

# Model Consent Forms & Related Information on Tissue Banking from Routine Biopsies

*Compiled by the:*

National Action Plan on Breast Cancer  
Tissue Banking Working Group

*With comments by the:*

PRIM&R/ARENA Tissue Banking Working Group

# Memorandum

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**To:** Directors/Chairpersons and Members, Institutional Review Board  
(IRBs)  
**From:** Joan Rachlin, Executive Director, PRIM&R  
**Date:** 1/23/98

Enclosed are several documents related to a national effort to improve the quality and effectiveness of the informed consent process for tissue banking from routine clinical surgical procedures. PRIM&R and ARENA are disseminating these documents as part of its ongoing mission to serve the medical research community by fostering sound research practices. These documents, and the processes that led to their development, will be discussed at the PRIM&R meeting in Boston on December 8 and 9, 1997. It is the hope of PRIM&R and ARENA that the information and documents provided here will be helpful and utilized by IRBs and others to strengthen their informed consent procedures and enhance protection of human subjects in medical research.

The following narrative briefly summarizes the origins of the enclosed documents and provides descriptive information to assist in the review and understanding of the documents. Many in the clinical and research community may be aware already of this information; PRIM&R and ARENA hope that this communication will help to provide greater awareness, common understanding, and broad usage. The level of discomfort shown by IRBs with issues related to tissue banking is high. This is illustrated by the fact that, when an earlier draft of this model system was presented in a multi-center clinical oncology protocol with tissue banking as an option, two-thirds of the institutions choose to opt out of the banking component. Suggestions and comments regarding the enclosed information may help to shape future actions by PRIM&R/ARENA related to the larger issues of tissue banking and informed consent.

## **The Development of a Model Informed Consent Document**

On June 2, 1997 the National Action Plan on Breast Cancer (NAPBC), Public Responsibility in Medicine and Research (PRIM&R), Applied Research Ethics National Association (ARENA), the National Cancer Institute (NCI), and the National Institutes of Health Office of Research on Women's Health co-sponsored a meeting "Informed Consent and IRB Review: A Model for Review and Discussion." At that meeting, NAPBC's National Biological Resource Bank Working Group (NBRBWG) presented both a model consent form for permission to store tissue from routine surgical procedures, and other related documents. The model consent form had been developed by NBRBWG using information and ideas from

existing IRB-approved forms, discussions with representatives of the breast cancer clinical and research communities, and 27 focus groups that drew from racial/ethnic and socio-economic groups of adults within and outside the health care community. A summary of the focus group's findings is available from the NAPBC.

In undertaking this project to facilitate research, NAPBC had three goals:

- To elevate the role of the tissue donor to that of an active partner;
- To develop a user-friendly consent process meaningful to both patients and researchers; and
- To develop a set of standards for specimen use upon which researchers could rely.

The premises and assumptions underlying this project are provided in the Executive Summary Report of the June 2 meeting, a copy of which is in the enclosed set of materials. It is important to note, however, that one assumption was that materials, practices, or methodologies developed for breast cancer specimens probably would be applied eventually to all types of specimens. It is with this generalizability of the model in mind that its broad dissemination and discussion is now being pursued.

In addition to the model consent form, the NAPBC also presented two other documents at the June 2 meeting: an information sheet about the use of human tissue specimens in research that could serve to answer the types of questions likely to arise from patients and their families; and a set of principles designed to assist IRBs in deliberations on tissue banking issues. Copies of all three of these documents--the model consent form, the information sheet, and the principles for IRB use--are enclosed.

### **Further Review of the Model Consent Form and Tissue Banking Issues**

Following the meeting of June 2, 1997, I asked a small group to develop further commentary on the documents. This PRIM&R/ARENA Tissue Banking Working Group was asked to give particular attention to sections of the documents that may need special consideration by IRBs and to provide a working guide for IRBs, utilizing feedback given by participants at the June 2 meeting as a starting point. They met via conference call throughout the summer. The comments of the group are also provided in this mailing, in an *additional* set of the three documents. The group's comments are written in non-bold text and integrated into relevant sections of the original documents' **bold** text. Where the group suggested changes in the original document, those suggestions are shown by non-bold text to replace ~~struck-through~~ text.

Some of the specific areas in which there was much discussion include the following:

- a) disclosure of research results
- b) commercial use of specimens
- c) consent form issues including benefits language and permission to re-contact subjects
- d) tissue bank concerns including the oversight board and duties of the tissue trustee

Other areas in which concerns were raised, and for which the NAPBC is providing further follow-up include:

e) implementation concerns including time needed to obtain consent and the tracking of forms—being addressed with professional groups including surgeons, and

f) costs associated with such a system—being addressed by other groups including the National Cancer Institute.

The intent of the PRIM&R/ARENA Working Group's comments is to provide a basis for further discussion by IRBs. However, it should be noted that with the criteria presented here, including initial informed consent, distribution of coded samples and coded follow-up information by a tissue/specimen bank trustee, and the almost-total prohibition against return of results, the PRIM&R/ARENA Tissue Banking Working Group decided that this system involves risks comparable to those found in daily life, and thus presents minimal risk to subjects.

### **Future Considerations and Request for Feedback**

It was the shared view of those who participated in the June 2 meeting that the NAPBC has provided an important model that might be widely used for improving the quality of the informed consent process for tissue collection in clinical practice. PRIM&R/ARENA hopes that the documents distributed here will be useful to IRBs and to the medical research community.

PRIM&R/ARENA will continue to serve as a forum for discussion and sharing of perspectives and a voice for improvements that will serve both research needs and the needs of individual patients and their families. To that end, I am also including a feedback form, and ask that you provide us with some description of your reactions and experiences, both positive and less positive. At some time in the near future, we want to be able to provide follow-up information about the usefulness of these documents and commentaries. Similarly, if you are already using consent forms or other materials related to tissue collection and use, we would very much appreciate a copy of those documents, so we can establish a library resource of examples of such materials.

It is important to note that, as you read this information, the National Bioethics Advisory Commission (NBAC) has taken up issues related to tissue banking and genetic testing as a current topic of study and review. NBAC is a Presidentially appointed committee providing guidance to federal agencies on the ethical conduct of current and future human biological and behavioral research. NBAC anticipates a report on the topic of tissue banking by early 1998.

PRIM&R and ARENA wish to thank the individuals who served on the Tissue Banking Working Group (see attached list), and others including Karen Hansen who contributed written feedback on the NAPBC documents. Thanks also go to Leah Conn of PRIM&R/ARENA, Darla Moss of Prospect Associates, Debbie Saslow of the NAPBC, and Helene Quick of Prospect Associates for coordinating Working Group conference calls and

distributing documents, and for facilitating all other administrative aspects of this Project . Special thanks to Paula Panissidi also from Prospect Associates for compiling the written summary of the June 2 meeting, and for her always competent and cheerful handling of the details surrounding the planning of that meeting.

Finally, this work could not have been completed without the leadership of Christine Howe and Rose Mary Padberg, the PRIM&R/ARENA Working Group Co-Chairs. It has been their commitment to the synthesis, analysis, and widespread distribution of the proceedings of the June 2 meeting which has led to the production of these materials. They have truly been the "fixative" for this phase of the Project, and we appreciate not only their hard work, but also their consistent good humor and impressive efficiency! We hope that you will find this packet useful and encourage you to share any comments you might have with a member of our Working Group (please see below). We also look forward to your continued involvement in this complex and sensitive area, which will ultimately affect us all....

PRIM&R/ARENA Tissue Banking Working Group

**Christine L. Howe**; Co-Chair; **Rose Mary Padberg**; Co-Chair, Patricia Barr, William Freeman, Susan Z. Kornetsky, Robert J. Levine, Philip A. Ludbrook, Gwenn Oki, Ernest D. Prentice, Patricia M. Scannell, Ada Sue Selwitz .

# **Model Consent Forms & Related Information On Tissue Banking from Routine Biopsies**

A.  
June 2<sup>nd</sup> Meeting Summary

B.  
Feedback Form

C.  
PRIM&R/ARENA Comments on the NAPBC IRB Principles

D.  
PRIM&R/ARENA Comments on the NAPBC Information Sheet

E.  
PRIM&R/ARENA Comments on the NAPBC Consent Form

**INFORMED CONSENT AND IRB REVIEW:  
A MODEL FOR REVIEW AND DISCUSSION**

**National Action Plan on Breast Cancer (NAPBC)  
Public Responsibility in Medicine and Research (PRIM&R)  
Applied Research Ethics National Association (ARENA)  
National Cancer Institute (NCI)  
NIH Office of Research on Women's Health (ORWH)**

**National Institutes of Health  
Bethesda, Maryland  
June 2, 1997**

**Introduction and Welcome**

Ms. Joan Rachlin, Executive Director, Public Responsibility in Medicine and Research (PRIM&R), welcomed those in attendance and provided a brief summary of two of the meeting's co-sponsors, PRIM&R and ARENA. PRIM&R is an advocacy and educational organization that focuses on the areas of bioethics (animals and humans), research and development, and clinical and basic research, including behavioral research. PRIM&R's sister organization, Applied Research Ethics National Association (ARENA), is a membership organization that supports and promotes professional development for those who administer or serve on Institutional Review Boards (IRBs) and Animal Care and Use Committees.

Dr. Vivian Pinn, Director, NIH Office of Research on Women's Health (ORWH), welcomed attendees on behalf of NIH, ORWH, and the National Cancer Institute (NCI), noting that the field of bioethics is at an exciting juncture. The problems of informed consent; confidentiality; and the need for, use of, and access to tissue span all of medical research and are of great importance to the issues of genetics and women's health, especially breast cancer. As researchers look forward, developing workable solutions to these problems will become increasingly important in the diagnosis, management, and treatment of disease as well as in future discoveries. Such resolutions will require input from all players: diagnosticians, patients and consumer advocates, pathologists, surgeons, ethicists, and lawyers.

