

Early Detection Research Network

Manual of Operations

Version 4.0

Revision History

Version	Date	Change
1	01-11-01	Created Sections 1, 2, 3, 4, 5, 6 and Appendices I, II, III
1.1	07-19-01	Created Appendix IV
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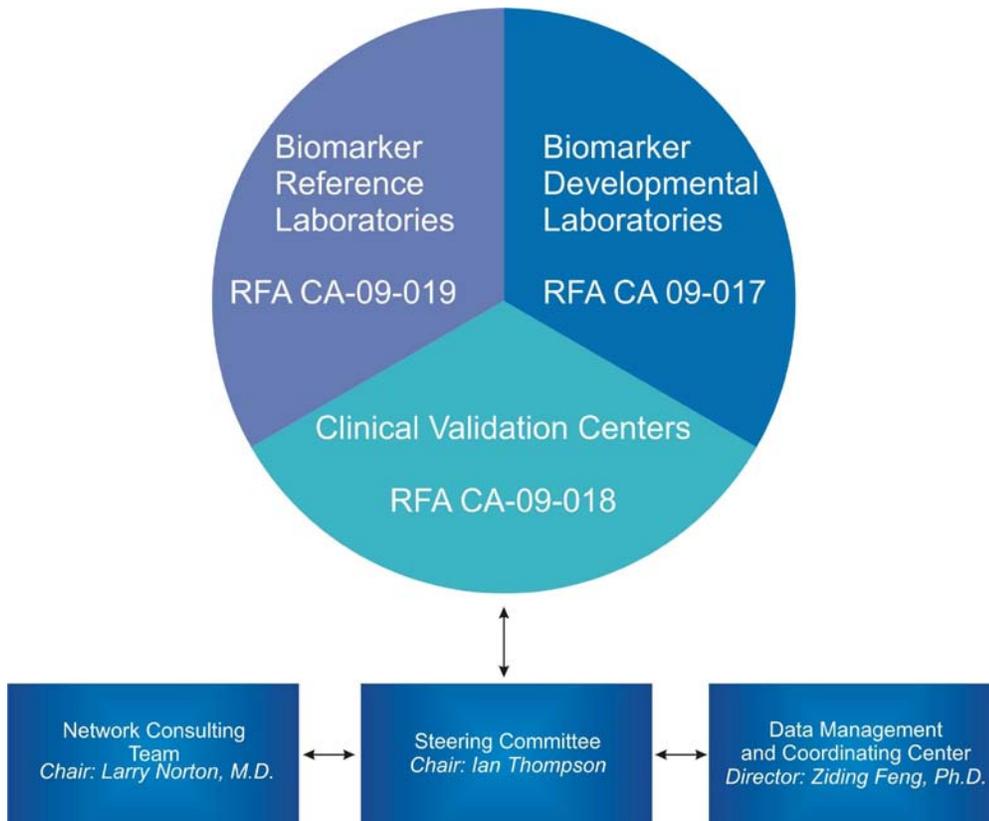
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SECTION 1 ORGANIZATION AND DEVELOPMENT

The Division of Cancer Prevention in the National Cancer Institute created the Early Detection Research Network (EDRN) to support investigator-initiated, collaborative research on molecular, genetic and other biomarkers for cancer detection, risk assessment, prognosis and diagnosis. A number of programmatic review groups at NCI recommended that the EDRN be created and continued.



Funded separately through peer-reviewed Cooperative Agreements, the EDRN has four components:

- Biomarker Developmental Laboratories (BDLs): The BDLs are responsible for the development and characterization of new or refinement of existing biomarkers. BDLs may be multi-PI.
- Biomarker Reference Laboratories (BRLs): The BRLs serve as a Network resource for clinical and laboratory validation of biomarkers that include technological development, refinement and quality control. BRLs are expected to work with EDRN BDLs and CVCs.
- Clinical Validation Centers (CVCs):. The CVCs conduct clinical research on the validation of biomarkers and participate in Network-wide clinical validation of biomarkers.

- **Data Management and Coordinating Center (DMCC):** The DMCC supports statistical and computational analysis and informatics infrastructure, coordinates network-wide meetings and conferences and serves as the Coordinating Center for validation studies.

