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Understanding 'Minimal Risk' in SBR: NRC Recommendations for Proposed Changes to the Common Rule

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**Changes to the Common Rule:
Challenges and Opportunities for IRBs**

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The Significance of the Minimal Risk Classification

- “Minimal Risk” is a regulatory “sorting” or “gateway” mechanism
- It permits IRBs to waive certain human subject protection requirements and approve certain types of research with vulnerable populations.
- E.g., Expedited review, waiver of elements of IC, procedures involving children with no prospect of direct benefit



Minimal Risk Barriers to SBR Research

Ambiguity of regulatory minimal risk definitional language

Overly broad SBR examples qualifying for expedited review



Over-estimation of risk: “Eggshell Participant”

Consent “warning clauses” jeopardizing scientific validity

Unnecessary Full Board Review



ANPRM Requested Comments on Minimal Risk Definition

§ 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 Definitional Problem Who's Life is it Anyway?

General Population/Uniform Standard: 1977 – 1979 National Commission & HHS recommended “healthy person”

Subject Population/Relative Standard: 1981 Preamble “subjects of the research”



Whose Life? Who Knows?

However...neither “healthy persons” or
“subjects of research” was included in the final
definition of the Common Rule



Ambiguity for Subparts A, B & D

* *“Healthy persons” was preserved for Subpart C*



NRC (2014) Recommendation: General Population Standard

IOM, 2004; SACHRP, 2005

- Participants should *not* be exposed to greater research risk simply because they are exposed to greater risk in their daily lives or routine health examinations
- MR should be indexed to the daily life or routine physical or psychological examinations or tests ordinarily experienced by “*healthy persons living in safe environments*”



General Population Standard: Avoiding Risk Under-Estimation

Examples

- **SBR:** A study testing the effectiveness of exposure therapy for severe phobias will initially elicit high levels of anxiety. It should not be judged as minimal risk simply because phobic patients experience high levels of anxiety in their daily lives.



NRC Recommendation: Age-Indexed MR Criteria

- *The general population standard should be age-indexed to adequately reflect the magnitude and probability of harms and discomforts in the daily lives and routine health examinations of children and adolescents*

IOM, 2004; SACHRP, 2005, SRCD/Fisher et al 2013



Over-estimation of Adolescent Risk Research

- SBR includes surveys and prevention programs on adolescent sexual behavior, gender identity, substance use, bullying and other developmental risks
- Many IRBs categorize these surveys as greater than minimal risk
- Full Board Review & Denial of Guardian Permission Waiver under CFR46.408/116
- Adolescents refuse to participate if guardian permission is sought
- Research is not conducted or conducted with a biased sample



Age-Indexing and Minimal Risk Review of Adolescent Survey Research

Routine visits to physician or psychologist: Sexual health and behavior, substance use, sleep disorders, anxiety, depression, peer and family relationships (SACHRP, 2005)

Adolescent Daily Life

- School health curricula include information and tests on sexual behaviors, substance use, conflict resolution; information on school staff who handle harassment, bullying, or discrimination complaints.
- Regular use of Internet to learn and discuss these issues with peers



NRC Recommendation: Expand Minimal Risk Definition to include “Procedures”

The terms “examination” or “tests” do not adequately cover routine procedures used by health and mental health practitioners

- **Stress reduction techniques**
- **Conflict resolution strategies**
- **Evidence based cognitive-behavioral techniques**
- **Cognitive enhancement techniques**



NRC Recommendation: MR Definition to Include “Educational”

- Although many SBR research conducted on normal educational practices are exempt, traditional educational tests (e.g. reading comprehension, problem solving) are often used outside of the school setting
- “.....routine physical, psychological and educational examinations, tests or procedures.



NRC Criteria for Expedited Review

- The OHRP expedited list should include constantly updated SBR examples, and....
- Guidance that IRB decisions should not be limited to these examples, but based on “risk equivalence”



NRC Recommendation: Criteria for Minimal Risk Equivalence

- Level of harm/discomfort
- Duration
- Cumulative characteristics
- Reversibility of harm

SACHRP, 2007



Distinguishing Research Vulnerability from Social Vulnerability:

- CFR 46.111 requires “additional safeguards” for “populations vulnerable to coercion or undue influence”
- However, Subparts B, C, and D already provide adequate safeguards
- CFR 46.111 inadvertently encourages IRBs to apply undefined “additional protections” to undefined “vulnerable” populations and leads to risk over-estimation



Distinguishing Social from Research Vulnerability

- Just because their life history may be characterized by high levels of psychological or other risks, does not mean that S will be more likely than the general population to experience higher levels of research harms or discomforts
- Example: Study on career training effectiveness involving recent Iraq veterans some of whom are diagnosed with PTSD



NRC Recommendation: Redefining Research Vulnerability

- HHS should eliminate CFR 46.111 from the Common Rule
- OHRP should provide guidance on distinguishing research vulnerability from social vulnerability



Defining Minimal Risk Through Risk Minimizing Procedures

- § 46.110 Expedited Review
IRBs should classify as minimal risk protocols that include
“reasonable and adequate procedures that are implemented so
that risks related to invasion of privacy and breach of
confidentiality are not greater than minimal”

<http://www.hhs.gov/ohrp/policy/expedited98.html>



NRC Recommendation: HHS Should Harmonize Regulations

- IRBs should classify as minimal risk protocols that include “reasonable and adequate procedures that are implemented so that risks related to invasion of privacy, breach of confidentiality and physical and psychological discomfort or harm are not greater than minimal”



Example: Minimal Risk Research with Socially Vulnerable Population

Research on HIV educational prevention program for PWID; Measures include drug use, HIV knowledge & behaviors

- Informational risk is minimized through CoC & other privacy protections
- Ss screened for intoxication/craving to ensure IC
- Research procedures do not exacerbate/create drug use or HIV behaviors



ANPRM New “Excused” Category:

- Only “informational risk” no greater than minimal or
- Data protection plans reduce risk of disclosure to no greater than minimal
- IRB registration, but No IRB review: Periodic oversight
- HIPAA as appropriate data protection plan *NRC rejects HIPPA model*



NRC Examples of SBR “Excused” Research

- **Familiar benign low or no risk interventions:** Ethnographic or survey study on how rail users, technicians and officials talk about experiences with high speed travel
- **Minimal informational risk:** Anonymous survey of personality traits leading to different leadership styles among business executives.
- **Deception that does not include physical or psychological discomfort:** Healthy adults play cooperative/competitive game against “another person”, but is in fact playing against a computer—debriefing follows.



NRC Criteria for Distinguishing Excused & Expedited Categories

1. Ss decisional vulnerabilities requiring enhanced informed consent protections
2. Study designed to produce clinical changes in health, health related behaviors or symptomology
3. Recruitment can jeopardize participant physical safety or reveal criminal behavior



NRC: Distinguishing Expedited from Exempt Categories

4. Data requires specific plans for disclosure/reporting
5. Deceptive techniques designed to induce psychological or physical discomfort
6. Ss has relationship with research staff that would compromise voluntary participation



Levels of Review of SBR

Protecting Ss: Reducing Burden

Excused/Expedited SBR default review



Decision that research poses greater than MR should be evidence-based and...



Risk cannot be adequately reduced through risk-minimizing procedures



Protect participants, reduce burden and advance Science



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Questions/further discussion





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