Research With Stored Biological Samples

What Do Research Participants Want?

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Background: There is widespread disagreement about the type of consent needed for research with stored biological samples. Many believe consent for each future use is required to respect individuals. Others worry this approach may block important research.

Methods: We analyzed 1670 consent forms signed by research participants at the Warren G. Magnuson Clinical Center, National Institutes of Health, between January 1, 2000, and May 31, 2002, that offer options for future research with participants’ biological samples. The research participants were healthy volunteers, family members of affected individuals, and individuals with a broad range of medical conditions enrolled in clinical research studies with and without the prospect of direct medical benefit.

Results: Overall, 87.1% of research participants given the option chose to authorize future research on any medical condition. More than 85% permitted unlimited future research with their stored biological samples regardless of sex, age, geographic location, or whether the individual was affected by the disease being studied or a healthy volunteer. Only 6.7% of those given the option to refuse all future research did so. Although African Americans were less likely to permit future research, 75.0% of African Americans still authorized unlimited future research with their samples.

Conclusions: Most research participants authorize the unlimited future research use of their biological samples when given the opportunity to do so. These findings suggest that providing research participants with a simple binary choice to authorize or refuse all future research might allow individuals to control use of their samples, simplify consent forms, and allow important research to proceed.

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Figure. Examples of options offered regarding future use of participants' biological samples.

Example A
I give permission to use my blood cells or DNA sample(s) in future research, under the following conditions:

- I give my permission to use my blood cells or DNA sample(s) in future research studies about (my condition) as judged important by the investigators.
- I wish to be recontacted if future research studies are considered using my blood cells or DNA sample(s). After the study has been explained, I will then decide if I want my samples to be included in the study.
- Under no circumstances shall my blood cells or DNA sample(s) be used in future research.

Example B
I give permission to use my DNA sample(s) in future research studies, under the following conditions:

- These samples may be used for any research project; it does not matter to me if the sample is identifiable as mine. You do not need to contact me if my samples are used for other research.
- Future studies can be completed without contacting me if all identifying information is removed so that the sample is not able to be identified as mine.
- I wish to be recontacted if further studies with my samples are considered. After the study has been explained, I will then decide if I want my samples to be included in the study.
- Under no circumstances shall my samples be used for future studies.

Example C
1. My blood or tissue may be kept for research to learn about, prevent, treat, or cure (my disease) and related diseases. Yes____ No____
2. My blood or tissue may be kept for research about other health problems (for example: diabetes, Alzheimer’s disease, and heart disease). Yes____ No____

Table 1. Characteristics of the 1298 Participants*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>% of Participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>46.8</td>
</tr>
<tr>
<td>Female</td>
<td>53.2</td>
</tr>
<tr>
<td>Age, y</td>
<td></td>
</tr>
<tr>
<td>0-17</td>
<td>12.3</td>
</tr>
<tr>
<td>≥18</td>
<td>87.7</td>
</tr>
<tr>
<td>Race</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>81.9</td>
</tr>
<tr>
<td>African American</td>
<td>8.2</td>
</tr>
<tr>
<td>Hispanic</td>
<td>3.8</td>
</tr>
<tr>
<td>Asian American</td>
<td>4.8</td>
</tr>
<tr>
<td>Native American</td>
<td>0.3</td>
</tr>
<tr>
<td>Unknown</td>
<td>1.9</td>
</tr>
<tr>
<td>Residence</td>
<td></td>
</tr>
<tr>
<td>Virginia, Maryland, or District of Columbia</td>
<td>55.6</td>
</tr>
<tr>
<td>Other part of the United States</td>
<td>41.5</td>
</tr>
<tr>
<td>International</td>
<td>2.9</td>
</tr>
<tr>
<td>Participant type</td>
<td></td>
</tr>
<tr>
<td>Affected individual</td>
<td>53.1</td>
</tr>
<tr>
<td>Family member</td>
<td>20.8</td>
</tr>
<tr>
<td>Healthy volunteer</td>
<td>26.0</td>
</tr>
<tr>
<td>Unknown</td>
<td>0.1</td>
</tr>
<tr>
<td>Study type</td>
<td></td>
</tr>
<tr>
<td>Prospect of direct medical benefit</td>
<td>20.1</td>
</tr>
<tr>
<td>No prospect of direct medical benefit</td>
<td>79.9</td>
</tr>
</tbody>
</table>

*Excludes research participants who left forms blank or made inconsistent or uninterpretable choices.