The primary purpose of the meeting was to present and then discuss drafts of a model patient consent form and a set of IRB principles. These materials were developed by the National Biological Resource Banks Working Group of the National Action Plan on Breast Cancer (NAPBC) in an effort to assist IRBs in their work, particularly when facing the complex issues associated with entry into large-scale clinical trials and tissue banking.

**History of the Project**

Ms. Patricia Barr, member of the National Breast Cancer Coalition (NBCC) and Chair of the Ethical Issues Subcommittee of the NAPBC National Biological Resource Banks Working Group, gave the history behind the materials presented for discussion, outlining the Working Group's assumptions, goals, and special concerns. The next steps in this process, Ms. Barr explained, are to incorporate the ideas and comments generated during the meeting into these materials and then transfer these items and related activities to appropriate groups or institutions that will, in turn, become responsible for further changes and implementation.

*Assumptions*

In its ongoing efforts and discussions, the Working Group made the following general assumptions: (1) that the materials, practices, or methodologies developed for breast cancer specimens probably would be applied eventually to most or all specimens; (2) that the vast retrospective specimen collections currently in use would not be part of the

Group's work; and (3) that the Group would focus on future actions and include consumers and patients in discussions on how their tissue could be used, allow researchers access to tissue as deemed acceptable by the patient, and develop a mechanism to facilitate research. The two key legal/ethical issues for researchers, as identified by the Working Group, were IRB requirements for prospective tissue/specimen use and informed consent.

#### *Goals and Special Concerns*

From this vantage point, the Working Group then developed the following goals: (1) to elevate the role of the tissue donor (i.e., the patient or consumer) to an active partner, (2) to develop a user-friendly consent process meaningful to both patients and researchers, and (3) to develop a set of standards for specimen use upon which researchers could rely. Special related concerns identified by those in the Working Group included: (1) specimens tied to the patient's medical records are most valuable to researchers, and anonymous specimens are of limited use to researchers; (2) the burdens associated with maintaining tissue repositories fall primarily with pathologists; (3) allowing patients to decide in advance how their tissue might be used probably is not practical; (4) not all specimens will be used for genetic research; (5) recontacting the specimen source (i.e., the donor) as acceptable versus an invasion of privacy; (6) most current general consent forms do not adequately address the full range of issues associated with tissue banking and related research; and (7) defining the nature of the resource (which tissues to collect, who should have access to this tissue, who decides the issue of access, etc.). The Working Group attempted to balance these issues and concerns as it worked through the consent form and the IRB principles.

#### *New Issues*

The Working Group incorporated several novel features into its proposed "tissue banking enterprise," including (1) the notion of trust between the donor of the tissue, the surgeon collecting the tissue, and the researcher using the tissue; (2) the development of standards for consent; (3) the prohibition of recontact unless the patient gives specific consent for recontact; (4) the prohibition against sharing of individual results; and (5) a role for an appointed panel to review researchers' requests.

### *Goals for Today's Meeting*

Ms. Barr suggested that the following issues be discussed during the meeting:

- Review and comment on the proposed model consent form, the informational brochure, and the IRB principles;
- Consider the model for the proposed tissue banking enterprise;
- Identify practical concerns for the future; and
- Identify the next steps in the implementation of the IRB principles and consent form.

### **Proposed Model for Obtaining Specimens for Research**

Moderator: Dr. Barbara Handelin, President, Handelin Associates

As noted by Dr. Sheila Taube, Associate Director, Cancer Diagnosis Program, National Cancer Institute, the issues associated with tissue banking and research have changed and evolved as available research technologies have evolved. Dr. Taube added that the proposed model and principles apply not only to breast cancer but to other cancers and diseases as well.

The model proposed by the Working Group was guided by two primary premises:

Premise 1: Human tissue specimens are critical for research to improve the ability to treat disease and ultimately to impact the health of the population.

Premise 2: Private information about the individuals from whom the specimens are collected must remain private, and the medical care of that individual cannot be compromised by the use of the specimens for research.

In an effort to incorporate these guiding principles into a new model for tissue banking and use of tissues in research, the Working Group first examined current practices. The Group recognized that most specimens are obtained through routine care of patients and then processed and retained by pathologists and pathology departments, as directed by federal and state regulations; in this scenario, most patients do not know whether their tissue will be used for research. In contrast, some specimens are collected specifically for research purposes; under these conditions, extensive guidance and consent have been developed and already are in place, and patients are aware of how their tissue may be used. In recognition of these differences, the Working Group decided to focus on developing principles and a patient consent form that could be used in cases in which tissue is collected during routine care and may be used for research purposes. The model was developed for prospective collections, but its principles also may be applicable to archival collections.

The proposed model seeks to adequately inform the patient of potential uses of his or her tissue for research and protect the patient's care and privacy while still allowing certain anonymous or delinked information, such as the patient's age, gender, and prior treatments, to flow to the researcher. The components of the model include the patient, the clinician, the pathologist, the repository or trustee (which may or may not be the pathologist), and the researcher. The critical feature of the model is the flow of information. Interaction between the patient and the clinician is two way, as is the interaction between the clinician and the pathologist. However, the flow of information between the pathologist or repository and the researcher must be one way; the delinking of specimens from source identifiers most likely would occur at this stage. Including this step, Dr. Taube pointed out, is the only way to protect the patient, ensure that research results are not used for patient care and are not entered into the patient's medical records, and ensure that the researcher never knows the source of the tissue. The consent by the patient enables this general model; consent for recontact can accommodate follow up.

### **Response**

Dr. Virginia LiVolsi, Professor and Vice Chair for Anatomic Services, University of Pennsylvania Medical Center, considered the proposed model a good starting point for academic pathologists, noting that the model recognizes the importance of pathologists in patient care and research. The model presents some unique challenges, however, to pathologists in general and academic pathologists in particular, including:

- The use of the "honest broker model" in which tissue specimens must be available to researchers and, at the same time, patient privacy and confidentiality must be protected.
- The clerical (e.g., data entry, data management) and technical (e.g., the dissection, preparation, and classification of tissue sections) costs, materials, and resources and professional level of effort of maintaining a tissue repository -- above and beyond current efforts and costs -- must be built into the model. Dr. LiVolsi cited the Cooperative Human Tissue Network (CHTN) as an example of a system that incorporates these features.
- Addressing the issue of archival collections and the pathologist as the resource person for that material.
- The multiple roles of the pathologist -- as a researcher, collaborator, broker, and tumor registrar/specimen collector.

The proposed model needs to address these points more fully and explore approaches to ensure that pathologists and associated resources and staff are not overburdened or undercompensated. For example, the model may be revised to suggest that one pathologist serve as the broker for a companion pathologist who actually conducts the research of interest.

#### Position of the College of American Pathologists

Dr. William Grizzle, Professor, Department of Pathology, University of Alabama at Birmingham, presented the College of American Pathologists' (CAP) position regarding tissue banking and research with reference to the proposed model.

One area that may require special attention in further development of the model is genetic testing and genetic research; for example, newly defined guidelines and principles should be flexible and dynamic enough to accommodate and appropriately interpret evolving and accumulating scientific data. CAP supports the continued availability of specimens for research and agrees with the proposed model's premise that research results should not be used in an individual's care; that protecting the patient's privacy and confidentiality is a fundamental ethical issue; and that pathologists are directly involved in the retention, integrity, and maintenance of tissues. The role of pathologists as researchers, however, needs to be more clearly defined by CAP and those in the pathology community. CAP takes a somewhat different view from the Working Group in believing that current systems and processes, such as those promulgated by IRBs and the Office for Protection from Research Risks (OPRR), provide adequate oversight of patient privacy and strike a balance between informed consent and research needs, especially as applied to archival collections. CAP recognizes the possible need to fine tune current regulations but does not support major changes in the present system or its basic concepts of informed consent and confidentiality, especially as applied to existing tissue banks, archival collections, and banks of medical information.

#### Presentation of IRB Principles

Moderator: Ms. Ada Sue Selwitz, Director, Sponsored Programs Development and Research Subject Office, University of Kentucky

Ms. Selwitz noted that the purpose of this session was to examine the NAPBC 's recommendations for IRB principles governing prospective tissue collection and banking. The proposed recommendations are timely in that many

institutions across the country currently are engaged in re-reviewing consent principles and protocols for tissue collections, which pose legal, social, ethical, and regulatory challenges to IRBs. Issues raised at the University of Kentucky, for example, include identifying situations in which it may be acceptable or reasonable to waive consent, assuring that certain safeguards are in place to ensure patient privacy and confidentiality, and discussing the rights of populations in addition to individuals. The principles presented during the meeting provide a standardized framework to guide IRBs in reviewing protocols for prospective tissue collection.

Karen Rothenberg, Director, Law and Health Care Program, University of Maryland School of Law, began her presentation by pointing out that advances in medicine usually are not based on research subjects per se, but, rather, are much more largely based on findings obtained through routine patient care. This observation is important because: (1) Routine patient care is not the typical paradigm under consideration by OPRR, IRBs, and the larger research community, and, thus, the proposed enterprise challenges traditional thinking and approaches; (2) the patient perspective and the role of the patient in the enterprise must be taken into consideration. Most individuals are not aware of the reasons why their tissue is being stored; thus, they often lack true informed consent. However, through improved consumer/patient education about the value of tissue resources to the development of future treatments and cures, the medical research community most likely will foster a strong sense of trust in patients which, in turn, should encourage more, not less, research.

These two concepts should drive the development of what have been termed, for the purpose of this meeting, "IRB principles." Whether the IRBs ultimately take on all the responsibilities outlined in these principles should be less of the focus during the meeting than trying to reach consensus that these principles should guide the informed consent process and the collection, storage, and use of tissue collected during routine patient care. It should also be noted that some of the organizations that collect and distribute specimens are cooperative groups, NCI-funded institutions and organizations, academic institutions, and commercial banks.

The primary goals of the principles are:

- To facilitate research, using specimens that are linked to outcome data. At this time, both federal and state-mandated registries with name-linked data exist. These registries could serve as the vehicles by which specimens and outcome data are connected.
- To address ethical issues, such as privacy, contact/recontact, and availability of research results, while keeping a balance between access and confidentiality within the context of the trust relationship and partnership.
- To simplify and standardize the patient choice process. What do donors want to know versus what they need to know, how can this best be conveyed, and how does this type of informed consent fit into the proposed model for tissue collection and distribution?
- To move toward a standard of review that allows researchers to focus on their research.