The network is governed by the Steering Committee, consisting of the Principal Investigators of the EDRN and NCI staff. The Network also has a Network Consulting Team composed of non-EDRN investigators appointed by EDRN Steering Committee to review the progress of the Network and to recommend new research opportunities.

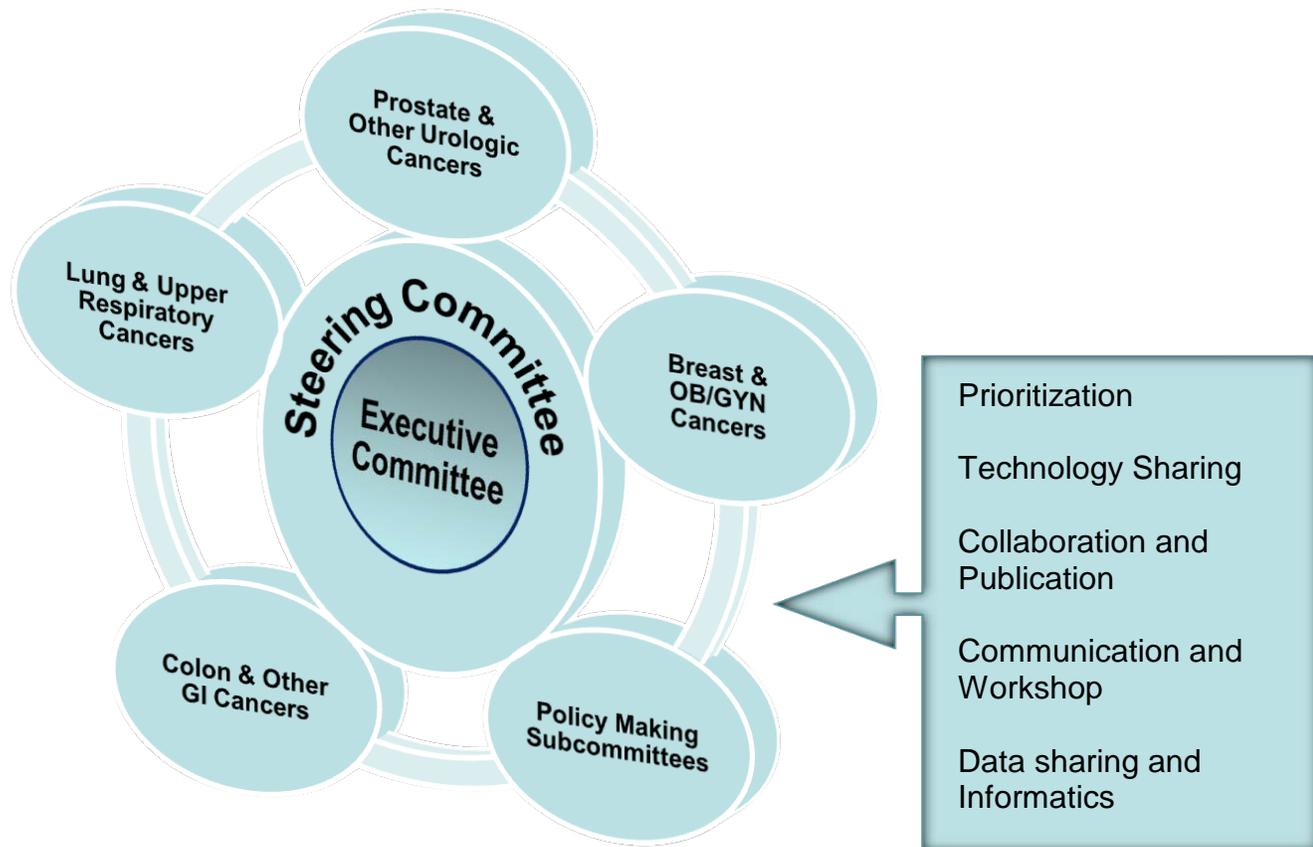
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These procedures provide guidance for the administrative and operational activities of the EDRN and may be modified or revised by approval of the Steering Committee as experience and need dictates. Any member in good standing (i.e., a member who attends at least one Steering Committee meeting per year) may propose amendments to the EDRN Manual of Operations.

