

Response of the
Department of Health and Human Services
to NBAC's Report
Research Involving Human Biological Materials:
Ethical Issues and Policy Guidance

Response of the Department of Health and Human Services to NBAC's Report *Research Involving Human Biological Materials: Ethical Issues and Policy Guidance*

- [Cover Letter](#)
- [Executive Summary](#)
- [Analysis and Proposed Actions Regarding The National Bioethics Advisory Commission \(NBAC\) Report *Research Involving Human Biological Materials: Ethical Issues and Policy Guidance*](#)
 - [Introduction](#)
 - [General Comments](#)
 - [Discussion of Terms Used in Report](#)
 - [Specific Issues of Note](#)
 - [Future Considerations](#)
 - [Comments on Specific Recommendations](#)
 - [Recommendations Regarding Interpretation of the Existing Federal Regulations](#)
 - [Recommendations Regarding Special Concerns About the Use of Unlinked Samples](#)
 - [Recommendations Regarding Requirements for Investigators Using Coded or Identified Samples](#)
 - [Recommendations Regarding Obtaining Informed Consent](#)
 - [Recommendations Regarding the Criteria for Waiver of Consent](#)
 - [Recommendations Regarding Reporting Research Results to Subjects](#)
 - [Recommendations Regarding the Considerations of Potential Harm to Others](#)
 - [Recommendations Regarding the Publication and Dissemination of Research Results](#)
 - [Recommendations Regarding Professional Education and Responsibilities](#)
 - [Recommendations Regarding the Use of Medical Records in Research on Human Biological Materials](#)
- [Appendix](#)

[Printable \(PDF\) version of the report](#)

[National Bioethics Advisory Commission Publications](#)

[REDACTED]

Recommendations Regarding the Criteria for Waiver of Consent

Recommendation 11. *In determining whether a waiver of consent would adversely affect subjects' rights and welfare, IRBs should be certain to consider*

- a) *whether the waiver would violate any state or federal statute or customary practice regarding entitlement to privacy or confidentiality,*
 - b) *whether the study will examine traits commonly considered to have political, cultural, or economic significance to the study subjects, and*
 - c) *whether the study's results might adversely affect the welfare of the subject's community.*
- [REDACTED]

Recommendation 11

The second criterion for waiver of consent emphasizes that consent may not be waived if such action would adversely affect subjects' rights and welfare.

Recommendation 11(a) refers to the question of whether a waiver of consent for a proposed study might violate any federal or applicable state statutes or customary practices regarding entitlement to privacy or confidentiality. Current DHHS regulations (45 CFR 46.107(a)), supported by existing guidance,³¹ require IRBs to be knowledgeable about relevant statutes and practices. In addition, 45 CFR 46.116 (d) (2) does not allow an IRB to grant a waiver of consent if the proposed research would adversely affect the study subjects' rights.³² Application of recommendation 11(a) therefore requires a factual response: granting a waiver of consent for the proposed study either violates or does not violate state or federal laws regarding entitlement to privacy or confidentiality. If it does, a waiver of consent may not be granted.

The Working Group believes that 11(b) and (c) should be regarded as conditions that will require a higher level of scrutiny of a proposal by the IRB but which, even if they existed in a given research proposal, do not preclude granting of a waiver of consent. As long as the IRB determines that a study examining traits considered to have political, cultural or economic significance to the study subjects does not adversely affect the subjects' rights and welfare, such a study should be eligible for a waiver of consent. Finally, in 11(c) NBAC focuses on the risk that a study might adversely affect the welfare of a subject's community. Federal regulations

governing waiver of consent address the rights and welfare of the *individual* (emphasis added) study subject. The IRB would therefore need to consider whether, if there were reason to believe that a study could cause harm to a group, such group harm would also adversely affect the rights and welfare of individual study subjects. The Working Group notes that the subject of group harm is addressed more fully in Recommendations 18 and 19.

Recommendations Regarding the Considerations of Potential Harms to Others

Recommendation 17. *Research using stored human biological materials, even when not potentially harmful to individuals from whom the samples are taken, may be potentially harmful to groups associated with the individual. To the extent such potential harms can be anticipated, investigators should, to the extent possible, plan their research so as to minimize such harm and should consult, when appropriate, representatives of the relevant groups regarding study design. In addition, when research on unlinked samples that poses a significant risk of group harms is otherwise eligible for exemption from IRB review, the exemption should not be granted if IRB review might help the investigator to design the study in such a way as to avoid those harms.*

Discussion

The Working Group shares NBAC's concern that some research using human biological materials may be potentially harmful to groups. However, as NBAC points out, "federal regulations governing the protection of research subjects extend only to individuals who can be identified."³³ Thus, the regulations do not include federal oversight of research that may pose risk of group harm (beyond the risks to study participants who are members of the group) except insofar as the requirements for IRB membership provide some protection for vulnerable groups.

Notwithstanding the silence of federal regulations on this point, the Working Group agrees that investigators should plan research in a manner that minimizes potential harm to groups. Consultation with representatives of relevant groups may identify potential harms and other problems as well as benefits and opportunities in the proposed research that may not have been evident to the investigator. Appropriate consultation may thus minimize harms, maximize benefits, and increase the likelihood that the research will be carried out successfully.

