement specifically designed interventions for emergency treatment.

In rare cases, social and behavioral research methods themselves can increase the probability of high-magnitude physical harms. For example, in some contexts a study on conflict resolution involving a group of individuals previously diagnosed with explosive anger disorder may reasonably be associated with a higher-than-minimal probability that physical violence among participants may arise. However, such risks may be reduced to minimal if the research design has built in research staff procedures for recognizing evidence-based thresholds of anticipatory behaviors preceding aggression and methods for preventing these behaviors from escalating into actual aggression.
As discussed in the next section, physical harm may also be an indirect result of inadequate confidentiality protections in social and behavioral research. At present, IRBs do not have sufficient guidance in distinguishing among physical harms that may be the consequence of inadequate disclosure protections, indirect harms associated with an ineffective intervention, and the very small number of direct physical harms that may be induced by the research procedures themselves.

Potential Harms Resulting from Inadequate Confidentiality Protections for Social-Behavioral Research

The ANPRM devotes considerable attention to issues of informational risk, which it contends represents one of three relevant categories of potential harm: “physical, psychological and informational” (76 Fed. Reg. 44,515). It defines informational risk as resulting from harms that “derive from inappropriate use or disclosure of information, which could be harmful to the study subjects or groups. For instance, disclosure of illegal behavior, substance abuse, or chronic illness might jeopardize current or future employment, or cause emotional or social harm” (76 Fed. Reg. 44,516). The topic of informational risk will be discussed in greater detail in Chapter 5, but these potential harms are addressed in this section by using the term “confidentiality risk” to distinguish the ethically relevant issues of breach of confidentiality that could result in the potential harm to study participants.

Confidentiality Risk Minimization

Social and behavioral science investigators will face unnecessary barriers to excused and expedited review if IRBs overestimate the confidentiality risks described below by focusing on all possible harms that might arise from a breach of confidentiality rather than following current regulatory language on the HHS website, which directs IRBs to classify as minimal risk protocols that include “reasonable and adequate [investigator implemented] protections” that would ensure that “risks related to invasion of privacy and breach of confidentiality are no greater than minimal.” The committee believes the final regulations should reaffirm this directive and incorporate it directly into the Common Rule.

Confidentiality Risk and Physical Harm

Social and behavioral research may involve populations who live in unsafe environments where disclosure of research participation may result in physical retaliation from family members or peers. For example, failing to take adequate precautions to protect public disclosure of a woman's participation in a study on interpersonal violence might increase the risk of partner abuse. Similarly, recruitment procedures for a study on gang member violence that fail to protect the identity of those recruited may result in participants being subjected to retribution by other gang members who perceive such participation as a betrayal. The risks of such harms are serious and are best evaluated in terms of the adequacy of the recruitment and confidentiality protections to minimize such risk.

Confidentiality Risk and Social Harm

Social harms may involve negative effects on relationships or in interactions with other people if an individual's research participation or responses become available to the public. For example, sexual minorities (LGBTQ—lesbian, gay, bisexual, transgender, questioning) currently suffer from social and legal discrimination both within the United States and internationally. They are thus vulnerable to social, economic, and legal harms if their participation and/or responses in a study focused on sexual minority health were publicly disclosed. In this example, the potential social harms of study participation are not a consequence of the research procedures themselves but would result from inadequate confidentiality and data security protections.
Confidentiality Risk and Economic Harm

Economic harm involves financial loss, loss of employment opportunity, increase in health care or other insurance costs, or other consequences with a negative monetary value that result from public disclosure of an individual's research participation or individual data (e.g., organizational studies on job behaviors or attitudes undesirable to employers, studies on cheating among college students). As in the case of social harms, these potential harms are not a consequence of the research's experimental methods but would result from inadequate confidentiality and data security protections.

