

EDRN Pre/Validation Reference Set Specimen Sharing Guidelines

The approved guidelines for standard specimen reference sets.

(Guidelines approved by the EDRN Steering Committee on September 22, 2005)

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It is the goal of specimen reference sets to promote the aims of the Early Detection Research Network, i.e., testing and implementation of biomarkers useful for the detection of solid malignancies for the purpose of down-staging incident cancers in the population. Much of the biomarker work to date has been performed on convenience samples from cases and controls. Since these samples have been collected in a variety of ways, comparisons have been difficult. Further, cases and controls may not have been selected and matched using appropriate rigor to reduce bias. Finally, since there has not been a common resource with sufficient amounts of sample, comparison or integration of multiple markers has not been feasible. With the creation of shared and common sets of specimens from well characterized and matched cases and controls from specific disease spectra, the EDRN will overcome many of the logistic and design issues in preliminary and advanced biomarker validation. This resource will be accessible to any investigator within or outside of the EDRN based upon a common and transparent set of criteria used to evaluate applications. It is anticipated that results from these studies will be made publicly available.

The Specimen Resource Sharing Committee was created within the EDRN to draft a process through which these specimen reference sets could be accessed. It is the opinion of this committee that no completely common set of criteria could be used to evaluate biomarkers from the disparate cancers encompassed by these sets. Each cancer site has its own particular requirements, barriers, and opportunities for detection. Therefore, the appropriate organ-specific Collaborative Group should handle the detailed scientific evaluation of applications for samples. However, it was also recognized that certain common guidelines and procedures could be developed and implemented without reducing the scientific and programmatic input of the Collaborative Groups. After providing specific details related to the specimen reference set(s) being requested and institutional approval to use these sets, the investigator is then expected to address the following topics as provided on the application form in relation to his/her biomarker and future intentions:

- Clinical Relationship
- Background and Significance
- Preliminary Data & Methods
- Data Analysis Plan
- Collaboration
- Future Plans

If additional review criteria or application queries for any specimen reference set are stipulated by the corresponding Collaborative Group, the appropriate NCI Program Director will provide this additional material to the investigator. In essence, each Collaborative Group will determine the stringencies for granting access to specimen reference sets they have oversight of. These standards should be established by the Collaborative Groups before the set(s) become available. For each review conducted, it is expected that every Collaborative Group will include an adequate biostatistical critique, either from within a participating laboratory of the Collaborative Group, or by involvement of the DMCC, to ensure that appropriate consideration is given to statistical concerns of the proposal.

Upon receiving an inquiry or request regarding access to specimen reference set(s) the appropriate NCI Program Director will be notified to send an application form and any other relevant documents to the investigator. After the completed application has been returned, the Program Director will then forward it to

the respective Collaborative Group. The Collaborative Group, in a timely manner (within one month) will review and discuss the application and offer a recommendation of whether 1) the investigator should be sent the requested specimen reference set(s), 2) further clarification or revision are needed, or 3) the request is deemed to be of low priority and deferred or denied.

1. If approval is given, the EDRN Executive Committee will be notified at its next monthly meeting by the Collaborative Group chair (or co-chair). If extenuating circumstances require a more timely response, the Executive Committee will be notified by email of this decision and the Committee must respond to the Collaborative Group chair within 48 hours if they have any concerns. As the Executive Committee provides oversight for global EDRN activities, it needs to be informed of requests for specimen reference sets that have been received and reviewed within EDRN. In principle, the Executive Committee will concur with all approvals recommended by Collaborative Groups unless special issues are raised. NCI Program Staff will then notify the facility in Frederick to prepare the materials needed for sending the appropriate specimen reference set(s).
2. If further clarification is needed, the Collaborative Group will inform the Program Director of what concerns or questions remain with the application. The Program Director will then communicate with the investigator of these issues to ask for a resubmission.
3. If deferral or denial is made, the Collaborative Group will provide the rationale to the Program Director why the request was turned down. The Program Director will then relay this decision and its reasons to the investigator.