The Working Group considered the following issues as it developed the proposed IRB principles:

- The difficulties associated with securing consent for unspecified future research studies. To what is the patient actually consenting at the time he/she is consented, and how can a compromise be reached so that the patient has some control over use of his/her tissue and a sense of being part of the process?

- Increasing sensitivity to the issue of privacy, especially in genetic research and in projects involving special populations.
- Acknowledging the patient as a partner in the consent process and in research.
- Addressing practical concerns and difficulties associated with collecting, storing, and distributing specimens.

The Working Group noted that the application of these principles is for prospective collections, although the Group acknowledged the value of archived specimens and recognized that some if not all of the proposed principles could be relevant to previous collections. The principles should be considered in conjunction with the specific materials developed (i.e., the model consent, the Q & A brochure) and the results of the field testing. Finally, the principles should be used by centralized institutions as part of a system of broad access.

## IRB Chair Response

Dr. Robert Levine, Professor of Medicine, Yale University School of Medicine, identified several issues for discussion, including defining the role of IRBs; determining whether the proposed principles will lead to the development of a standardized consent and collection process and actually facilitate research; identifying the additional technical, clerical, and professional costs associated with the new enterprise; scrutinizing the credibility of the proposed enterprise; and determining for which of the principles IRBs should be responsible. Dr. Levine noted that IRBs are facing numerous challenges and increased responsibilities, including resolving both real and potential problems involving research on human subjects. At the same time, IRBs are receiving less and less feedback from federal oversight agencies, such as the FDA, NIH, and industrial sponsors. The continued, time-consuming efforts of IRBs and their members generally go unrewarded, further undermining motivation and the ability to retain current or recruit new members. Finally, the increased presence of managed care vendors is creating a tremendous imbalance in time and resource commitments, availability, and generation among faculty members.

Dr. Levine proceeded through the set of principles, commenting on each as follows:

- IRBs cannot ensure that adequate consent is secured among all tissue donors as planned or expected. It can review the timing, personnel, setting, content of the form, and even the means of documenting the dissemination of the form. The final document should clearly distinguish between informed consent and the consent form.
- IRBs should not have to develop their own standards for confidentiality and privacy; rather, NAPBC (or the responsible party) should develop a set of standards to guide IRBs.
- Prohibiting recontact without prior consent to recontact is not a good idea because (1) it potentially irreversibly closes the door on what could be solid research, (2) it is contrary to prior standards (consider case-control studies), and (3) there is a high probability of refusal upon recontact (consider uninformed refusals). Keeping these points in mind, it was suggested that this principle be reconsidered.
- Prohibiting patients to have access to the results of research on their tissue is a sound principle but is costly. Are there any situations in which the research results should be given to the treating physician and the patient? If so, these must be clearly defined. (Dr. Levine noted that at Yale, a high-level committee scrutinizes, on a case-by-case basis, situations in which research data are returned to the doctor and/or the patient.)
- Establishing a panel of both scientists and consumers is a solid concept that recognizes the importance of community involvement. However, IRBs do not necessarily have the specific expertise or training to address issues presented to the panel. Perhaps each institution should be allowed to decide how to implement this activity locally. The same approach applies to the remaining principles.

### Response from the Office for Protection from Research Risks (OPRR)

Dr. Tom Puglisi, Director, Division of Human Subject Protections, OPRR, pointed out that, for the past year and a half, OPRR has been providing specific guidance to IRBs regarding the establishment, operation, and maintenance of tissue repositories that is consistent with clearly articulated regulations. OPRR continues to work on developing guidance that is consistent with more challenging regulations and operations. Some of the issues still under consideration by OPRR include (1) what level of protection is appropriate to ensure privacy and confidentiality, (2) what is the appropriate standard for this protection, and (3) what level of protection would be needed to satisfy the criteria that allow for the waiving of informed consent. OPRR believes that it should receive input from the National Bioethics Advisory Committee (NBAC) before moving forward with such substantive issues.

Dr. Puglisi raised the following issues and concerns regarding the IRB principles presented for discussion during the meeting:

- What should the standards of privacy and confidentiality, as set forth by the IRB, entail? At what point is protection adequate to grant reasonable certainty that privacy and confidentiality concerns will be maintained? Because no system is iron clad, the IRB must then make a subjective decision about setting the parameters for protection. The NAPBC and NBAC should provide further elucidation of this point.
- Prohibiting recontact without prior permission and prohibiting release of research results generally are good ideas. However, the repository IRB should include in its guidance situations in which it is possible to ask the IRB for specific permission to go back to the donor or treating physician.
- It is reasonable to expect the establishment of a panel or group that will control access to the repository. This panel will be responsible for determining whether a proposed research project is worthy of receipt of requested materials. Related issues include the IRB's role in setting guidelines and direction for and governing the panel, as well as how the repository shares tissues.

### **Presentation of the Model Consent, Patient Brochure, and Focus Group Results**

Moderator: Ms. Susan Kornetsky, Manager, Research Protocol Administration, Children's Hospital

Ms. Kornetsky opened the afternoon session by noting that informed consent is an interactive process that includes the clinician, the patient, a consent form, and related educational efforts such as print or audiovisual materials and further discussion, as needed. Those attending this meeting as well as those involved in further development of any new enterprise need to identify the elements required to meet informed consent and then determine whether the form meets those requirements and also complies with federal regulations. The concepts of patient choice and rights and research uses and benefits should be addressed, including the option to recontact. The final consent form should address these issues, be comprehensive enough to give the patient enough information to make an informed choice, and finally, be easy to understand.

Ms. Barr reported that all of the issues identified by Ms. Kornetsky were addressed and debated by the Working Group and the subcommittees assigned to develop the model consent form and related materials. A fundamental concept driving the development of these items was that consent for use of tissue from routine practice in research must be separate from the basic surgical consent. Working Group members agreed that both patients and researchers could be better served by moving beyond the simple consent statement on the surgical form.

Ms. Barr noted that early discussions sought to reduce the burden to patients and focused on identifying patients' needs, such as what patients would want to know, when patients should be consented (probably not at the time of surgery), who should administer the consent, and with whom patients would want to consult in addition to their doctor. The Working Group decided that the form should be used as a tool to facilitate consent and not as the absolute consent; the Working Group thus streamlined the information presented in the form to the bare minimum and developed the Q & A brochure

with the guidance that the brochure must accompany the form. For example, the form does not go into detail about the benefits and risks of agreeing to participate in research. The Working Group also decided to keep the extent of choice that patients have about use of their tissue for research to a simple yes or no, rather than offering a choice for each possible type of disease that could be investigated; the yes/no choices were thus limited to cancer and "other health problems." In addition, the form includes an option for recontact, and the patient again is given a yes/no choice for participating in future research. These decisions should facilitate another goal proposed by the Working Group: to try to consent as many individuals as possible and to make this process a part of standard practice.

As the process of development and revision of the forms continued, the Working Group recognized that, although the patient's concerns need to remain a priority, informed consent cannot be obtained in a vacuum without input from clinicians. As Ms. Barr noted, both nurses' and doctors' groups were included in the focus group testing, and input from the surgical and pathology communities in particular was sought. The Working Group has identified several factors, however, that it believes may hinder the further development and subsequent implementation of the enterprise, such as cost and resistance to change; the medical community is encouraged to try not to let these issues interfere with moving ahead with the proposed process but, rather, suggest alternatives to overcome these potential obstacles.

Dr. Craig LeFebvre, Chief Technical Officer, Prospect Associates, provided a summary of results of the focus group testing. He noted that, although health professional focus groups were convened, the primary focus of the testing was on understanding the perspectives, needs, and reactions of consumers and patients and their families to the proposed consent form and process. Moderator guides targeted the needs and reactions of each categorical focus group. Moderators also asked participants to raise issues and questions that were not covered by the moderator or in the form.

As Dr. LeFebvre noted, the results and the analysis of the results of the focus group testing are qualitative rather than quantitative; further, he pointed out, the study results do not necessarily statistically represent any particular target group. With those points in mind, the following are highlights of the results of the focus group testing:

- A large proportion (75 percent) of those in the consumer groups did not understand and/or were not familiar with the concept of tissue banking.
- The form was easy to understand ("it was like reading a newspaper"), but participants indicated that many of the questions could not be answered comfortably because of a lack of sufficient information. An informational/educational Q & A booklet or brochure to accompany the form was suggested by several focus group participants.
- The form seemed to imply that additional tissue would be taken. It was suggested that the form be clarified so that the "additional tissue" mentioned (i.e., that will be used for research) refer more clearly to the tissue remaining after the individual tests are completed. In addition, the form should more clearly delineate when and why extra tissue may not be maintained; this issue was particularly important to the patients and their families.
- The form should more strongly reinforce the confidentiality of the donor of the sample.
- The form should address the impact of genetic testing on the individual and the family.
  
- Participants requested that the form provide additional examples of the types of research conducted using tissue samples and emphasize that consenting to have one's tissue used for research and the research itself will not impact the individual's care. Many participants expressed concern about the motives and intentions of the research.
- Most participants indicated that physicians should administer the form several days in advance of the procedure, allowing the patient time to reflect on the critical issues at hand and to consult with family members and friends, as

needed.

Copies of the executive summary report of the focus group testing will be forwarded to participants who request them.

#### Practical Experience with the Consent

Ms. Joyce Mull, Director of Regulatory Affairs, National Surgical Adjuvant Breast and Bowel Project (NSABP), described use of an early draft of the model consent form by institutions participating in the NSABP, an NCI-funded cooperative group project begun in 1958 to study breast and rectal cancer in the context of clinical trials. Membership of the NSABP includes some 6,000 physicians, nurses, and research personnel at major academic and community settings across the United States and Canada. The NSABP conducts the Breast Cancer Prevention Trial, the largest breast cancer prevention trial to date; the study is designed to determine the possible role of tamoxifen in preventing breast cancer.