Confidentiality Risk and Legal Harm

Legal harm can include arrest, conviction and incarceration, loss of probation or parole, and civil lawsuits. Such harm can result when research recruitment procedures create risks for public disclosure of illegal behavior. For example, street recruitment for participation in ethnographic or other studies of illegal drug activities or gang-related behaviors could lead police to identify and arrest individuals approached by research staff. While participants need to be protected from such harms, the legal liability in such cases arises not from the types of questions and interviews that might be conducted as part of the research but from inadequate privacy protections instituted during the recruitment phase.

There are, however, social-behavioral research studies in which the design of the study has a high probability of producing data that may require mandatory disclosures, such as situations in which state law requires that certain types of researchers report particular activities, such as child or elder abuse. The legal harms to participants posed by these studies are a function of these reporting responsibilities, and these harms should be distinguished from harms produced from the experience of answering questions about these issues. In such circumstances, investigators need to know their legal reporting responsibilities and those of their research staff, determine evidence-based criteria for determining that a legally reportable disclosure has occurred, and ensure that informed consent procedures adequately describe these reporting obligations, to ensure participants make an informed participation choice (Fisher and Goodman, 2009; Fisher et al., 2002).

Recommendation 3.2: To ensure just distribution of research benefits and risks across diverse populations and to avoid subjective overestimations of potential research harms, HHS should eliminate current regulatory language at 45 C.F.R. § 46.111(b) identifying certain populations as “vulnerable to coercion and undue influence” and requiring additional but unspecified human subjects protections.

Guidance Recommended: To ensure adequate subject protections as well as fair access to the benefits of research, OHRP guidance should be provided to assist in distinguishing between vulnerabilities in participants' lives and their vulnerability to research risks.

Procedural Improvements Needed: IRBs could take steps to avoid confusing the risks participants may face in their daily lives from the risks of potential harms produced solely by their participation in research.

Recommendation 3.3: HHS should harmonize regulations such that decisions regarding the level of potential informational, physical, and psychological research harms must take into account whether reasonable and appropriate protections will be implemented to reduce the probability and magnitude of harm or discomfort to no more than minimal.

Guidance Recommended: OHRP guidance should be issued to assist in
• determining whether steps to minimize risk are sufficient for research designs to be categorized as minimal risk; and

• distinguishing between physical and psychological harms associated with informational risk (e.g., the harm derives from inappropriate use or disclosure of information, which could be harmful to the study subjects or groups) and those caused by the research procedures themselves.

**Procedural Improvements Needed:** In decisions regarding level of risk, IRBs could consider

• avoiding overestimation of research harms by ensuring that their members consider the extent to which risk-minimizing procedures reduce the probability and magnitude of physical and psychological harms to not more than minimal risk; and

• avoiding erroneous judgments that research that may elicit negative psychological reactions of low magnitude in some participants is by default greater than minimal risk.

Reactions, such as anxiety in anticipation of having a blood draw or answering questions about health-compromising behaviors, may be probable but of small magnitude, short duration, transient, and reversible. In the majority of cases, the probability and magnitude of such reactions is not intrinsically different from similar reactions experienced in daily life or during the performance of routine physical or psychological examination or tests.

**Research Needed:** Research is needed to provide empirical evidence for effective procedures for minimizing potential physical, psychological, and informational research risks to no more than minimal risk levels.

**EXPEDITED REVIEW**

The ANPRM has proposed to (a) expand the category list for expedited review, (b) provide a default presumption in the regulations that a study which includes only activities on the list is a minimal risk study, (c) eliminate the requirement of routine annual continuing review of research that has been approved under the expedited procedure, and (d) appoint a standing federal committee to periodically review and update the expedited review list, based on a systematic, empirical assessment of the levels of risk (76 Fed. Reg. 44,516-44,517). The committee concurs with these proposals and offers recommendations in this section to ensure that social and behavioral research receives equitable consideration in IRB review.