1.1 Statement of Objectives

- To support and facilitate a broad spectrum of research activities that address early development and initial validation stages of molecular biology and genetics, including biomarkers that can be applied in cancer risk prediction, early detection, primary prevention of cancer and diagnosis.
- To coordinate national and international research programs for the development of clinically useful biomarkers in preneoplastic lesions that accurately predict the risk of invasive cancer or the presence of early cancer in asymptomatic individuals not previously diagnosed with the disease.
- To support the development of databases on the utility of biomarkers and expression patterns that will serve as background information for larger validation and efficacy studies.
- To promote collaboration and communication with other programs at the NCI, other Institutes within NIH, organizations with the National Cancer Program, and academic and industrial leaders from relevant disciplines.

SECTION 2 COMMITTEES



2.1 Steering Committee

2.1.1. Overview

The Steering Committee (SC) has major scientific management oversight and responsibility for developing and implementing a collaborative Network research program including protocols, publications, and design. The Committee consists of a Chair, Co-Chair, the EDRN Principal Investigators or a designee, and the NCI Program Coordinator or a designee. A Principal Investigator cannot designate an Associate Member to replace him/her at an SC meeting. Members of the SC review all data collected in Network studies, monitor study results, follow-up, and report to the full SC upon request of the Chair. Each member has one vote.

According to the requirements of the Cooperative Agreement, there are 2 SC business meetings per year and one scientific workshop each 18 months that EDRN members should attend; additional meetings may be called as needed. The time and site for these meetings are determined by SC members. The Principal Investigator(s) from each Cooperative Agreement are required to attend at least one SC meeting each year. However, there must be at least one representative from each Cooperative Agreement, at every SC meeting. The minutes of the SC meetings are prepared by the

DMCC as a matter of record and distributed to the members of the SC for approval at the next meeting. NCI reserves the right to terminate a grant for failure to attend or have representation at SC meetings.

The PIs of a U01/U24 will serve as a voting members of the Steering Committee and will attend the Orientation meeting and two Steering Committee meetings in the first year and in subsequent years attend two Steering Committee meetings and an EDRN-Sponsored Gordon Conference or an EDRN-sponsored workshop every 18 months. The attendance of PI(s) at these meetings is considered an essential part of the grant.

Applicants must budget for travel and per diem expenses for SC meetings. In the first year, applicants should plan for two investigators, the principal investigator and an additional senior investigator, to attend a Planning Meeting and two SC meetings. In the second and subsequent years, applicants should plan for the PI and another investigator to attend two SC meetings and one workshop every 18 months.

The EDRN Steering Committee is comprised of EDRN Principal Investigators and NCI Program Coordinator. Exceptions to this membership can be brought to the Steering Committee for approval. Such exceptions may include the nomination of PI, funded by the NCI through another peer-review mechanism, for which the NCI has determined his/her inclusion to be of significant EDRN programmatic interest.

2.1.2. Responsibilities and Privileges

- Develop guidelines for operating the EDRN
- Coordinate the research program within the EDRN
- Develop criteria for reviewing progress of the EDRN
- Establish and track milestones
- Develop and implement rules for sharing data and resources
- Disseminate information on the availability of resources (tissues, new technologies, and patients) within the EDRN
- Develop criteria for selecting an Associate Member of the EDRN
- Develop criteria on the use of the Core Funds
- Develop and approve protocols for clinical research through the EDRN
- Develop criteria on evaluating and reviewing data on potentially promising new biomarkers
- Prepare annual Progress Reports for submission to NCI at the end of each fiscal year

2.1.3. Chair

The Chair and Co-Chair are elected by the full SC. Any member of the SC can offer nominations for the Chair and Co-Chair. The term of office for the Chair is five years with eligibility for re-election for one additional term (for a total of 10 yrs). The term of office for the Co-Chair is 2.5 years with eligibility for re-election for one additional term (for a total of 5 yrs). The Chair makes all appointments in consultation with the SC.

