

SWOG

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Policy Memorandum No. 39
Subject: Tissue and Other Patient Specimens
Departments Affected: All

Page 1 of 5 pages
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**ACQUISITION, MAINTENANCE AND USE IN RESEARCH
OF TISSUE AND OTHER BIOLOGIC PATIENT SPECIMENS**

1. All biologic materials obtained from patients taking part in SWOG protocols that are stored for future research use are to be obtained, stored, banked, inventoried, and used in medical research as directed by these guidelines.
2. When a SWOG protocol requests biologic materials from patients, these materials must be obtained only after appropriate informed consent of the patient. This informed consent must include appropriate elements required by the National Cancer Institute. Waiver of the requirement for informed consent will only be considered for retroactive banking and/or use of specimens that were originally collected solely for nonresearch purposes, where the proposed use of the specimens meets all criteria for waiver of consent as defined under HHS regulations or is exempt from the requirement for consent (e.g., research entirely involving anonymous specimens or specimens from deceased individuals).
3. All biologic materials obtained for research from patients taking part in SWOG protocols will be held in biospecimen banks. "Stored" biospecimens are collected for use that is defined at the time of sample submission. Collection of stored specimens is time-sensitive and will be audited during the course of the clinical study. "Banked" biospecimens refers to the use and distribution for future studies not specified at the time of collection. The operation of these banks will be the responsibility of the person so designated by the Group Chair.
4. Each bank will be reviewed and approved by its local Institutional Review Board and on an annual basis will be re-reviewed. The bank will keep records of this review and approval process.
5. Each bank will have a manual of operations detailing the major elements of the bank's operation. This manual must be approved by the Group Chair on an annual basis or more often as appropriate. These elements will include:
 - a. Protection of patient confidentiality: Patient specimens are to be stored in a manner in which direct patient identification is not possible. Specimens will be stored without any direct patient identifiers and only identified by Group patient number and other numbers used by the bank. This regulation does not pertain to specimens during their initial receipt in a bank, or to initial quality control steps to ensure that submitted material is appropriate for banking. However, after such steps these regulations come into force for specimens to be stored.
 - b. The electronic data bases containing laboratory data about patients must not contain patient names and information that can be used to directly identify patients, nor may they be directly linkable to data bases that contain this information. The bank may maintain an electronic data base that contains patient identifiers and sample numbers, but this data base must be separate from the data base with laboratory data, and must be "fire walled", password protected, and with access to only a small number of identified individuals.

- c. Personnel handling the specimens must be adequately educated about and agree to the confidential handling of specimens.
 - d. Specimen security: Specimens are to be stored in a secure limited access area with an appropriate environment for their preservation and with adequate disaster preparedness..
 - e. Specimen accessibility: A plan detailing how specimens can be accessed for use, returned or marked for non-use in an expeditious manner is maintained by the Group Chair's Office. Authorization for specimen distribution will follow a standard operational procedure.
 - f. Quality assurance: A plan detailing how the quality of the material will be assessed when appropriate (e.g., confirming the presence of tumor material within a paraffin block) at receipt of specimen or at distribution of specimen to investigator.
 - g. Specimen handling: A plan detailing how specimens will be handled to minimize degradation, contamination, and specimen wastage.
 - h. System for keeping data on patient samples: This system is to be in a limited access system. It is not to contain information that would allow direct patient contact, patient demographic data or medical information, or patient outcome data. This system is to keep a history tracking individual sample use. It should contain information for estimates of the amount of material in a specimen remaining if such information is available.
 - i. Plan to minimize the possibility of complete exhaustion of materials in specimens that might in the future be relevant to clinical decision making.
 - j. Communication link with the Statistical Center for confirming receipt and quality assurance of biologic materials, and that the SWOG database documents the appropriate level of informed consent for their storage and use. Access to the laboratory and clinical outcomes data will be restricted to the SWOG Statistical Office and the Group Statistician. Only select personnel will have the ability to match the SWOG identification number with clinical endpoints. Results from the analysis of biospecimens shall not be published or presented in any manner that allows identification of any patients. Contractual agreements and understandings on the use of biospecimens will be specified in the SWOG Material Use Agreement (MUA).
 - k. Estimates for recovery of costs associated with processing and shipping requested material for research.
6. Material will not be processed within or removed from the bank without authorization of the Group Chair and the Executive Committee, or the corresponding Intergroup committee when appropriate, except when returned to the patient or their medical designee as detailed by the protocol. When a specimen return is requested, this material should be sent by a route in which the receipt can be documented, and in most instances sent to the site from which the material was received.
7. Requests for authorization to use materials for research will be directed to the Group Chair. The request will be evaluated as follows:
- a. The authorization for materials from Intergroup trials can be obtained by a process involving first the disease specific appropriate Intergroup Translational Medicine Committee. Approval of a concept by this committee is only to be considered final when the investigators enter into a research agreement with the cooperative group coordinating the clinical aspects of the specified clinical trial, according to that cooperative group's standard procedures for data analysis, data confidentiality, authorship, and intellectual property sharing. Materials from any Intergroup trial will not be released by a SWOG bank until that bank receives authorization from the SWOG Operations Office that such an agreement has been reached with the Intergroup Correlative Science

Committee and the group coordinating clinical aspects of the trial. Also required is a verification that the site to receive the materials has appropriate local IRB approval for the proposed study, and that a satisfactory agreement has been reached with the Southwest Oncology Group about the cost of processing and shipping of the samples.