METHODS

SETTING AND PARTICIPANTS

We evaluated all research consent forms at the Warren G. Magnuson Clinical Center, National Institutes of Health, signed between January 1, 2000, and May 31, 2002, that offered options regarding the future research use of participants’ biological samples. We identified 61 studies enrolling a total of 1670 participants. For research participants enrolled in more than one study during the evaluation period, we assessed only the most recent consent form. Choices regarding future use of pediatric samples were made by the parents. Overall, 372 of the consent forms contained inconsistent or unclear choices or were left blank, leaving 1298 forms (77.7%) with interpretable choices.

DATA CODING

The 1298 consent forms offered a total of 23 different sets of options regarding future use of participants’ biological samples (Figure). By using a consensus process, 5 of us (D.T.C., D.L.R., F.G.M., E.J.E., and D.W.) coded these options into 4 general types: (1) refuse all future research, (2) authorize future research on the same medical condition for which the sample was obtained, (3) authorize future research on any medical condition, and (4) request recontact for consent before any future research. The option to request recontact was offered in 3 different versions: request recontact or refuse all future research; request recontact or authorize all future research without recontact; or request recontact, authorize all future research without recontact, or refuse all future research. Research participants were categorized as affected with the disease under study, family members of affected individuals, or healthy volunteers. The research studies were categorized as offering the prospect of direct medical benefit or not. The studies varied widely from normal physiological studies to studies involving cardiopulmonary, developmental, endocrinologic, immunologic, neurologic, oncologic, psychiatric, and sight/hearing/speech disorders.

STATISTICAL ANALYSIS AND PARTICIPANT PROTECTIONS

The research participants’ characteristics and choices were summarized as frequency counts and percentages with exact binomial confidence intervals. Univariate associations between choices and participants’ sociodemographic characteristics were tested by the χ² test for independence. Differences were deemed significant at P<.05. Because all personal identifiers were removed from the data, the study was deemed exempt from institutional review board approval by the Office of Human Subjects Research at the Warren G. Magnuson Clinical Center.

RESULTS

RESEARCH PARTICIPANTS’ CHARACTERISTICS

Overall, 53.1% of individuals were affected by the disease under study, 20.8% were family members, and 26.0% were healthy volunteers (percentages do not total 100 because of rounding) (Table 1). Of all participants, 87.7% were 18 years or older; there were nearly equal numbers of women and men. More than 50% were residents of Mary-
land, Virginia, or the District of Columbia. Of all individuals, 79.9% were enrolled in a research study that did not offer the prospect of direct medical benefit (Table 1).

### RESEARCH PARTICIPANTS’ CHOICES REGARDING FUTURE RESEARCH

Overall, 87.1% (775/890) of those given the option authorized future research on any medical condition. Of research participants given the option, 90.8% (403/444) authorized future research on the same medical condition for which the sample was obtained. Only 1.2% (2/165) of research participants who were given the option indicated their biological sample could be used for research on the same medical condition, but refused research on other medical conditions. Just 6.7% (71/1060) of research participants who were given the option refused to allow their samples to be used for future research. Participants’ choices regarding recontact depended strongly on the alternatives they were offered. Of those participants given the choice of recontact or refusing all future research, 90.6% (116/128) chose recontact. Conversely, of those given the choice of recontact or authorizing all future research, only 17.2% (10/58) asked to be recontacted. Of research participants given the choice of recontact, authorizing all future research, or refusing all future research, 26.2% (91/347) chose recontact. Univariate analysis indicates that more than 85% of research participants allowed all future research on their stored biological samples (Table 2). Only African Americans were less likely to allow unlimited future research compared with non-Hispanic whites ($P < .001$). Nevertheless, when offered the option, 75.0% (63/84) of African Americans allowed all future research.