2.1.4. Duties of the Chair

- Preside at all meetings of the full SC
- Appoint and re-appoint members of Subcommittees, Review Groups, and designate special assignments
- Appoint the Chairs and Co-Chairs of Subcommittees, Review Groups, and Collaborative Groups
- Appoint ad-hoc committees as needed
- Invite consultants as needed to Subcommittees, etc.
- Appoint EDRN liaison members to other organizations
- Serve as a Co-Chair of the Executive Committee
- Serves as an ex-officio member of all Subcommittees, ad hoc Committees, and Task Forces
- Submit annual EDRN Progress Reports to NCI and the Network Consulting Committee

- Prepare the agenda for the SC meetings

2.1.5. Duties of the Co-Chair

- Serve as acting Chair during absence of the Chair
- Serve as chair of the Executive Committee

2.1.6. Quorum

For holding meetings, including conference calls, a quorum is defined as the presence of the majority of SC members. If a quorum is not present, the meeting will be cancelled.

2.2 Executive Committee

2.2.1. Overview

The Executive Committee (EC) consists of a Chair, Chair of the SC, Chairs of Collaborative Groups, at least one Principal Investigator from a BDL, BRL, CVC, and DMCC (if not represented in the Collaborative Group Chairs), and the NCI Program Coordinator or a designee. The Committee is chaired by the Co-chair of the SC. The term of office for the Chair is 2.5 years with eligibility for re-election for one additional term (for a total of 5 yrs). The EC meets as necessary to conduct the business of the EDRN, typically once a month on a conference call, or at the discretion of the Chair of the EC or SC. The minutes of the EC are prepared by the DMCC as a matter of record and distributed to the members of the EC for approval at the next meeting.

The Committee expedites the work of the SC and assists the Chair of the SC. It coordinates the administrative and research activities of the EDRN on a regular basis and provides a mechanism for communication on the management of the EDRN. The Committee makes recommendations on major policy issues to the SC.

2.2.2. Responsibilities and Privileges

- Facilitate the work of the SC and assist the Chair of the SC
- Coordinate the administrative and research activities of the EDRN on a regular basis and serve as a forum for communication on the management of EDRN
- Conduct routine business to consider distribution of funds and to review and recommend for approval all research proposals submitted to the SC
- Approve Associate Members
- Recommend the release of Restricted and Core Funds to NCI
- Act for the SC on administrative and scientific matters between the semiannual SC meetings
- Oversee responsibilities of the Collaborative Groups

2.2.3. Duties of the Chair

- Serve as Co-Chair of the SC
- Preside over meetings of the EC
- Prepare the agenda for EC meetings

2.2.4. Duties of the Co-Chair

- Serve as acting Chair during absence of the Chair
- Serve as chair of the Steering Committee

2.2.5. Quorum

For holding meetings, including conference calls, a quorum is defined as the presence of the majority of EC members. If a quorum is not present, the meeting or conference call will be cancelled.

2.3 Network Consulting Team

2.3.1. Overview

The Network Consulting Team (NCT) an ad-hoc group of extramural scientists, is independent of the programmatic oversight provided by the NCI who are appointed by the Director of the Division of Cancer Prevention, NCI. The NCT is a non-voting committee, composed of non-federal scientists, clinicians, patient advocates, and ethicists who are devoid of financial and/or collaborative affiliation with EDRN where a conflict of interest exists or may be apparent. At the recommendation of the Chair, EDRN SC ,ad-hoc consultants may be recommended to serve on the NCT. Ad hoc consultants may be called upon for consultation in areas where specific expertise is needed yet lacking in the NCT. Ad hoc consultants may be federal or non-federal scientists, clinicians, patient advocates, and ethicists.

2.3.2. Responsibilities and Privileges

The primary role of the NCT is to assist the EDRN in evaluating the overall Network concept. The NCT will assist in the evaluation and operation of the EDRN by:

- Exchanging facts, materials, or information pertaining to the review of progress and planning of research within the EDRN
- Providing non-binding advice of individual members (not consensus advice or consensus recommendations) to the EDRN SC or EC, when appropriate
- Reviewing the progress of the EDRN, which may include a member's participation in site visits
- Considering new research initiatives to ensure the EDRN is responsive to promising opportunities in early cancer detection research and risk assessment

- Serving as members on ad-hoc committees of the EDRN, including Review Groups, Working Groups and Collaborative Groups, and as Consultants to Subcommittees
- Assisting the EDRN SC in planning and organizing workshops and symposia
- Participating in EDRN workshops and symposia
- Serving as a liaison between the cancer research community and the EDRN
- Meeting with NCI and EDRN leadership at the request of the Chair, NCT, NCI, or Chair, EDRN SC

2.3.3. Chair

Appointed by the Director of the Division of Cancer Prevention, NCI for an initial 5-year term and is renewable for an additional 5-year term.