**Including Social and Behavioral Science in the Expanded List for Review Categories of Research**

The committee welcomes the ANPRM proposal to expand the list of research categories appropriate for expedited review. Although the current category 7 list of expedited research includes a wide range of social and behavioral research methods, IRBs too often use intuition rather than scientific data to classify social and behavioral research studies as greater than minimal risk and to either require that the protocol undergo full board review or require the research investigators to modify their protocols to address psychological reactions of high magnitude but very low probability. We believe that a more specific breakdown in the category list of social and behavioral research procedures, perhaps equivalent to the category 1 through 4 examples of biomedical methods, may assist investigators and IRBs in identifying when a protocol merits expedited review. We also applaud the ANPRM recommendation for a standing committee for timely updating of the expedited list. We note that this standing committee needs sufficient representation from social and behavioral science disciplines, including researchers with expertise in studying a wide range of populations.
Expedited Review of Research Involving Children

Commenting on the ANPRM, the SRCD Task Force concluded that, historically, the perception of children as a population vulnerable to research harms has denied them the full benefits of scientific knowledge and evidence-based interventions essential to their health and well-being:

IRB reviews have often subjected research involving children to over-zealous protectionism (Hoagwood et al., 1996). The 1998 NIH mandate for the inclusion of children in research created a sea change in the interests of government and industry to fund pediatric and developmental research. This increase was not however matched by sufficient reassessment of whether existing ethical frameworks and regulations were appropriately calculated to the twin goals of access to and protection governing the responsible conduct of pediatric and developmental research (Kodish, 2005). (Fisher et al., 2013, p. 13)

To date, pediatric and developmental research scientists still encounter obstacles to scientifically valid and socially valuable research as a result of beliefs that all research involving children must be subject to full board review or to risk/benefit assessments that overestimate the harms and discomforts of procedures meeting expedited review criteria (Fisher et al., 2013, p. 3; Shah et al., 2004). These beliefs persist despite the fact that the current categories for expedited review explicitly state that, with few exceptions, “the categories in this list apply regardless of the age of subjects”.

IRB decisions are often motivated by value-laden concepts of vulnerability in areas such as adolescent sexuality research, resulting in institutional barriers to the quality and conduct of socially critical research that has the potential to improve the health and welfare of children and youth (Mustanski 2011; [Wendler et al.] 2005). One reason for this over-protective IRB stance is that Common Rule regulation § 46.111a[3] refers to children as a “vulnerable” population requiring additional protections—but the regulation neither defines vulnerability nor references the additional protections provided in Subpart D…. In some cases, paternalistic protections that discourage research involving children create a population of “therapeutic orphans,” unable to accrue the benefits derived from scientific advances (Leonard et al. 1996). (Fisher et al., 2013, pp. 3-4)

To help remove these unsupported obstacles to valuable research, the committee has recommended, in its Guidance Recommended, that OHRP underscore the applicability of the expedited categories to research involving children and provide specific age-indexed examples.

Risk Equivalence and Expedited Review

No list can adequately include all the variations in minimal-risk research procedures that should be eligible for expedited review. And waiting for the list to be updated may result in unnecessary barriers to responsible science. There are many ways to judge the risk equivalence of research procedures including the duration and frequency of the procedure, the cumulative risk posed by a set of procedures, and the degree to which any harms, if they do occur, are transient and reversible. OHRP thus needs to make clear that the list of expedited review categories is an example rather than an exhaustive, limited set of procedures. Further, procedures not specifically listed in the expedited categories should be considered minimal risk if their risks can be determined to be functionally equivalent or less in probability and magnitude of harms and discomforts to listed procedures.
Ensuring Adequate Classification of Excused and Expedited Categories

The committee welcomes the current ANPRM proposal to classify surveys, educational tests, interviews, focus groups, and specified types of benign interventions used in social and behavioral research as excused if they only present informational risk (see Chapter 2). However, additional guidance is needed to help investigators and IRBs appropriately distinguish between minimal risk procedures that are appropriately classified under the excused versus the expedited review categories. For example, under current conditions IRBs have had difficulty distinguishing social and behavioral research procedures, such as surveys that meet criteria for exemption, from those that should undergo expedited review. Without explicit guidance, this confusion may extend to instances in which research that should be classified under the new proposed category of excused research is erroneously subjected to expedited review.