Ms. Mull described how the text in the NSABP consent form was adapted from an early version of the NAPBC 's consent form, the process by which the NSABP collects and uses specimens, who has access to that tissue, and the reactions of IRBs and patients to the NSABP consent form. While no direct feedback from patients was reported, feedback from an IRB survey indicated that the form was well-received, prompted little questions or comments, and required very little revision. Ms. Mull also stated that the issue of recontacting a patient with research results is discussed and planned for at the time of the initial NSABP approval of a study; any decision made is incorporated into the consent form. In most cases, patients will not be given individual research results.

Ms. Mull noted that the NSABP looks forward to input from NAPBC and other groups to keep the consent process moving forward and is interested in assisting NAPBC in its endeavors.

#### An IRB Response

Ms. Paula Knudson, IRB Executive Coordinator, Research Support Committees, University of Texas Health Science Center, congratulated the NAPBC Biological Resources Working Group and all others involved in successfully taking on the challenge of developing the model consent form and related materials. The NAPBC 's form is clear, simple, and easy to understand, and appears to be easily revised to suit individual settings and research projects without losing its clarity or simplicity. Recontact/future contact is addressed directly (the patient can answer "no" on the form) and thus is really not an issue.

The role of the IRB in this new enterprise remains an issue, however. Critical to this discussion is the recognition that IRBs already have so many responsibilities, including reviewing numerous existing consents and protocols. Under the new enterprise, IRBs must persuade administrations to impose another consent when most hospital admissions forms indicate that a patient's records and specimens may be made available for research. IRBs also will have the added responsibility of convincing pathology departments to keep new records and tissues and to ensure that they live up to the promises articulated in the consent. Further, IRBs will be faced with the challenge of having to convince surgeons to add to their consent process for treatment the consent for specimen banking and unspecified future research activities.

#### **Panel Discussion: Practical Concerns About Informed Consent; Moving Toward Implementation**

Moderator: Dr. Ellen Wright Clayton, Associate Professor of Pediatrics Vanderbilt Children 's Hospital  
Participants: Dr. Kim Jessup, Associate Professor, Deaconess Hospital; Dr. Michael Cibull, Professor of Pathology, University of Kentucky Medical Center

Speaking for the surgical community, Dr. Jessup stressed that surgeons will be most attracted to the new consent enterprise if it is a highly focused project that (1) has narrow goals; (2) is restricted to a specific disease of interest (e.g., cancer); and (3) is simple and can be administered in a minimal amount of time, with the surgeon talking briefly with the patient about research and consent in the first visit and then obtaining consent during the subsequent visit. Those involved in moving the enterprise forward also should strive to form a very strong alliance with advocacy groups to

generate enthusiasm in patients. Patient care should be the top priority, with research coming second. One area that remains a challenge is the physical movement of the document from the doctor's office to the operating room; the process must ensure that the signed consent travels with the patient and then with his or her tissue to the pathology department.

Dr. Cibull stated that the proposed endeavor is very possible and that the problems discussed are not insurmountable, assuming that:

- The consent is for procurement and banking only. Consent for the actual or potential use(s) of the tissue is a completely different issue.
- Local IRBs remain in control of structuring their own institution's tissue bank or repository. However, the IRB should not be involved in the day-to-day operation or oversight of the bank.
- OPRR develops much clearer guidance for IRBs.
- The consent for procurement and storage of the tissue be physically part of the OR/surgical consent. The only piece of paper that is guaranteed to travel with the patient to the operating room and then be in close proximity to the tissue as it is removed is the operative consent. Assurance that the patient has agreed to have his or her tissue harvested for research can then be rechecked at the time of the operation.
- The current form, which is very well written, is shortened even further, perhaps to one side of one page.

### **Wrap Up**

Ms. Barr provided a brief summary of the day's primary issues and identified possible next steps. The three separate items discussed during the meeting -- the overall model or enterprise, the consent form, and the IRB principles -- should be considered together and integrated into one process.

The greatest concerns raised about the model included (1) cost, (2) pressures on the pathologists, and (3) time constraints and demands on surgeons in obtaining consent and becoming an active player in the enterprise. The next steps in this process are to work on cost-related issues and field test the design.

The current draft of the consent form responds most directly to the needs and concerns of the patient, especially as expressed in the focus groups. The form will be revised again, taking into account the comments and suggestions from this meeting; the Ethical Issues Subcommittee will be reconvened for this purpose. Ms. Barr pointed out, however, that the final form probably will not be entirely satisfying to medical researchers and physicians in terms of genetics protections and the extent to which issues are defined or explained. Because the current form was generally well received today, NAPBC will proceed with this draft as a working document that will be modified as needed.

The principles (1) create an excessive burden on IRBs, (2) may not have identified the most appropriate venue for execution, and (3) remain unresolved regarding absolute prohibition of recontact versus prohibition with provision for exception. PRIM&R is open to the suggestion that a special working group be established to address these concerns and develop practical guidance for IRBs, either at the level of the specific role of the IRB in overseeing tissue banks, or at different levels of the enterprise (e.g., IRBs having a role in research, procurement, and/or distribution). Those interested in participating in such a working group should contact Joan Rachlin at PRIM&R.

Another issue that needs to be addressed more fully in the future is the role of commercialization in tissue banking. Whether NCI or another institution should oversee this project has yet to be determined. Finally, crystallization of broad policy concerns must occur, perhaps through NBAC, OPRR, or representative IRB organizations.

Ms. Barr thanked all those in attendance for their interest and input.

### **End Note**

PRIM&R is co-sponsoring a conference in November, 1997, that will focus on expanding the categories of research that can be expedited. The annual fall IRB meeting, scheduled for December 7-9, 1997, will be co-sponsored by ARENA and PRIM&R.

**The following questions and concerns were raised during the discussion sessions conducted after each presentation:**

**Proposed Model for Obtaining Specimens for Research**

Moderator: Barbara Handelin, Handelin Associates

- Those developing and ultimately implementing this model must consider the reality of practice, specifically, that patient protections currently are not in place. The model must clearly define what information can and cannot be forwarded with the tissue, and patients and consumers must be involved in this process. Further, if archived tissue is to be used for research purposes, patients should be recontacted for the purposes of recontact if not already done.
- Confidentiality is of concern not only to patients but to all players in the model. In addition, confidentiality and privacy are not the only concerns of patients; other issues include the type of research to be conducted on tissue and the concept of a partnership between the patient and researchers.
- Is it necessary to have another group or groups (in addition to IRBs and disease and protocol-specific committees) review protocols? On the other hand, it was stated that not all protocols are forwarded to IRBs and, further, that IRBs probably cannot resolve all problems regarding consent and use of tissue for research.
- Who is responsible for the cost of procurement and banking? Should this component be incorporated into the research grant process?
- Does the possible dual role of pathologist as tissue banker/trustee represent a conflict of interest?
- How do researchers/pathologists/primary care physicians handle cases in which there is an obvious discrepancy between the patient's diagnosis and the research result? Isn't going back to the patient (or his or her physician) a violation of one of the fundamental principles of this model? Although this probably is a rare occurrence, this scenario needs to be addressed.

**Discussion Session: Practical Concerns About IRB Principles and Tissue Availability**

Moderators: Dr. Sheila Taube, National Cancer Institute, and Ms. Ada Sue Selwitz, University of Kentucky

- At some institutions, specific consent language and information about tissue banking and research have been added to the standard surgical consent form. However, experience with this type of amended form suggests that the addenda are not discussed, consent is not given, and the specimen cannot be placed in the repository/bank. The underlying problem with this approach appears to be that surgeons have no vested interest in the ultimate fate of the tissue, especially when they are not given priority access to the tissue.
- Competition for tissues is high. Some institutions find themselves competing with cooperative groups, other clinical centers, etc., for their own tissue. In some cases, outside institutions will incorporate a request for unspecified but mandatory use of tissue into a clinical trial protocol.
- Is prohibiting the release of research results to the treating physician and/or donor unethical? Some consumer and cooperative groups consider this principle in violation of the patient's rights if those data

prove to be scientifically valid and of clinical utility. A related concern is the obligation (legal as well as moral and ethical) of the physician or researcher to report back adverse results. Another issue is whether the research results are valid; for example, research-based laboratory tests are not necessarily considered applicable to patient care.

- Is it necessary to have a full-blown consent, or is an abbreviated form sufficient?
- Have the various levels of risk inherent in the proposed model been defined and assessed? For example, the differences between somatic and germline mutations; incidence and prevalence data versus genotype and phenotype-based research. Dr. Taube responded that at this point, the Working Group and others are trying to set up a system in which specimens taken as part of routine care can be used in subsequent research; the protocols within this system will need to be evaluated in the future, i.e., at the time of implementation, for risk. Ms. Selwitz commented that developing policies for assessing risk may be less difficult and problematic if the first principle of ensuring adequate consent for the collection and dissemination of all donated tissue is implemented.
- The Working Group needs to understand that the broad inclusiveness of the proposed consent form may be a basis for rejection by IRBs.
- Should there be an absolute bar on recontacts? Many have argued that this action involves more than minimal risk and should, therefore, be bypassed. The definition of risk defined by federal regulations, however, relativizes the judgment of risk in the setting of a routine office visit. In a standard office visit, potentially highly confidential information is collected; improper release of such information would present a serious breach of confidentiality. On that basis, many IRBs have reached the conclusion that merely collecting information that could cause social injury through a breach of confidentiality is minimal risk; other IRBs have decided that this is not minimal risk. It was suggested that the issues of risk and recontact should be handled initially, with the patient being informed of the potentially uncertain and, although unlikely, possibly improper uses of his/her tissue.
- Prof. Rothenberg pointed out that the proposed principles must be considered within the context of the consent process. The consent form and process are relatively simplistic, she explained, as a practical tradeoff to reduce or eliminate the risks at the other end of the enterprise (i.e., at the point of the researcher). Thus, a closed and clear protection of patient privacy and confidentiality is essential. Allowance of exceptions (e.g., the obligation of a researcher to go back to the patient, perhaps, with adverse results) must be carefully scrutinized in keeping the model intact.
- Differences between cooperative group and institutional studies, and hospital versus cooperative IRBs, were outlined. Cooperative group studies are usually of a confirmatory nature that establish the criteria for clinical care and institutional individual exploratory studies. Those developing the enterprise may want to consider incorporating a three-tier type system into the model, whereby institutions conduct phase 1 studies, regions conduct phase 2 studies, and cooperative groups conduct phase 3 studies (clinical care). This type of system has been implemented at Harvard.
- The proposed model implies a sharp demarcation between medical research and clinical practice; clinical trials, however, span both areas. How does the enterprise address this? If it does not, the group overseeing the further development of the model should re-examine this issue. Dr. Taube noted that the model proposes a continuum of relationships versus clearly distinct interactions. She pointed out that the model assumes that tissues are being collected in the context of a patient's standard medical care rather than as part of a research protocol.