2.3.4. Duties of the Chair

- Presides over all meetings of the full NCT
- Serves as liaison with the NCI Program Coordinator or designee and the Director of the Division of Cancer Prevention, NCI

SECTION 3 SUBCOMMITTEES

3.1 Overview

Subcommittees are the policy-making Working Groups of the EDRN and report to the SC when requested by the Chair. Subcommittees meet twice a year in conjunction with the SC business meetings. Conference calls are made any time on the recommendation of the Chair of either the SC or Subcommittees. Formal meetings between the semiannual meetings require approval by the Chair of the SC.

Voting members of the Subcommittees are Principal Investigators in the EDRN. Co-investigators, Associate Members, and other interested parties, however, are welcome to attend Subcommittee meetings as consultants. The Chair of the SC appoints members to the Subcommittees although SC members can express their preferences on which Subcommittee they would like to serve. Members cannot serve on more than one Subcommittee simultaneously. Members are appointed for 2.5 years and can be re-appointed for a second, 2.5 year term. Each Subcommittee member has one vote. Consultants for Subcommittees can be appointed by the Chair of the SC or by the Chairs of the Subcommittees as non-voting members.

3.1.1. Chairs

The Subcommittee Chairs and Co-Chairs are appointed by the Chair of the SC and must be EDRN Principal Investigators. Term of office is 2.5 years with eligibility for reappointment for one additional consecutive term (for a total of 5 yrs). It is the duty of the Subcommittee Chairs to determine whether a quorum is present before opening the meeting. The Chair has the responsibility to prepare the agenda and to report to the Steering Committee.

3.1.2. Quorum

A quorum for all Subcommittee meetings, including conference calls, is defined as the presence of the majority of the voting Subcommittee members. If a quorum is not present, the meeting or conference call will be cancelled.

3.2 Collaboration and Publication Subcommittee

3.2.1. Objective

The objective of the Collaboration and Publication Subcommittee is to define procedures and conditions for formal collaboration within the EDRN and with investigators outside the Network, and defines publication policies.

3.2.2. Responsibilities and Privileges

- Develop procedures for formal research collaboration within and outside the EDRN, including collaboration with individual investigators, industry, academic centers, community hospitals, government agencies, international investigators, and Cooperative Groups
- Determine collaborative relation with private industry, especially with regard to IP issues
- Develop procedures for collaborating with other NCI Programs, such as SPORE, CGAP and the Cancer Family Registries
- Determine the role of the SC in monitoring collaborative research within and outside EDRN
- Develop guidelines for order of authors, standard credits, statement for source of support, and common formats for the publication of EDRN research
- Assist in developing common EDRN materials needed for obtaining approval for EDRN studies from Institutional Review Boards

3.3 Technology and Resource Sharing Subcommittee

3.3.1. Objective

The objective of the Technology and Resource Sharing Subcommittee is to establish the rationale and conditions for sharing technology and other resources among investigators within and external to the EDRN.

3.3.2. Responsibilities and Privileges

- Develop guidelines for sharing novel technology, reagents, and resources within the EDRN
- Develop guidelines for external Network sharing
- Develop guidelines and responsibilities for considering IP issues

3.4 Communication and Workshop Subcommittee

3.4.1. Objective

The objective of the Communication and Workshop Subcommittee is to achieve the full potential of biomarkers as tools to facilitate early detection of cancer by disseminating research goals and findings with the broader research community. To accomplish this objective, the Communication and Workshop Subcommittee defines formats for exchange of scientific findings such as workshops, seminars, and electronic information resources that serve to inform the research communities of scientific advances.