In its response to the ANPRM, SACHRP noted that evaluation of the harms and discomforts of the research should take into account (a) the nature of the study procedures; (b) other study characteristics; (c) characteristics of subjects to be enrolled in the research, including an evaluation of subject susceptibility, vulnerability, resilience, and experience in relation to the procedures; and (d) steps taken to minimize risk.8 Research appropriate for expedited review includes studies that, because of the specific nature of the research procedures and/or the characteristics of the subject population, require consideration of human subjects protections beyond those normally applied, in order to ensure that harm or discomfort created solely by the research procedures are not greater than minimal risk.

Recommendation 3.4: HHS should clarify in regulations the conditions under which research methods, that might otherwise be classified under the new excused category, are appropriate for expedited review because the specific nature of the research procedures and/or the characteristics of the subject population require consideration of human subjects protections beyond those normally applied for excused research, in order to ensure that harm or discomfort created solely by the research procedures are not greater than minimal risk.

Guidance Recommended: The committee offers below elements of a guidance statement that would help investigators, IRBs, and research and academic institutions understand when studies implementing the methods described under the excused category require expedited review. Such guidance, if issued by OHRP, would assist investigators and IRBs in developing risk-minimizing human subjects protections appropriate for the following special situations, in which protections are needed beyond those required to minimize informational risk:

a. The participant population is known to have decisional vulnerabilities empirically established to require enhanced informed consent protections for the type of study to be conducted.

b. The study is designed to produce clinical changes in health, health-related behaviors or symptomology, and includes identifiable information.

c. Public awareness of recruitment procedures can jeopardize participant physical safety or reveal criminal behavior.

d. The nature of the research data collected requires specific plans for reporting illegal behaviors, providing emergency treatment, or protecting a participant or third party from physical harm.

e. Use of deceptive techniques includes procedures that are specifically designed to induce psychological, social, or physical discomfort.

f. Additional protections are necessary to avoid harms produced by an existing professional or service relationship with research staff that would compromise voluntary participation.
Below are some examples of research, keyed to the special situations listed in the Guidance Recommended above, for which it would be appropriate to assign the research protocol to expedited review:

a. A study involving individuals diagnosed with obsessive-compulsive disorder and a nonclinical population designed to assess the validity of a scale to detect malingering.

b. A survey study asking adults with intellectual disabilities about their adaptation to independent living housing.

c. Research comparing the effectiveness of a peer- versus counselor-led education program to reduce alcohol consumption among college students found in violation of institutional rules against drinking on campus.

d. A study recruiting street-drug users in public spaces that has the potential to alert local police to prospective participants' illegal behaviors.

e. A focus group study on parenting styles that asks for specific examples of physical discipline that may elicit reports meeting criteria of child abuse that an investigator is required by law to report.

f. A deception study using a confederate to assess participants' emotional reactions to peer rejection.

g. A study on nursing aides' attitudes toward patients hospitalized for HIV-related infections, conducted by a senior psychologist on staff.

**Guidance Recommended:** The following actions would facilitate the adequate classification of excused and expedited risk categories:

- OHRP should expand the list of research eligible for expedited review to include additional specific examples of social and behavioral research to assist investigators and IRBs in identifying when a protocol should be submitted for expedited review.

- The standing committee appointed by OHRP to review and update categories for expedited review should have sufficient representation from researchers with expertise in social and behavioral research involving a wide range of populations.

- OHRP should take steps to ensure that investigators and IRBs appropriately apply categories for expedited review to research involving children and adolescents and do not by default require research involving children to undergo full board review.