- The issue of patient privacy and confidentiality in federal and state-based registries was discussed. It was noted that these registries have been established and that information is entered into these registries without the consent or knowledge of the patient. Further, patients whose information is included in these registries can and may be contacted by researchers for participation in studies. The reporting of information to public health officials, which is done largely through mandated registries, exempts the requirement for informed consent; consent is required, however, if the patient enters a research study. Many participants agreed that distrust seemingly would be fostered by this type of system. Concerted efforts to educate consumers about registries and the information and evaluations being conducted using data in these public registries should be encouraged.

**Discussion Session: Practical Concerns About Informed Consent and Satisfying IRBs:  
Are the Ethical Issues Adequately Addressed?**

Moderator: Ms. Susan Kornetsky, Children's Hospital

- Informed consent does not necessarily equal notification, which may be a particular problem with regard to public registries. Just because these registries are mandated by law does not excuse clinicians or others involved in the system from the responsibility of notifying consumers of what is happening with these registries. Early steps in the education of health professionals and the public about the validity of issues such as the existence of these registries, notification of registry activities, the flow of information in the registry, consent, and reporting requirements are underway. Such outreach is critical and will require concerted, continued efforts.
- The NAPBC focus group testing included only English-speaking groups and no Native American groups or Asian breast cancer survivor groups; further, the Asian groups were divided into male Japanese and Filipinos and female Koreans and Chinese, which seems misrepresentative of Asian populations. Most survivors also appeared to be highly educated and at the high income level. How can these discrepancies and deficiencies be reconciled, especially given recent mandates to increase recruitment and retention of underserved populations?

To the above question, Dr. LeFebvre responded by noting that the focus group testing was limited by several factors, including time, cost, and logistics. These factors, in turn, forced certain decisions that limited the number of groups that could be conducted and also the materials and resources that were available (i.e., no translations, thus, no non-English speaking groups). The initially proposed 64 groups were thus reduced to the 26 final groups. All Asian groups were based in Los Angeles, and recruitment to these groups was especially difficult. The project staff worked through focus group agencies and placed advertisements in local newspapers to facilitate recruitment. It was noted that all of the issues and questions raised by the audience member were addressed and discussed as the focus group testing was being planned. Ultimately, those involved in the focus group testing decided to move forward with the project, despite its limitations, in an effort to generate at least some feedback to the model. Dr. LeFebvre agreed that more comprehensive and inclusive research should be conducted. Piloting the revised consent form hopefully will address at least some of these issues.

Some questions/suggestions/comments on the consent form included:

- Should question 3 (i.e., about recontact) be included in the form? What if the patient changes his or her mind in the future? (The form states that the patient can opt out at the time of signing the form, or later; if later, that patient's tissue and accompanying information will be removed from the bank.) Because this form is planned for use in routine patient care (rather than with patients already diagnosed with cancer who have more of a vested interest in the disease), does this question actually work against consenting for participation in a research project?

- Should question 1 retain the word "cure"? Is this too strong?
- Should question 2, which indicates that tissue may be used to investigate the causes of diseases other than cancer, be revisited? (The Q & A brochure provides additional information about possible future research projects.)
- The distinction between cancer and other diseases is much less significant than the differences between germline and somatic mutations. (Incorporating these distinctions into the forms and/or the brochure was discussed by the Working Group, which ultimately decided to not include these distinctions in the current draft.)
- Won't requiring a witness add to the expense and time needed to administer the form? Aren't we trying to simplify the process?
- Will all identifiers actually be stripped from the specimens, as indicated in the text of the form? Isn't this misleading, even if the identifier is simply a code? Doesn't coding allow someone to trace the sample back to the donor? The consent should define what identifiers are and are not used.
- The consent does not provide enough assurance about possible misuse of the tissue and/or private medical information. This topic should be explored further and expanded upon.
- Instead of saying, "My tissue may be kept . . ." the form might be changed to say, "My tissue may be shared . . ." It must be clear, however, that the tissue will not be sold or used directly for commercial gain.
- The form should state, up front, that there are no benefits to the patient.
- The simpler the form the better; cumbersome forms are prohibitive, whether administered to low-literate or highly educated persons. Thus, the current form and its companion brochure are on the right track and are applicable to all individuals. Simpler forms also may be more attractive to the physicians and nurses who administer the consent (or oversee the consent process).
- Is the form too simplistic and short? Will it get lost when appended to a research protocol? (The audience was reminded to think of the form in the context of general medical care and to meet the needs of patients going into surgery and not in the context of a clinical trial, for which a system and standards of support, consent, and education are well established.)
- It is the responsibility of the larger medical community to ensure that patients really are well informed. However, they must avoid being too paternalistic in their approach.
- Audience members were disappointed to hear that such a large proportion of IRBs opted out of the banking component of the NSABP trials when given the option.
- The Alliance for Genetic Support Groups has developed guidelines for informed consent; although these guidelines originally were designed for consumers, they also are used widely by health professionals, including researchers. The model consent form proposed today is a good start but should take into account the role of the patient in determining how his/her tissue may be used; this will help contribute to developing trust.
- Media (over)exposure of a few unethical situations contributes greatly to mistrust of the medical research

community by consumers. A related point is that whistle blowers within the medical and scientific research communities often are treated poorly. Further, "good news" rarely seems to gain the attention that "bad news" does. What kinds of messages are being received by the public? Who watches whom? Which groups should monitor ethical issues? Can we continue to stretch IRBs? Should new institutional entities be established for this purpose?

- The risks associated with consent are not really quantitative but qualitative in nature. It was noted that the Q & A brochure discusses the concept of risk as well as specific risks (e.g., insurance and workplace discrimination) more fully than the consent form. Delinking of personal information from specimens, and allowing information to flow in only one direction out of the repository, should help reduce risks significantly. However, it must be kept in mind that the pathology department, which has access to an individual's medical records, often serves as the repository. Certain safeguards must be in place before implementation of this or any other model.
- The responsibilities of IRBs are not inconsequential. However, it is important to not duplicate efforts. OPRR and similar organizations can be helpful in convening expert consumers and scientists and reaching consensus.

### **Discussion Session: Practical Concerns About Informed Consent; Moving Toward Implementation**

Moderator: Dr. Wright Clayton, Vanderbilt University

Participants suggested that the brochure be given to patients at the first visit so that any questions the patient has could be raised in the second visit, when the form would be signed. Some suggested making the brochure more generic (e.g., delete references to a specific institution) and converting it into a tri-fold pamphlet.

Other comments/questions included:

- The process of consent must be efficient, and if surgeons are to be involved in administering the consent, the time component of the process may have to be compromised somewhat, as it is unlikely that surgeons will devote 30 minutes to accomplish this task. The possibility of offering hospitals, surgeons, pathologists, and others incentives for participation, such as laboratory accreditation programs, should be considered.
- Can the IRB serve as the gatekeeper for determining the outcome of the consent? For example: At the time that the tissue may be used for research, if the consent is adequate, then recontact to use the tissue is waived; if the consent is inadequate, then a decision about recontacting is made.
- Identifying criteria for overriding the prohibition of recontact should include a discussion of whether the research results in question are truly of clinical significance or are simply of scientific interest. The discussion should also address whether researchers can somehow return to the donor if confounding factors are subsequently identified. Cases in which recontact may be permitted might include unexpected epidemiologic findings identified after the tissue is collected and an unexpected research finding specific to a patient that significantly affects that individual's diagnosis and treatment. The person or group responsible for recontact and the person or group to be recontacted also should be identified.
- Does the tissue need to exist at the time the research is proposed? (Yes.)
- Attempts to standardize national cancer registries are underway so that registry data are not easily released without appropriate IRB reviews. Efforts are also being made to ensure that all states have IRBs. The

issue of requiring prior patient consent for entry of information into public health databases is under debate and may rest with finding a balance between right to know and right to privacy. Opening the discussion to all stakeholders, as in the current meeting, may help set social consensus, which, in turn should help resolve some of the issues at hand.

- Contrary to the comments of some speakers, OPRR guidance is appropriate and adequate, and further regulation is not the answer. The key to progressing this enterprise is sound, ethical decision making, both in a broader social context and at the more narrow, local institutional level.
- Pilot studies not only should include diverse populations but should also be conducted in a variety of settings (e.g., academic center, community hospital, community clinics).
- Establishment of three different types of IRBs (one at the researcher level, one at the institutional level, and another at the patient level) and then developing a model by which the three groups could reach consensus on overlapping issues was proposed.
- Those developing the enterprise seem to be aware that the general public and some special populations tend to distrust the medical research community. Targeting specific groups for research ultimately may benefit the health of members of those groups; however, publication or release of "adverse" data or information about a certain group can also serve to stigmatize that group and cause further distrust. Fostering the sense of a partnership and promoting research as a means to reach a greater good for all (or for specific groups) may help allay concerns and distrust.
- Guidance for the dissemination and distribution of materials should be developed. One type of research being conducted that should be included in this discussion is multi-center, industry-sponsored drug trials. Nearly all, if not all, of these studies collect at least some tissue/blood samples for unspecified future research. It maybe worthwhile to investigate how consent for these collections is handled. It was noted further that commercial organizations are very interested in accessing new and archival collections.