3.4.2. Responsibilities and Privileges

- Organize workshops to inform other components of the research community of the opportunities and needs to implement biomarkers in clinical screening, clinical trials, and early detection, etc.
- Develop long-term strategies that facilitate the translation of research advances into screening and detection practices
- Identify mechanisms to extend biomarker research to enable commercial development of diagnostic tools through public-private partnerships or collaborations
- Interact with organizations that facilitate the use of biomarkers in the clinical arena and discuss the long-term implications of biomarkers as screening and detection tools in population health
- Identify key audiences to engage/inform about EDRN research activities, goals, etc.
- Communicate with oncology groups, cancer research societies, immunology, biochemistry, pathology groups, epidemiology and biostatistical communities, biotechnology/bioengineering developers; technology transfer offices, voluntary health organizations, public health organizations, managers of health care, and regulatory agencies, etc.
- Organize workshops to inform other components of the research community of the opportunities and needs to implement biomarkers in clinical screening, clinical trials, and early detection, etc.
- Develop other communication mechanisms to facilitate information dissemination (e.g., electronic media (websites, listservs) for communication among centers, data registries, newsletters, supplements to journals).
- Oversee liaisons

3.5 Prioritization Subcommittee

3.5.1. Objective

The objective of the Prioritization Subcommittee is to establish procedures for prioritizing research and allocating resources within the Network.

3.5.2. Responsibilities and Privileges

- Define the decision criteria needed for the evaluation of biomarkers beyond the discovery stage and set up a review process for implementing them in the EDRN
- Develop guidelines for coordinating the prioritized projects across the Network including obtaining involvement of the NCT
- Establish guidelines for utilization of the Core Funds and allocation of research resources
- Ensure integration of various components of the EDRN with the NCI Bypass Budget

- Develop metrics for evaluating the progress (success) of EDRN. Establish annual and overall milestones for EDRN that will be used for evaluating Network progress and reporting to the NCT, NCI Executive Committee, NCI Board of Scientific Advisors, and National Cancer Advisory Board

3.6 Data Sharing and Informatics Subcommittee

3.6.1. Objective

The objectives of the Data Sharing and Informatics Subcommittee are to establish guidelines for the EDRN data structure and common data elements, and to provide a forum for biostatisticians/analysts within EDRN to collaborate on research pertinent to EDRN.

3.6.2. Responsibilities and Privileges

- Develop EDRN Informatics Enterprise System compatible with NCI Informatics Enterprise and NCI standards (caBIG and CTEP systems)
- Develop guidelines for security levels of the centralized database
- Develop guidelines for internal and external data sharing that include mechanisms to ensure that the data are used appropriately
- Develop guidelines for statistical design and evaluation of biomarkers
- Monitor the quality of biomarker data captured and curated in biomarker database
- Develop guidelines for posting materials on the secure website
- Review patient privacy requirements for EDRN in conjunction with the relevant Subcommittee
- Develop methods to promote data sharing with NCI programs such as CGAP, CGN, SEER, etc.

SECTION 4 GROUPS

4.1 Standing Review Group

The Standing Review Group is responsible for reviewing Associate Membership applications. Members are nominated by the Chairs of the Collaborative Groups and/or NCI Program and appointed by the Chair of the SC. The Group consists of two Principal investigators from each of the Collaborative Groups (one Principal Investigator from a BDL and one Principal Investigator from a CVC), one Principal Investigator from a BRL, the Principal Investigator or designee from the DMCC, and one representative of the NCI Program. Additional EDRN and non-EDRN consultants can be added at the discretion of the EC. Details on the application and review processes are under the 'Policies and Procedures' section of this manual. Term of office is 2.5 years with eligibility for reappointment for one additional term (for a total of 5 yrs).

4.2 Working Groups

Working Groups shall be created for specific, finite projects as deemed needed by the SC or EC. Members of Working Groups are volunteers and appointees from the EDRN membership. Examples of Working Groups include:

- Proteomics Interest Working Group
- Genomics Interest Working Group
- ERNE Working Group
- IRB Working Group
- Imaging Interest Working Group

SECTION 5 ACTIVITIES TO PROMOTE COLLABORATION

5.1 Collaborative Groups

Collaborative Groups are organ-specific groups designed to promote the exchange of information on organ related biomarkers and identify research priorities within EDRN. Members of the Collaborative Groups are the members of the SC, their co-investigators, Associate Members, and other interested parties. Members are encouraged to participate on the Collaborative Group that best reflects the expertise presented in their original peer-reviewed application. Members cannot serve on more than one Collaborative Group simultaneously. There are four Collaborative Groups: Breast/Gynecology, Prostate and Urologic, Lung and Upper Aerodigestive Tract, and G.I. and Other Associated Cancers.