- OHRP should clarify that the types of research listed in the expedited category are examples rather than an exhaustive, limited set of procedures. Further, it should be clarified that procedures not specifically listed in the expedited categories should be considered minimal risk if their risk can be determined to be functionally equivalent or less in probability and magnitude of harms and discomforts to listed procedures. In addition, to ensure equal protection and opportunities for participation for all populations, equivalent risk evaluations should not be based solely on the content area covered by an examination or test (e.g., health behaviors) but on whether the content, method, and language of inquiry is population-appropriate and whether the investigator has the training required to treat participants with sensitivity and respect.

**Procedural Improvements Needed:** Investigators and IRBs might consider for expedited review research protocols whose risks can be determined to be functionally equivalent to research methods specifically described in current expedited review categories. Estimates of risk equivalence can include the duration and frequency of the procedure, the cumulative risk posed by a set of procedures, and the degree to which any harms, if they do occur, are transient and reversible.

Individuals who are vulnerable to risks in their daily lives should not be considered by default to be more susceptible to greater than minimal research risks than other populations. Rather, established scientific knowledge or professional expertise should be considered that indicates which specific types of research procedures are associated with an increase in the probability and/or magnitude of harms for specific participant populations.
RESEARCH INVOLVING GREATER THAN MINIMAL RISK AND REQUIRING FULL BOARD REVIEW

As discussed above, the majority of social and behavioral science research methods pose harms of no greater than minimal risk either in and of themselves or once appropriate human subjects protections are instituted that ensure the probability and magnitude of harm posed by research participation are minimal. Rare instances of greater-than-minimal-risk social and behavioral research might occur, for example, when a psychological or behavioral intervention study involving individuals with serious mental health disorders includes treatments that have a reasonable possibility of exacerbating distressful or maladaptive psychological or behavioral symptoms (for instance, a study testing effectiveness of exposure therapy for severe phobias). A second example might include the potential for physical harm indirectly associated with assertiveness training for victims of interpersonal violence who are still living with their abusive partners. A third example might include studies involving institutionalized individuals with declining or persistent neurocognitive or affective disorders whose ability to understand or assert their right to refuse or withdraw from participation may be compromised by the research context.

**Guidance Recommended:** To avoid overestimation of risk, OHRP guidance is recommended to clarify that expedited review should be considered the default procedure for evaluating social and behavioral science research that is not excused. In addition, decisions to require full board review should be based on established scientific or professional knowledge indicating a significant probability that participants will experience a magnitude of risk that is greater than minimal and that cannot be adequately reduced through risk-minimizing procedures.

OHRP guidance is also recommended to clarify that research involving children, prisoners, persons from economically or socially disenfranchised groups, individuals with mental disorders, those engaged in illegal activities, or other social groups traditionally labeled as “vulnerable” should not by default require full board review. IRBs should be directed to only assign such studies for full board review if the research procedures pose greater than minimal risk and appropriate human subjects protections may not be sufficient to reduce such risks to the level of minimal risk.

**Procedural Improvements Needed:** In determining whether research poses greater than minimal risk, investigators and IRBs should draw on established scientific or professional knowledge to help determine whether the probability and magnitude of harms associated with the research procedures themselves pose greater than minimal risk and that appropriate human subjects protections may not be sufficient to reduce them to minimal risk levels.

**STREAMLINING EXPEDITED AND FULL BOARD REVIEW**

The committee endorses the ANPRM recommendation that research approved under expedited review should not require continuing review (76 Fed. Reg. 44,517). However, this recommendation alone does not adequately address the problem of lengthy delays for IRB review of research in the expedited category (Gordon, 2003; Koski, 2002). We therefore recommend below that OHRP guidance to IRBs specify time limits in processing research under expedited review.