**Feedback Form on Specimen Banking and Use of the  
NAPBC Model for Banking of Routine Specimens**

Please return this form to PRIM&R/ARENA, 132 Boylston Street, 4th floor, Boston MA 02116, or fax to (617) 423-1185. Use extra sheets as needed.

Your Name \_\_\_\_\_  
Title \_\_\_\_\_  
Institution \_\_\_\_\_  
Address \_\_\_\_\_  
City, State, Zip \_\_\_\_\_  
Phone \_\_\_\_\_ Fax \_\_\_\_\_  
Email \_\_\_\_\_

A. Questions about tissue/specimen banking at your institution:

1. Approximately how many protocols does your IRB review each year? \_\_\_\_\_

2a. Has your IRB reviewed protocols which include specimen collection, use, or banking? Yes No

2b. What percent of protocols submitted to your IRB involve specimen collection or use? \_\_\_\_\_%

3. Do you have current policy for review and approval of such protocols? Yes No

If yes, what is your policy? (attach copy, or describe on a separate sheet)

4. Under what conditions, if any, does your policy allow for future undefined use of stored specimens (check all that apply)

a) further consent needed?	Yes	No
b) further review by IRB needed?	Yes	No
c) specimens must be anonymous?	Yes	No
d) reviewed on case by case basis?	Yes	No
e) no conditions need be met?	Yes	No
f) other? (please describe)	Yes	No

5. Do you currently rely only on a surgical consent form for research specimen use?

Yes No If yes, please send a copy of surgical consent.

6. Do you have additional consent documents or procedures for specimen use, beyond a surgical consent? Yes No

If yes, please send a copy of consent document.

7. Does your institution have, or contribute specimens to, any of the following types of specimen collections? Yes  
(please circle below) No Don't know

- a) existing pathological or diagnostic specimens, later used for research
- b) individual clinicians' (pathologists, surgeons, etc.) research specimen collections
- c) individual non-clinical researchers' specimen collections
- d) departmental research specimen collections
- e) institutional specimen banks, for research use by multiple investigators
- f) regional and national specimen banks [e.g. Cooperative Human Tissue Network, National Disease Research Interchange, Cooperative Family Registry for Breast Cancer, etc.]
- g) non-profit private specimen banks [e.g. LifeGift Foundation, Tucson AZ]

- h) for-profit organizations [for research use or for direct commercial use]
- i) oncology groups' collection of paraffin blocks or other specimens for specific research and/or for storage for future unspecified use
- j) others, please list

7k. If yes, does the bank have its own IRB protocol? Yes No If yes, please describe relevant details of approved protocol

8. Does your IRB take special concerns of cultural, religious, or ethnic groups into account in deliberations on tissue/specimen donation? Yes No If yes, how do you do so?

9. Have any concerns about your existing policy or decisions been voiced by

- a) surgeons/pathologists? Yes No
- b) researchers? Yes No
- c) epidemiologists? Yes No
- d) patients/families? Yes No
- e) IRB members? Yes No
- f) ethicists? Yes No
- g) lawyers? Yes No
- h) administrators? Yes No
- i) others? (please specify) Yes No

If yes, briefly describe concerns:

B. Questions about the NAPBC Model and Documents for Specimen Banking

10a. Has any discussion about the 3 NAPBC documents (Principles, Information Sheet, Consent Form) taken place with your IRB? Yes No

10b. If yes, has the discussion been useful in formulating or adapting your IRB's policies on specimen banking? Yes No

10c. If yes, were any new issues raised? Yes No If yes, please describe.

10d. If no, do you expect discussion to occur at a later date? Yes No

11. Have the comments on the documents provided by the PRIM&R/ARENA Tissue Banking Working Group been useful? Yes No

12. Are investigators at your institution planning to use the documents?  
Yes No Don't know

13. If the model documents were to be used at your institution, do you foresee any problems or issues that might be raised by providers (hospital administration, medical staff, legal staff, forms committee, etc)? Yes No If yes, please describe.

14. If the model documents were to be used at your institution, do you foresee any problems or issues that might be raised by patients or their families (additional questions, suggestions, etc)? Yes No If yes, please describe

15. If the model documents were to be used at your institution, do you foresee any problems or issues with logistics of implementation (having a consent form separate from the surgical consent; additional time involved in obtaining informed consent, additional work/costs associated with a tissue trustee, etc.)?

Yes No If yes, please describe

16. Do you have any suggestions for modifications to the model or to the specific documents?

THANK YOU! Please note: If you also send copies of specific consent forms, policy, etc, please make sure that you and your institution are named on the forms, so that proper attribution can be maintained with the documents as we collect them.

**IRB Principles** for Consideration by Institutional Review Boards (IRBs)  
Regarding Operation of Tissue/Specimen Banks  
(PRIM&R/ARENA Tissue Banking Working Group comments)

A more descriptive title for this document, to make it clear that there is no implication that the IRB necessarily has any or all responsibility for ensuring implementation of the following statements, was felt to be essential.

**In order to facilitate scientific research, the NAPBC National Biological Resource Banks Working Group recommends development of a system of specimen collection and distribution which will enable consumers to donate tissue and researchers to have tissue that is ~~de-identified~~ coded but, when necessary for research, will allow specimens to be linked, through an intermediary, to outcome data such as those available through the national cancer registry system.**

Slight changes in words were felt to make the description of the model system more clear.

The NAPBC Working Group 's focus was on the situation in which tissue is removed for purposes of routine care and where most patients do not know whether their left-over tissue may be used for research.

Issues of funding and costs related to the proposed model system were a major concern and discussion point. The clerical and technical costs, as well as the professional level of effort of maintaining a tissue repository, must be built into the system. It takes careful attention to code tissue, and the code must be maintained indefinitely without error. The National Cancer Institute is supporting several sites around the country to pilot this plan and to determine the costs as well as other logistical issues.

**The Working Group believes that when organizations with access to ~~tissue~~ specimens act according to the following criteria, it should generally be unnecessary to obtain further consent from patients.**

The document can be made more general by reference to specimens rather than just to tissue. By using the word "specimen," the document can be broadened to include tissue, blood, body fluids, and other samples regardless of fixation or storage condition.

Individual IRBs must still decide if waiver of informed consent for each future use of banked specimens might be approved. Opinions of IRBs vary on the issue of risk, usually discussed in the context of risk associated with uses of the tissues and the chance of improper release of confidential information. With the criteria presented here, including initial informed consent, distribution of coded samples and coded follow-up information by a tissue/specimen bank trustee, and

the almost-total prohibition against return of results, the PRIM&R/ARENA Tissue Banking Working Group believes that this system involves risks comparable to those found in daily life, and thus presents minimal risk to subjects.

The amount of protection needed to ensure privacy and confidentiality to the level that would allow for the waiving of informed consent remains under consideration by the Office for Protection from Research Risks (OPRR).

**Furthermore, if IRBs of those organizations collecting and distributing specimens fulfill their obligations to assure preservation of confidentiality and privacy, ...**

IRBs cannot necessarily assure preservation of confidentiality. The IRB can, however, review the mechanisms proposed by the tissue bank or institution which function to protect the patients. One consideration in this model is whether a pathologist can serve as the tissue/specimen trustee, or whether another individual would be better able to serve as the intermediate buffer between the physician (surgeon and/or pathologist) and the researcher.

The level of protection that is appropriate to ensure privacy and confidentiality, and the standards needed to obtain that level, are substantive issues that are still under consideration by OPRR. Certificates of Confidentiality may be requested for research protocols, but were not originally developed for broad use in all types of research.

A Certificate of Confidentiality is a prohibition that assists in guarding the privacy of research subjects from involuntary disclosure of identity. A researcher so authorized to protect the privacy of research subjects may not be compelled in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings to identify such individuals. A Certificate can be obtained through the Public Health Service for any type of research, whether or not it is federally funded. [PHS Act, ' 301(d),42 U.S.C. ' 241(d), as added by Pub. L. No. 100-607]

**...the need to recontact/reconsent patients or repeat the process of informed consent will be reduced.**

IRBs may be able to decide that a subject ' s response, as documented on this model consent form, would allow waiver of consent for any future research use of tissue. Any recontact, for purposes of repeating the process of informed consent, must be clearly distinguished from recontact for purpose of reporting of research results. Although the latter type of recontact is strongly discouraged, there may be, on rare occasions, compelling reasons/justifications to do so. In all situations, IRB approval must be obtained, and the subject ' s welfare must be foremost in this consideration.

**The Working Group proposes a model consent to be used within the recommended system.**

The June 2 meeting was held specifically to discuss this document, the consent form, and the information sheet drafted by the NAPBC. However, the concerns and issues brought up at the meeting can be used as a starting point for further discussion. Whether or not IRBs review protocols for tissue banks which follow NAPBC ' s guidelines and are "within the recommended system," IRBs are probably already reviewing protocols in which tissue/specimen banking or storage is proposed, even if such activity is only briefly or indirectly noted. Modifications and explanations of the forms and principles presented here might then allow their use in other situations where specimens are collected and later used for research. Many people, including some members of

this PRIM&R/ARENA Working Group, continue to work on and write about these larger issues.

**While these principles apply to prospective tissue specimen collection, the Working Group recognizes the vast and important research resource collected and kept by pathologists in their clinical practice. It is hoped that these principles, suggested specifically for organizations whose primary function is collecting and distributing specimens, can be adapted to allow those pathologists to make their collections available for research and, at the same time, protect the privacy and confidentiality of the tissue sources.**

Specimen collections, whether they are described as “banks” or not, are many and varied. They cover the spectrum from individual clinicians’ (pathologists, geneticists, etc.) research specimen collections, often gathered with no specific project in mind; to institutional “Tissue Banks,” such as Comprehensive Cancer Centers’ Shared Resource banks; to multi-center, industry-sponsored drug trials which usually collect at least some blood or tissue for unspecified future research.