- b. The authorization for materials from studies done solely by SWOG can be obtained by applying for permission for the use of the specimens to SWOG by submission of the SWOG Translational Medicine Research Proposal form. The review of scientific merit will take place weekly during Executive Conference calls, with prior input from the appropriate disease committee chair and translational medicine subcommittee chair. They will review the request then forward to the Group Chair. The translational medicine subcommittee chair will have the responsibility of organizing reviews and communicating on an annual basis in writing to the Group Chair the results of the reviews, and the current status of approved projects.

Formal written proposals will be evaluated by the SWOG Executive Committee on the basis of their clinical and scientific merit. Particular attention will be given to optimizing the translational aspects of these studies by selection whenever possible of Food and Drug Administration (FDA) approved methodologies or methodologies with well standardized reagents, materials that have high potential for translation into clinical use, and scoring or quantitation that is reproducible and accurate.

The proposal must be submitting via the Translational Medicine Request Proposal and Biospecimen Request Form. The text of these proposals is not to exceed five pages in length, but may include appendices with detailed information about methodologies and figures. The proposal must have:

1. A primary objective (hypothesis): Clearly state the hypothesis to be addressed. In general, because of the limited material available, validation studies will give priority over exploratory studies (which without preliminary data may be rejected).
2. Brief justification (including rationale and significance): Detailing the proposals special merit, how it adds to previous studies, and justifying the rationale for the use of bank material rather than materials from other sources.
3. Eligibility: Detailing what characteristics specimens are required to have, and/or what study(ies) specimens are being requested from. Of particular importance is a statement describing the state of the material requested for the studies (number and thickness of sections, etc.).
4. Experimental research techniques/tests employed and expertise of PI: This should include a section of preliminary results and demonstration that the methodologies are well standardized and reproducible. The experimental design should be included with a detailed discussion of methodology to be used. A description of the facilities where the work will be done is also required.
5. Statistical Plan: Statistical section to justify the number of specimens requested and the data analysis plan.
6. Expected timeline of project completion: Must be within 2 years of receipt of specimens.
7. Disclosure of conflict of interest: This should be included for each investigator.
8. A description of the proposed funding sources for the work.

The review and recommendations of proposals will be communicated in writing to the disease committee chair, translational medicine subcommittee chair for that disease

committee, the Operations Office, and to the applicant. Approval of a concept by this committee is only to be considered final when the investigators enter into a Material Use Agreement with SWOG covering data analysis, data confidentiality, authorship, and intellectual property sharing.

Biologic specimens will not be released by a SWOG bank until that bank receives authorization from the Group Chair and the Operations Office that agreements have been reached, that the site to receive the materials has provided documentation that it has appropriate IRB approval for the proposed study, and that a satisfactory agreement has been reached with the SWOG bank about the cost of processing and shipping of the samples. Documentation of the local IRB approval must be provided to the SWOG Operations Office prior to release of materials.

The letter of approval will mandate that no material released to a site for research may be used in any other research other than defined studies that are specifically approved. Distribution or use of biospecimens for unspecified research is not permitted.

This agreement will mandate that any material not used in the approved research will be returned to the bank in a timely manner, unless otherwise specified. Materials may not be held at non-bank sites awaiting analysis for more than 12 months, unless otherwise approved to longer storage outside the bank.

- c. The authorization for materials from Intergroup trials which do not fall under the purview of a disease specific appropriate Intergroup Correlative Science Committee will be evaluated using the mechanism described under the above section 7.2 for SWOG.
8. Materials sent to investigators will be sent with numbered identifiers and stripped of any information that could be used by investigators to identify patients.
9. Communication of research data to patients or to their physicians is explicitly forbidden as this falls outside what has been consented for, and usually these research data are not obtained in a manner authorized for clinical use. This prohibition does not apply to communications necessary for those studies approved within the protocol that are to be used for treatment decisions as specified by the protocol, or for quality assurance dealing with the conditions of the material received by the bank.
10. By January 01 of each year, each bank must send to the Group Chair an inventory reflecting activity during the previous year (by type of specimen and treatment study entered): 1) number of specimens remaining in the bank, 2) number of specimens added to the bank during that year, 3) number of specimens removed from the bank and distribution list 4) a copy of the manual detailing the compliance with the elements stated in this policy, and 5) proof of IRB approval. Banks may be inspected at on-site audits. Additional sub-reporting may be required. Use of the Specimen Tracking System is mandated for centralized database reporting for all biospecimens collected for SWOG studies. Inventory reports, specimen tracking and site compliance reports will be generated from this database.
11. There have been several versions of consent for biological specimen collection. The NCI has developed sample **consent** documents for bank activities which are the standard that SWOG has adopted. This consent will be used in SWOG to consent patients for specimen acquisition and banking for clinical studies. Patients will be allowed to participate without prejudice in treatment protocols without consenting for (refusing) specimen submission for research except in the following instances: 1) when a primary objective of the study is to address a question that requires tissue, 2) when specimen studies are being done to ensure patient safety, and 3) if the specimen is being used to stratify the patients (balance the patient subsets on the basis of known predictive variables). In these instances specimens can be mandatorily required and consented for as part of the consent for treatment, but if this limited consent is obtained the specimen may not be banked or used for other research without additional consent.

For studies where specimens are banked for future unspecified use, the NCI Informed Consent Template Document (<http://ctep.cancer.gov/guidelines/consent.html>) should be used with minor appropriate modification (i.e., substituting the appropriate descriptors for the word specimen); however, it is very important as an ethical and practical matter that there be uniformity in the text of the three check-box areas of consent. Modification of the consent template document must be consistent with SWOG's policies for banking and future sample use. SWOG cannot honor restrictions or limitation except for those originating from SWOG. The following notation is included in the instructions for every SWOG model consent template: "Please particularly note that the questions related to banking of specimens for future study are in bolded type and may not be changed in any way without prior approval from the Southwest Oncology Group Operations Office."