There will be instances in which a protocol submitted includes new research methodologies, population characteristics, or research contexts for which established scientific and professional evidence, the investigator's previous research experience, or clear guidance on human subjects protections may require full board review to ascertain whether or not the research presents no greater than minimal risk. To ensure appropriate human subjects protections, flexibility in assignment to expedited or full board review is required in such situations. Timeliness of review is
also required to ensure that the need for IRB deliberation does not cause delays that create undue barriers to the conduct of socially significant research and ethically responsible research. Consequently, regulations should specify time limits on the IRB processing of research under full board review, the time permitted to elapse before communicating a decision to the investigator, and, if the protocol is not approved, the specific nature of information communicated to the investigator to facilitate timely re-review.

**Recommendation 3.5:** To streamline expedited and full board review and procedures, HHS should eliminate the requirement for continuing review for expedited research.

**Guidance Recommended:** OHRP should offer specific guidance on time limits for conducting expedited reviews and processing research under full board review. For example, with rare exception, a decision on expedited review by the IRB should be communicated to the investigator within 2 business weeks. If the review does not result in an approval, the IRB should provide a specific rationale and directives for the specific information required for the review to proceed in a timely manner via deferral, specific directive comments, or a decision to submit the protocol for full board review.

Full board meetings would reasonably be scheduled approximately once a month to ensure timely review of research protocols. With rare exception, a decision by the IRB should be communicated to the investigator within 10 business days of the full board meeting. If the review does not result in an approval, the IRB should provide a specific rationale and directives for the specific information required for the review to proceed in a timely manner.

**ESTABLISHING AN EMPIRICAL KNOWLEDGE BASE FOR LEVEL OF RISK**

IRBs should recognize that daily life is not a risk-free affair. For example, car trips and sports have risk and are a part of daily life (Wendler et al., 2005). But even those normal daily risks may be context-specific, and the related benefits of the activities in context must be considered in assessing the risk. Moreover, there is limited empirical data about the risks of daily life (Fisher et al., 2007). Thus, even if there is consensus that a "general population" standard should be used for assessment of minimal risk, there will be continued disagreement as to what constitutes “routine experiences ordinarily encountered.” For much research, a better standard for comparison may be routine tests and examinations, especially when those routine tests are contextually similar to the research under consideration (Fisher et al., 2007; Resnik, 2005).

The committee does not take a position on whether the daily-life risks or those of routine tests or examinations should take precedence. Both aspects can help IRBs consider levels of risk. What is clear, however, is that those standards alone are not sufficient to guide IRBs. More empirical research is needed on the relative risks of the various bases used to assess a minimal level of risk. IRBs need concrete contextual examples to guide their deliberation. While greater clarity in regulatory language would no doubt be helpful, it does not eliminate the need for continued research and guidance.

**Research Needed:** Research is needed to study the effects of social and behavioral science research on research participants so that evidence-based assessments of “known and foreseeable” risk are more feasible. In particular, research is needed to properly address nonphysical risks of research and the methods that create them, rather than having IRBs rely on anecdote or moving to make drastic changes based on efficiency. Research is also needed on the effectiveness of confidentiality strategies in reducing risks of physical, social, economic, and legal harm.
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Footnotes

1 As explained in Chapter 1, “Common Rule” is used throughout this report to refer to 45 C.F.R. § 46, Subpart A.

2 The Office for Human Research Protection Institutional Review Board Guidebook (1993) did define risk as follows: “The probability of harm or injury (physical, psychological, social, or economic) occurring as a result of participation in a research study. Both the probability and magnitude of possible harm may vary from minimal to significant.” But neither the human-subjects research regulations nor the formal guidance from the Office for Human Research Protections define risk.

3 See the 2008 SACHRP Letter to HHS Secretary at http://www.hhs.gov/ohrp/sachrp/sachrpletter013108.html [December 2013].


5 See the 2011 SACHRP Letter to the HHS Secretary at http://www.hhs.gov/ohrp/sachrp/commsec/sachrpanprmcommentsfinal.pdf [November 2013].


8 See the 2011 SACHRP Letter to the HHS Secretary at http://www.hhs.gov/ohrp/sachrp/commsec/sachrpanprmcommentsfinal.pdf [November 2013].

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