**I. Coded specimens that facilitate ~~Facilitating de-identified but linked research that~~ and which **best protects the privacy and confidentiality of tissue donors requires a prohibition against reporting individual results to either the donor or his/her physician. Rare (E)xceptions to this rule should be examined with extreme scrutiny.****

Changes in words are proposed, in order to better describe the fact that a code is maintained, and to emphasize the importance of the near-prohibition against return of results.

The model consent form and information sheet are intentionally simple and brief. The trade-off for such simplicity comes with the limitation that no information about the research be placed in the medical record or given to the subject or his/her physician. The model also assumes that most use of tissue for research will likely occur a long time after the sample is taken and the patient has completed treatment.

Research tests usually do not meet the federal standards needed for results to be clinically valid [The Clinical Laboratory Improvement Amendments of 1988, with final rules published in 1992, (CLIA -88), Public Law 100-572, specifically requires the regulation of any facility that performs tests on human beings for the purpose of providing information for the diagnosis, prevention, or treatment of any disease or impairment. If the results of laboratory testing are used for individual treatment of the patient tested, the laboratory is subject to CLIA requirements. (57 FR 7015)].

There is a reluctance, however, to have a strict prohibition against revealing the results of research to subjects from whom tissue was used. Instances in which consideration might be given to return research results to subjects and/or their physicians include some, but not all, cases in which the results suggest a different diagnosis or treatment decision, when an unexpected epidemiologic finding is identified after the tissue is collected, or other situations where results would be of clinical significance to the patient.

Disclosure of a misdiagnosis could be of life-saving importance to the patient, if that information were found in a timely fashion. However, disclosure also constitutes a risk to the pathologist and the hospital in terms of malpractice liability. This presents a dilemma which is difficult to resolve, since pathologists might thus be reluctant to submit tissue which otherwise would be discarded.

If recontact were considered, the case must be referred to a review panel to determine the appropriateness of the disclosure of results (including clinical confirmation of research results, as needed), and the people to be involved in recontact.

**II. Organizations collecting and distributing specimens must have scientific panels (which include**

**consumer patient participants) reviewing and prioritizing material requests to assure that limited and non-renewable resources are used appropriately. Such panels must meet the standards of peer review.**

Substitution of a more specific word for consumer is recommended.

This panel may not require the IRB for establishment and oversight. The institution could be responsible for implementing and overseeing this activity. There are concerns of cost, logistics, and slowing of research progress if a panel were involved. IRBs should be aware that, if the institution provides funding for the oversight panel, it could potentially exert undesirable influence on the activities and deliberations of this panel.

The panel could deal with issues such as sharing of tissues by investigators who receive them from the bank, evaluation of whether proposed research projects are worthy of receipt of requested materials, commercial interests in obtaining tissue for research, and resolution of disputes over controversial protocols.

**III. IRB's of the organizations collecting and distributing specimens are**  
~~—charged with responsibility~~ can review and approve mechanisms **for:**

IRBs cannot and should not be responsible for ensuring the processes listed below. However, they can review and approve mechanisms that lead to the following results.

**A. Establishing standards for the maintenance of the collection.**

Establishment of standards might be the responsibility of the tissue bank or of the institution. Standards might vary depending on whether the tissue bank is operated by an investigator, a group of investigators, a cooperative clinical trial group, etc.

**B. Insuring that adequate patient consent is secured for all tissue donations; this requires approval of the consent process and a mechanism involving local institutions and/or pathologists for disseminating and collecting the consent forms.**

The IRB can review and approve the process for obtaining and documenting informed consent, and can approve the consent form, but cannot ensure that adequate consent is secured.

Some discussion revolved around whether consent would be obtained each time a patient had surgery, or whether a single consent would suffice for all subsequent donations of tissue. The original intent for the model consent was that it would be used for each specific tissue donation. However, this system would allow a different decision to be made each time, which might complicate logistical issues. Possible assumptions regarding the application of a subject 's answer to use of any specimens previously collected without informed consent should be approached with care.

In addition to pathologists and surgeons, the support of hospital CEOs will be critical in ensuring successful implementation of a consent process. CEOs oversee departments such as pathology and admission offices issuing surgical consent forms, as well as committees that review forms to be used in clinical care. Their involvement and understanding of the needs of all stakeholders are critical for providing an infrastructure for fulfilling research objectives of the institution.

**C. Validating the mechanism for prioritizing how limited and non- renewable resources are used.**

One of the most difficult issues in the model system is the resource allocation panel, described in Part II, above. The NAPBC recognizes that implementation of this principle requires significant discussion, and they are open

to any suggestions about how this important function could be adequately addressed.

**D. Maintaining the "trust" status of the repository.**

Intermediary tissue/specimen bank trustees are critical when it comes to protecting specimens and/or data. Efficient procedures are essential for well-protected tissue utilization or access to existing data or records. Some institutions have developed confidentiality pledges for use by trustees of specimen repositories and research data. Signed pledges serve to document IRB approval and other confidentiality provisions required. Trustees can also assist an institution ' s Technology Transfer Department, which may require a "Material Transfer Agreement" before release of specimens to unaffiliated researchers.

IRBs should question how the level of organization required for this tissue banking system will be maintained. What happens if tissue bank loses funding? How will the commitment made to the subject be honored?

Information Sheet  
**How is Tissue Used for Research?**  
(PRIM&R/ARENA Tissue Banking Working Group comments)

An additional title for this document makes it easier to refer to.

**Where does tissue come from?**

**After a person has had a biopsy (or surgery) and all tests have been done, there may be some left-over tissue. Sometimes, this tissue is ~~thrown away~~ not kept because it is not needed for the patient's care. Instead, a patient can choose to have the left-over tissue kept for future research. People who are trained to handle tissue and protect donors' rights make sure that the highest standards of quality control are followed by the xyz. Your doctor does not work for the xyz, but has agreed to help collect tissue from many patients. Many doctors across the country are helping in the same way. If you agree, only left over tissue will be saved for research. Your doctor will not take more tissue during surgery than needed for your care.**

There was concern that using the words “thrown away” might convey a sense of disrespect for the tissue and the person from whom it was removed.

“Left-over tissue” may be defined in the context of this model consent form as anything remaining from a specimen removed during a medically-necessary surgical procedure, after all tests and diagnoses have been performed. If the model consent is revised and broadened to include other leftover specimens such as cerebrospinal fluid or urine, all references to the word “tissue” should be changed to a more general word such as “specimen.” No extra tissue is taken for research purposes, and the decision to allow left-over tissue to be saved for research should in no way affect the surgeon, the surgery, or the pathology diagnostic procedures. On rare occasion, there might be additional diagnostically-important information in a left-over specimen. (See the discussion in the Principles document, part I.) IRBs should be aware of the potential for conflict of interest if the surgeon or pathologist, or other physician directly involved in handling the specimen, is personally interested in collecting some of the “left-over” tissue.

Tissue might be designated “left-over” if all of the whole, fresh sample is not needed to be looked at microscopically, at which point this “excess” tissue could be frozen or otherwise specially handled separately from the portion submitted for diagnostic procedures. Tissue also might be considered “left-over” only after all tissue has been processed into a paraffin block and slides made from part of the block for clinical diagnosis. It is important to note that there is no guarantee that any tissue will be “left-over,” especially when small samples are removed (e.g. biopsies). For biopsies, there might be enough tissue to make only one paraffin block, and the pathologist might decide that none of the tissue may be used for research, just in case it is needed for future care of the patient.

**Why do people do research with tissue?**

**Research with tissue can help to find out more about what causes cancer, how to prevent it, and how to treat it, ~~and how to cure it~~. Research using tissue can also answer other health questions. Some of these include finding the causes of diabetes and heart disease, or finding genetic links to Alzheimer's.**

Some concern was expressed that direct mention of a “cure” in this context might raise unrealistic expectations. Since successful treatment would include a cure, it was felt that words describing research on treatment should suffice. In the following paragraph, there is a much “softer” reference to a cure, but IRBs might discuss that reference as well.

**What type of research will be done with my tissue?**

**Many different kinds of studies use tissue. Some researchers may develop new tests to find diseases. Others may develop new ways to treat or even cure diseases. In the future, some of the research may help to develop new products, such as tests and drugs.**

**Some research looks at diseases that are passed on in families (called genetic research). Research done with your tissue may look for genetic causes and signs of disease.**

**How do researchers get the tissue?**

**Researchers from universities, hospitals, and other health organizations conduct research using tissue. They contact xyz and request samples for their studies. The xyz reviews the way that these studies will be done, and decides if any of the samples can be used. The xyz gets the tissue and information about you from your hospital, and sends the tissue samples and some information about you to the researcher. The xyz will not send your name, address, phone number, social security number, or any other identifying information to the researcher.**

An important concept in the model tissue banking operation envisioned by the NAPBC is the tissue/specimen bank trustee or intermediary who serves to protect patient privacy and confidentiality. This tissue/specimen trustee is the buffer between the surgeons and pathologists who know the patient's identity (and who supply tissue samples), and the researcher who will *not* know the patient's identity (but who uses the tissue and may have requirements for follow-up information about the patient).

The addition of the role of the tissue/specimen trustee represents increases in time and costs associated with a tissue banking enterprise, and this concern must be recognized. If costs increase, less research may take place. Funding agencies must be made aware of the need for specific budgeting for tissue.