However, as NBAC notes, "additional work is needed to identify appropriate mechanisms for

group consultation.³⁴ Identifying the appropriate groups to consult with may, in certain instances, be a complex challenge. The researcher may identify and consult with a group regarding the proposed research only to find that another or larger group claims that the originally defined group is in fact a sub-group whose views do not reflect those of the larger group. This larger group may disagree with, and even claim the authority to override, the decision of the initial group.

A group could be an informal collection of individuals, a formal organization with identified leadership, or include competing organizations with dissimilar opinions. Therefore, even when a group is identified, individuals or sub-groups within a group may have different opinions about the relative risk and value of the proposed research, who will be affected by the results, and the best research design for the study. Furthermore, some groups explicitly authorize only certain members to determine and express group opinion. These issues all contribute to the difficulty the researcher will experience in efforts to identify appropriate formal and informal spokespersons for a group. This uncertainty about how best to conduct group consultation militates against proposing a regulatory requirement in the near future.

Nevertheless, DHHS agencies are making efforts that are in keeping with the spirit of NBAC's call for improvement of mechanisms for group consultation. For example, NIH convened in September 2000 a community consultation to obtain input on the collection of tissue samples from members of identified populations; the results of this consultation are posted on the internet.³⁵

In the discussion preceding Recommendation 17, NBAC points out that, for many studies involving human biological samples, the "net gain to a particular population that results from being informed about its increased risk (especially when something can be done with this knowledge at an individual level) often will outweigh the harms that come from labeling the group as high risk."³⁶ In the United States, with one exception,³⁷ consultation with representatives of a group does not confer the right of veto over the research to those representatives. Nonetheless, bona fide consultation requires the researcher and the IRB to carefully consider the concerns, especially the perceived potential harms, of the group and of individuals in that group. If those potential harms cannot be sufficiently minimized, it is possible that the benefit to risk assessment may require that consideration be given to not proceeding with the research.

Under 45 CFR 46.101(b)(4) and 102(f), research on unlinked or anonymized samples is not subject to the Regulations. Individual institutions and IRBs have the authority to apply a more stringent standard than that required by the Regulations. Within an institution, an IRB may require that a proposal be submitted for review even if the proposal is otherwise not subject to federal regulations. The Working Group strongly encourages efforts to minimize group harm in all research, even research that is not subject to federal regulations. In this context, the Working Group encourages IRBs and institutions to consider risk of group harm in research involving unlinked or anonymized samples and to develop strategies to minimize such risk. However, absent revision to the Regulations, IRB review of proposals to which current federal regulations do not apply is not mandated.

Proposed Action

The Working Group proposes that the issue of group harm be addressed in the broader context of federal oversight of research involving humans that is being addressed in NBAC's forthcoming report on *Ethical and Policy Issues in Research Involving Human Participants*. In the interim, the Working Group suggests that DHHS continue to encourage further studies of strategies that would identify and effectively minimize group harm, including efforts to identify appropriate mechanisms for consultation with relevant groups.

Recommendation 18. *If it is anticipated that a specific research protocol poses a risk to a specific group, this risk should be disclosed during any required informed consent process.*

Discussion

The Working Group agrees that disclosure of foreseeable risk to groups should be included in the informed consent process. Potential subjects should have access to all information that could affect their decisions about participation. Individuals may wish to consider implications of the research design and/or results for their community in deciding whether or not to participate in a research study.

Proposed action

The Working Group proposes that OHRP, in consultation with FDA, consult with appropriate groups and organizations to develop guidance for implementation of this recommendation.

Recommendations Regarding the Publication and Dissemination of Research Results

Recommendation 19. *Investigators' plans for disseminating results of research on human biological materials should include, when appropriate, provisions to minimize the potential harms to individuals or associated groups.*

Discussion

The Working Group concurs with this recommendation. In language accompanying Recommendation 19, NBAC highlights the need to consider the risk of violating privacy rights when publishing written descriptions of patients, pedigrees, and other clinical or potentially identifying information about individuals, families, and associated groups. Some of these concerns are addressed in OHRP's Institutional Review Board Guidebook, Chapter 5 H (Human Genetic Research).

It is difficult to guarantee protection against identification of subjects, especially when publishing about an unusual or rare condition or about people from small groups. Strategies have been developed to reduce that risk, however, especially for presentation of pedigrees in the literature.

While it is difficult to ensure compliance with this recommendation, the Working Group believes that education of investigators regarding best practices can reduce risk to study subjects. It has also been noted that published materials do not always conform with professional editorial standards, such as those established by the International Committee of Medical Journal Editors in 1995.³⁸ Journal editors should therefore be mindful of the role that they can play in minimizing potential harm to individuals and to groups when publishing results. Finally, members of a small geographic or ethnic group or of a family can sometimes help the researcher more effectively mask individual or group identities and thus minimize the risk of disclosure.³⁹

Proposed Action

No DHHS action is required.