5.1.1. Responsibilities and Privileges

- Conduct routine literature reviews
- Write manuscripts describing the current state of biomarker development
- Review pre-proposals for EDRN Validation Studies
- Create opportunities for collaboration within each organ-based groups
- Provide leadership for identifying the most promising biomarkers

5.1.2. Chairs

The Collaborative Group Chairs and Co-Chairs are appointed by the Chair of the SC and must be EDRN Principal Investigators. Term of office is 2.5 years with eligibility for reappointment for one additional term (for a total of 5 yrs). It is the duty of the Collaborative Group Chairs to determine whether a quorum is present before opening the meeting. The Chair has the responsibility to prepare the agenda and to report to the Steering Committee. Former Chairs are ex officio members.

5.1.3. Quorum

A quorum for all Collaborative Group meetings, including conference calls, is defined as the presence of the majority of members. If a quorum is not present, the meeting or conference call will be cancelled.

5.2 Liaison Members

The purpose of liaison members is to ensure that members of key scientific organizations are aware of EDRN activities and to ensure that EDRN members are aware of activities of outside organizations that may impact EDRN. Liaison members to scientific and professional organizations, including scientific programs at NCI, are appointed by the Chair of the SC. Liaisons are appointed to 2.5 year terms with eligibility for reappointment for another two-year term. Liaison members report to the SC on activities by other organizations that are relevant to the EDRN during the semiannual SC meetings.

5.3 Sponsor

- Act as spokesperson for the Associate Membership
- Keep track of members progress
- Shares significant progress with SC and EC when called for
- Participate in evaluating the progress at the end of the grant period

SECTION 6 POLICIES AND PROCEDURES

6.1 Associate Membership

The Associate Membership is designed for investigators who are not affiliated with EDRN and wish to propose collaborative studies within the scope and objectives of the EDRN. There are three categories for Associate Membership. Associate Members are welcome to join a Collaborative Group on the basis of their expertise and interest.

Category A Members are domestic or foreign investigators who propose to conduct basic or translational research consistent with the priorities of the EDRN. Supplemental funds provided through Category A Membership are to be used as one-time "seed money" for pilot studies necessary to support applications for future independent funding. Funds are provided for a period of two years and are not renewable. Although support of Category A Members ceases after two years, they are considered to be Associate Members for the duration of the EDRN. Category A Associate Members are invited to participate in Workshops and Steering Committee meetings. The "seed money" will be \$50,000 direct costs per year for two years with additional "Facilities and Administrative" costs (F&A costs). The applicants must include in the budget funds to attend two EDRN SC meetings per year.

Category B Members contribute to the Network by sharing available technologies, contributing specimens, making available high-risk registries and cohorts, and providing other resources complementary to the Network and in conjunction with biomarker validation studies. They can be domestic or foreign. Category B Members can reapply for project-specific funds annually (total funding amount should not exceed \$100,000 in direct costs with additional "F&A costs", unless the Network needs as determined by the EC justify additional funding). Category B Members are considered Associate Members after funding ceases for the duration of the EDRN. Category B Associate Members are invited to participate in Workshops and Steering Committee meetings. Any clinical or laboratory site (other than current BDLs, BRLs and CVCs) participating in a validation study are considered Category B Members.

Category C, Corresponding Members, are scientists, organizations, clinicians, patient advocates, or ethicists who are interested in participating in Collaborative Group meetings and EDRN Workshops and Conferences yet do not receive funds from the EDRN. Category C Members will be invited to these meetings and conferences, but their expenses will not be supported by the EDRN. Category C members can be domestic or foreign. The application for Category C Members is the similar to that of other Associate Member applicants, with minor modifications: the budgetary document can be disregarded, and the proposal in the form of a letter addressed to the EDRN EC should explain how the applicant's participation at the meetings, workshops and other Network activities will contribute to the mission of EDRN. Category C Members are considered Corresponding Members for the duration of the EDRN. EDRN Members for which funding has ceased are considered Category C Members for the duration of the EDRN.