**-see other side-**

**Will I find out the results of the research using my tissue?**

**You will receive the results of your biopsy, but you will not receive the results of research done with your tissue. This is because research can take a long time and must use tissue samples from many people before results are known. Results from research using your tissue may not be ready for many years and will not affect your care right now, but they may be helpful to people like you in the future.**

**Why do you need information from my health records?**

**In order to do research with your tissue, researchers may need to know some things about you. (For example: Are you male or female? What is your race or ethnic group? How old are you? Have you ever smoked?) This helps researchers answer questions about diseases. The information that will be given to the researcher may include your age, sex, race, diagnosis, treatments, and family history. This information is collected by your hospital from your health record and sent to xyz. If more information is needed, xyz will send it to the researcher.**

**Will my name be attached to the records that are given to the researcher?**

**No. Your name, address, phone number and anything else that could identify you will be removed before they go to the researcher. The researcher will not know who you are.**

**How could the records be used in ways that might be harmful to me?**

**Sometimes, health records have been used against patients and their families. For example, insurance companies may deny a patient insurance or employers may not hire someone with a certain illness (such as AIDS or cancer). The results of genetic research may not apply only to you, but to your family members too. For diseases caused by gene changes, the information in one person's health record could be used against family members.**

**How am I protected?**

**The xyz is in charge of making sure that information about you is kept private. The xyz will take careful steps to prevent misuse of records. Your name, address, phone number and any other identifying information will be taken off anything associated with your tissue before it is given to the researcher. This would make it very difficult for any research results to be linked to you or your family. Also, people outside the research process will not have access to results about any one person which will help to protect your privacy.**

**What if I have more questions?**

**If you have any questions, please talk to your doctor or nurse, or call our research review board at ....(IRB's phone number).**

## **Consent Form**

(PRIM&R/ARENA Tissue Banking Working Group comments)

### **About Using Tissue for Research**

A fundamental concept supported by the NAPBC is that consent for research use of tissue from routine practice must be separated from the general surgical consent. However, this means that someone must persuade hospital administrations to “impose” another consent process when existing surgical consent forms (however inadequate that consent form really might be for research use) usually already indicate that patients’ medical records and excess specimens may be used.

Response from the focus groups indicates that most patients would prefer to have their physicians present the possibility of using their tissue for research several days in advance of the procedure, to allow time for the patient to reflect on the issue, and to consult with family and friends.

Response from the focus groups shows that one of the important strengths of this consent form is its simple language.

The time required, as part of the informed consent process, to explain the tissue collection project may be a problem for surgeons and others who have patient contact and who presumably will present the consent form. The information sheet and consent form should be only part of the process.

Surgeons will be most attracted to this new enterprise if it is restricted to a specific disease of interest (such as cancer), is simple, and can be administered briefly. Advocacy groups can play a role in education of patients, which may allow the process of obtaining consent to go more smoothly. The possibility of offering hospitals, surgeons, pathologists, and others incentives for participation, such as laboratory accreditation programs, might be considered.

The logistics of keeping track of each subjects’ answers so their choices can actually be honored is a serious concern and will need to be addressed. The physical movement of the consent document from surgeon’s office to pathology department will have to be thoughtfully considered, and might be more likely to succeed if it is physically part of the surgical consent form. Recording of the subjects’ responses so that they will be associated with the tissue samples will certainly require a large commitment from pathology departments. See other comments related to consent form logistics on the Principles document under Part III, section B.

**You are going to have a biopsy (or surgery) to see if you have cancer. Your doctor will remove some body tissue to do some tests. The results of these tests will be given to you by your doctor and will be used to plan your care.**

Tissues removed as part of care for non-cancerous conditions can also be used for research, as can normal tissue, and non-tissue specimens such as cerebrospinal fluid or urine. The consent form might be generalized to include these cases.

**We would like to keep some of the tissue that is left over for future research. If you agree, this tissue will be kept and may be used in research to learn more about**

**cancer and other diseases. Please read the ~~question and answer~~ Information sheet called "How is Tissue Used for Research" to learn more about tissue research.**

The title of “Information Sheet” has been recommended to be added to the question and answer sheet to make it easier to refer to. A large proportion (75%) of those in the focus groups did not understand or were not familiar with the concept of tissue banking, and the sheet is designed to help explain the process. It is important to note that there is no guarantee that any tissue will be “left-over,” especially when small samples are removed (e.g. biopsies).

**Your tissue may be helpful for research whether you do or do not have cancer. The research that may be done with your tissue ~~probably will not~~ is not designed to help you. It might help people who have cancer and other diseases in the future.**

Some felt that it should be made *clearer* that there is no direct benefit to the subject. U

**Reports about research done with your tissue will not be given to you or your doctor. These reports will not be put in your health record. The research will not have an effect on your care.**

See comments about return of results in exceptional circumstances on the Principles document, Part I.

### **Things to Think About**

**The choice to let us keep the left over tissue for future research is up to you. No matter what you decide to do, it will not affect your care.**

**If you decide now that your tissue can be kept for research, you can change your mind at any time. Just contact us and let us know that you do not want us to use your tissue. Then ~~the~~ any tissue that is left in the bank will no longer be used for research.**

An explicit limitation that only tissue remaining in the bank could be withdrawn was felt to be needed for clarity. If tissue has already been distributed to investigators, it would be difficult to track it down, and any tissue already used cannot be withdrawn. A clear method of contact to have tissue withdrawn needs to be added to the consent form (name, address, phone number of tissue/specimen bank trustee or other appropriate, institution-specific person).

**In the future, people who do research may need to know more about your health. ~~When~~ While the xyz may gives them reports about your health, it will not give them your name, address, or phone number, or any other information that will let the researchers find out who you are.**

It was thought important to make it clear that reports would not necessarily be given, but that if they were, no identifying information would be disclosed.

The issue of patient privacy and confidentiality in federal and state tumor registries was discussed. It was noted that these registries have been established and that information is entered without the consent or knowledge of the patient. Further, patients whose information is included in these registries can and may be contacted by researchers for participation in studies. Many participants agreed that distrust could likely be fostered by this type of system.

Concerted efforts to educate patients about registries and the information and evaluations being conducted using data in these registries should be encouraged. Just because these registries are mandated by law should not excuse clinicians or others involved in the system from the responsibility of notifying patients of what is happening with the registries.

**Sometimes tissue is used for genetic research (about diseases that are passed on in families). Even if your tissue is used for this kind of research, the results will not be put in your health records.**

When an earlier version of the model consent form was submitted to IRBs as part of an oncology group protocol, the majority of questions from IRBs focussed on this genetics section of the consent form. See discussion about return of research results in the Principles document, part I.

**Your tissue will be used only for research and will not be sold. The research done with your tissue may help to develop new products in the future.**

Commercial organizations are very interested in accessing new and archival tissue collections. Some of the concern about commercial use of tissue stems from prioritization of use of a limited resource. Specimens that are provided to researchers may ultimately be a foundation for profitable products. Opinions are many and varied regarding the need for information about any legal or ethical “rights” to share in possible future profits.

The focus group members were uncomfortable with comments suggesting that their tissue (or a product of their tissue) would be sold. Many participants in the focus groups expressed concern about the motives and intentions of the research. The consent form could be changed so that the phrase “...and will not be sold” is deleted. However, it might be difficult, if not impossible to promise that there will not be commercial use of specimens. Research using tissue might be supported by funding from commercial enterprises. Tissue is not “sold,” but money often changes hands for “services” associated with tissue collection, and might be an area that IRBs should examine for possible conflict of interest.

### **Benefits**

**The benefits of research using tissue include learning more about what causes cancer and other diseases, how to prevent them, and how to treat them, and how to**

**cure them.**

Some concern was expressed that direct mention of a “cure” in this context might raise unrealistic expectations. Since successful treatment would include a cure, some felt that words describing research on treatment might suffice.

### **Risks**

**~~There are very few risks to you. The greatest risk to you is the release of information from your health records. The xyz will protect your records so that your name, address, and phone number will be kept private. The chance that this information will be given to someone else is very small.~~**

It was thought that the first sentence, minimizing risk, should be deleted. Some feel that not enough information is provided about possible misuse of tissue or information.

The concerns about about tumor registries, mentioned above, also apply to these statements.

### **Making Your Choice**

**Please read each sentence below and think about your choice. After reading each sentence, circle "Yes" or "No." No matter what you decide to do, it will not affect your care. If you have any questions, please talk to your doctor or nurse, or call our research review board at ....(IRB's phone number).**

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**1. My tissue may be kept for use in research to learn about, prevent, or treat, or cure cancer.**

Yes                  No

Concern was expressed that direct mention of a “cure” might raise unrealistic expectations. Since successful treatment would include a cure, it was felt that words describing research on treatment should suffice.

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**2. My tissue may be kept for use in research to learn about, prevent, or treat about other health problems (for example: ~~of causes~~ diabetes, Alzheimer's disease, and or heart disease).**

Yes                  No

Changing the wording of this question so it parallels the first question was recommended.

Tracking of the specific choices of the subject will add to the complexity of the system. However, the NAPBC felt it was important to allow the subject at least this simple choice between cancer research and “other” research, as a reflection of the partnership of the donor to the research effort.

Although some think that the distinction between use of tissue for research on cancer versus other diseases is much less significant than the difference between research on germline versus somatic mutations, the NAPBC Working Group ultimately decided not to include these genetic distinctions.

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**~~3. Someone from xyz may contact me in the future to ask me to take part in more research.~~**

~~Yes~~ — ~~No~~

The NAPBC Working Group included this question in the consent form because of concern that repeated contact of research subjects by investigators was a risk. However, the PRIM&R/ARENA Working Group recommends deletion of the question for the following reasons.

Prohibiting recontact without prior consent for recontact might not be a good idea because it potentially irreversibly closes the door on what could be important research, and is contrary to prior standards such as case-control studies. Because the consent process is planned for use in routine care (rather than with patients already diagnosed with cancer who might have more interest in research on the disease) there might be a high probability of refusal for recontact (uninformed refusals).

The form might give the impression that a subject can decline to be contacted and, by their answer on this form, completely prevent any future contact. However, subjects might be contacted by researchers from other institutions, or by others who have no knowledge of this tissue banking consent form; this might lead to distrust of the system.

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**Please sign your name here after you circle your answers.**

**Your Signature:** \_\_\_\_\_

**Date:** \_\_\_\_\_

**Signature of Doctor/Nurse:** \_\_\_\_\_

**Date:** \_\_\_\_\_

**Witness:** \_\_\_\_\_

**Date:** \_\_\_\_\_

Requirement for a witness signature may add to the expense and time needed to administer the form, and probably would not usefully increase the protection afforded to research subjects. Any such requirement should be thoughtfully considered if it is not mandated by law. Some states require the signature of a witness, and IRBs can add appropriate lines to the consent form as needed.

**5/15/97**

