The American Society of Human Genetics
Policy Statement

ASHG Response to National Bioethics Advisory Commission on the Ethical Issues and Policy Concerns Surrounding Research Using Human Biological Materials

January 15, 1999

Harold Shapiro, Ph.D., Chairman
Eric Meslin, Ph.D., Executive Director
National Bioethics Advisory Commission
6100 Executive Blvd., Suite 5B01
Rockville, MD 20892-7508

Dear Drs. Shapiro and Meslin:

In response to your request for feedback from the American Society of Human Genetics, a subcommittee of the ASHG Executive Committee has read the NBAC draft document entitled "The Use of Human Biological Materials in Research: Ethical Issues and Policy Guidance." We recognize that the views of the three individuals, Uta Francke, M.D., President, Ronald G. Worton, Ph.D., President-Elect, and Stephen I. Goodman, M.D., Treasurer, are not likely to represent the opinions of all members of the Society, or even of its Board of Directors. Given the shortness of time available, this was the only practical way for us to come up with a response.

First, we would like to congratulate you for having created a thorough and balanced report. This document provides a broad and in depth analysis of the current use and availability of human biological materials for research. It considers current regulations, practices and ethical issues from different viewpoints. Ambiguities in current regulations are identified and policy guidelines are issued in the form of recommendations. This report and its recommendations are of immediate relevance to research in human genetics that is conducted by members of the ASHG. We realize the difficulty in striking a balance between the protection of human subjects in research and regulations that place an undue burden on the researchers and inhibit the timely progress of research. In general, we believe that many of the recommendations should be acceptable to the majority of Society members and the public. The following points of concern are those that all three of us agreed upon during a conference call.

Recommendation 1:

The issue of rendering existing samples unidentifiable to avoid requirements of IRB review is of utmost importance. The main objectionable point of the entire document is the opinion that coded samples are considered identifiable. By requiring that samples be rendered unidentifiable with no possibility to link any research results back to the donor, numerous potential benefits of the research are being discarded [for example, let's assume that a new virus infection is threatening the world and that limited amounts of vaccine are available. Prior genetic testing of coded samples has revealed whether or not individuals are genetically susceptible to this infection]. We recommend that NBAC consider a way of coding samples by a third independent party who would keep the codes inaccessible unless there are specific circumstances in which the

code needs to be broken. While criteria for such instances should be laid down, each individual case would need to be examined by a ruling body. The decision to break the code should not be made lightly.

Recommendation 3:

The last sentence in this recommendation should not preclude the possibility of recording ethnic information that could lead to benefits of research results for particular ethnic groups. For genetic association studies, it will be extremely important to determine accurate allele frequencies for sequence variants in diverse populations. Existing samples with identifiers stripped could be used for these studies. The value of the research results is greatly enhanced if results can be grouped by ethnic origin of donors. For other studies, it might also be valuable to retain information on age and sex. Therefore, we strongly recommend considering the possibility for retention of ethnic background information when samples are rendered unidentifiable.

Recommendation 4:

We disagree. As pointed out under Rec. 1, we prefer that the "linkers" be placed into the hands of a disinterested third party, coupled with regulation as to when the code could be broken.

Recommendation 6:

We strongly disagree with this "additional measure of protection". Not only is it unnecessary, but potentially harmful. Contacting subjects with the "opt-out" message may raise fears and concerns where none existed before. These are meant to be cases where the consent requirement has been waived.

We cannot accept the concept (page 133, line 16-21) that individuals "could be wronged, if not harmed" if their discarded tissue were used for research to which they may object on moral grounds, even though they have no knowledge of the research and the samples used are unidentifiable.

Recommendation 7:

The last sentence should be deleted. In genetic research, it is common practice that samples obtained with consent for one study are used as controls for other studies; the identity of the donor is stripped and/or irrelevant for these other studies. It is impractical and potentially disturbing to recontact the donors each time this occurs. Perhaps, consent forms should be designed to include a clause about permitting use of the sample as a control for unrelated studies. The subject would have a choice to say yes or no to this clause at the time when the original consent is signed.

Recommendation 8:

The term "certificate of confidentiality" should be defined.

Recommendation 9:

We reject this recommendation. If acceptable regulations to maintain confidentiality of medical research results are in place, there is no need for an extra level of protection for so-called sensitive research. On the preceding page, "sensitive research" is defined to include behavior genetics studies, studies of differentiating traits among ethnic or racial groups, or research of potentially stigmatizing characteristics such as addictive behavior. Based on our knowledge, we feel that it would be impossible to draw a clear line and determine which type of research would be subject to this recommendation. For example, studies on sickle cell anemia would be affected, as well as studies on genes that predispose to Alzheimer disease or studies on metabolic pathways whose deregulation may affect brain function. This recommendation appears to reflect an attitude against any research being conducted on human behavior or ethnic differences, for fear of genetic determinism. We ask that this recommendation be removed.

Recommendation 10:

In the last sentence, it is recommended that the IRB pay attention to "any incentives offered for allowing use of the sample". The issue of incentives for allowing use of samples has not been discussed anywhere else in this document. It conjures up the scenario of a bidding war between biotech companies in their desire to obtain samples from a family with a rare potentially informative disease. The brief statement in this recommendation could be interpreted to mean that the NBAC would condone the use of incentives. The surrounding issues should either be discussed in much more detail or this sentence should be deleted.

Recommendation 15:

The report's recommendations place a large amount of decision power into the hands of individual IRBs. In principle we agree with that, but we recognize that local IRBs are only as sophisticated and unbiased as the people who volunteer to work on them. Given the geographic and political diversity across the country, the decision power of the local IRBs does not ensure even application of the national policy guidelines. The flow charts 1-4, designed to guide the decision-making process, are considered an excellent part of the document. As part of the OPRR's education program and to further aid IRB members, a glossary could be developed with specific examples for each decision box.

Recommendation 16:

In current publication practice, manuscripts that contain human subject data include a statement in the "Subjects and Methods" section that the project was approved by an IRB and informed consent was obtained. We believe it should not be necessary to specify whether the samples were identifiable, coded or anonymous, as long as an IRB has examined the study protocol (which includes the possible determination that the study does not need formal IRB review and approval). We further reject Recommendation 16 because it implies that editors will be required to make sure that this requirement is met. This puts an obligation on journal editors that they should not be burdened with.

Other Comments:

On page 110, the "Tri-council of Canada" is described as if it were a structural entity. This is not the case. In fact, representatives of three Councils of the Canadian science system, the Medical Research Council, the Social Sciences Research Council and the Natural Sciences and Engineering Research Council got together only to issue a joint policy statement. Therefore, the NBAC report should be reworded to refer to the "Tri-council policy statement" rather than to the Tri-council as an organizational entity.

On page 142, lines 7-10, the wording is convoluted and the meaning is not clear. This sentence, starting with "Doing so" and immediately preceding the paragraph "Informing individuals about research" should be reworded.

Thank you for allowing us to comment on this important document.

Sincerely yours,

Uta Francke, M.D.
President, American Society of Human Genetics