### COMMENT

When given the option, most research participants in this study prospectively authorized unlimited future research on their biological samples. These data on the actual choices and preferences of research participants suggest that offering individuals the straightforward choice of authorizing or refusing all future research on their biological samples shows respect for them while allowing important research to proceed.

In the present study, more than 85% of research participants authorized unlimited future research with their biological samples. This finding is essentially equivalent to the 86.9% of oncology research participants who authorized future research on “health problems” in general. Similarly, approximately 85% of individuals who participated in the National Health and Nutrition Examination Survey agreed to contribute biological samples for future unlimited research. The present study found strong willingness to allow samples to be used for unlimited future research across all groups of research participants—men and women, old and young, those residing near the research center and those who had to travel great distances, participants with the dis-
ease being studied and healthy volunteers, and those participating in research that offered the prospect of direct medical benefit to the participants and those participating in research without the prospect of direct benefit. Although African Americans were statistically significantly less likely to authorize unlimited future research compared with non-Hispanic whites, 75.0% of African Americans chose to allow all future research when given the option. Given the relatively small number of African Americans in our study, future research will be necessary to confirm these data.

The present data suggest that a simple binary choice of allowing or refusing any future research on stored biological samples would permit research participants to control use of their samples without blocking important research. Conversely, requiring individuals to complete a checklist of options may complicate consent forms and divert attention away from research decisions that are more important to participants. Because most research participants are not concerned with which diseases will be studied, the costs required to track the limits imposed on each sample likely would provide little benefit to participants. These costs also do not seem justified by a significant increase in the number of samples that would be available for research purposes.

The fact that most research participants support unlimited research with their samples suggests that research on previously collected samples is consistent with the preferences of most research participants. This level of support suggests it may make sense to establish a relatively low threshold for waiving consent for minimal-risk research on previously collected research samples on the grounds that obtaining consent for such research would be “impracticable” as stipulated in the federal regulations.34 When the reviewing institutional review board decides that obtaining consent for research on previously collected research samples would be practicable, the present findings suggest that an approach of sending individuals a letter explaining the plan to make their samples available for all future research studies, unless the individual actively objects, might make sense. This approach would allow the few individuals who do not want their samples used for research to opt out, without requiring the majority who support unlimited research to go through the steps to provide active consent (Jordan J. Cohen, MD, Association of American Medical Colleges, written communication, 1997).

This study has several limitations. First, we assessed the choices of research participants from across the United States and 24 foreign countries at a major research institution. Like other major research institutions, the Warren G. Magnuson Clinical Center conducts a broad range of research studies, almost one fourth (233 [22.4%] of 1038) of which are multisite studies conducted simultaneously at other academic medical centers and research institutions (Teresa Doged, BA, Medical Records Department, Warren G. Magnuson Clinical Center, oral communication, 2003). As a result, our findings may be limited to major research institutions, and may not be generalizable to research institutions or private practices with smaller research portfolios. Second, because our study was conducted at a research institution, the findings may not apply to samples obtained in the course of routine clinical care. Third, more than 80% of participants were white, and the results may not reflect the decisions of racial or ethnic minority groups. Fourth, we omitted blank forms from our analysis. It is possible that some sections were left blank because individuals did not want their samples used for future research. Analysis considering blank forms as refusals, however, still results in 74.4% of research participants authorizing unlimited future research.

In conclusion, this study demonstrates that more than 85% of research participants authorize unlimited future research use of their biological samples when given the opportunity to do so. This finding was consistent regardless of sex, age, or geographic location (Table 2). Similarly, greater than 85% of research participants who had the disease being studied, family members, and healthy volunteers permitted unlimited future research on their stored biological samples. Although African Americans were somewhat less likely to allow future research compared with non-Hispanic whites, most African Americans still consented to unlimited future research on their biological samples.

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