To apply for an Associate Membership, applicants must be sponsored by an EDRN Principal Investigator. For details on the application procedure please see the EDRN website: <http://edrn.nci.nih.gov/>.

NIH policies (<http://deainfo.nci.nih.gov>) are observed for accepting revised applications. The number of amended (revised) versions of an application is limited to one, and this must be submitted within two years of the original submission. The Introduction must also include responses to the main criticisms and issues raised by the reviewers.

The Standing Review Group's comments should be included in the revised application packet. The application must include an Introduction of not more than 1 page that summarizes substantial additions, deletions, and changes. The Introduction must also include responses to the criticisms and issues raised by the reviewers.

Associate Members will agree to follow EDRN policies and procedures and include a copy of their annual progress report to their Sponsor and NCI.

6.1.1. Responsibilities of the Sponsor

Sponsors of Associate Members are responsible for submitting the initial membership application, representing their interests in SC meetings, and inviting them to EDRN meetings.

Sponsors are responsible for ensuring that their Associate Member is accountable, follows all EDRN policies and procedures, and, if requested, provide an update on their Associate Member's progress.

6.2 Funds

6.2.1. Definitions

There are two sources of funds available through EDRN: Restricted Funds and Steering Committee Core Funds.

Restricted Funds are funds that are set aside from the annual budget of BDLs, BRLs, DMCC and CVCs for Collaborative Studies.

- After the first year investigators from BDLs and CVCs must set aside 20% of their annual budget for Network Collaborative Studies.
- Investigators from BRLs must set aside up to \$150,000 per year (the exact amount is specified in the Notice of Grant Award) for collaborative studies. Collaborative studies must be submitted as part of a team of BRL or with at least one other component of EDRN (BDL and/or CVC). Funding for multiple years will be allowed subject to annual approval and the completion of the interim milestones approved for the project. The use of set-aside funds will be restricted to collaborative projects relevant to the Network's objectives, and must be reviewed and approved by the EDRN EC and the NCI. Investigators from BRLs must also set aside up to \$100,000 (the exact amount is specified in the Notice of Grant Award) for individual Developmental Studies. Applicants must submit a research proposal for a developmental study for one or multiple years as part of their application. In case that a one-year developmental project is submitted with this application, developmental

studies proposed in future years will be reviewed and approved by the EDRN EC and NCI.

- Investigators from BDLs and CVCs must set aside 20% of their annual budget after the first year for Network collaborative studies. The reimbursement will be based on the complexity and amount of clinical data, specimen types, duration of follow-up, and other factors within collaborative studies as decided by the Executive Committee.
- The DMCC must set aside 30% of its funds for Validation Studies.

Applicants for the release of Restricted Funds must include their specific plans for responding to the terms and conditions section of their grant award notice. The use of these set aside funds is restricted and must be reviewed and approved by the EDRN EC and then recommended to, and approved by the NCI before release from the individual U01 or U24 awards.

Steering Committee Core Funds are reserved for post-award collaborative Network research and for expanding participation within the Consortium. These funds can also be used to assist in moving a marker through the validation process. Examples of validation funding needs include accrual of patients, scaling-up of reagents, contracting to other laboratories or companies to scale-up production and maintain the quality of reagents. Funds can also be used for data management, travel, meetings, and other collaborative activities of the Network.

6.2.2. Release and Use of Restricted Funds

A Principal Investigator may only apply for the Restricted Funds within his/her Cooperative Agreement award. Restricted Funds may only be used for projects that complement the scope of the Cooperative Agreement award and/or support an approved EDRN Validation Study. More than one investigator may request the release of Restricted Funds for one collaborative project. A Principal Investigator may apply for more than one year's Restricted Funds, however, a status report must be submitted to NCI and should specifically detail how the Restricted Funds were used before subsequent year funds are considered for release. The status report may be submitted as part of the annual progress report submitted by the Principal Investigator. The applications for the release of Restricted Funds are reviewed by the EC at their monthly meetings. Applicants must apply for renewal within 90 days of their anniversary date of their Type 5 application. Validation Study applications for release of set aside funds are considered priority over other requests.

6.2.3. Application Requirements for Release of Restricted Funds

The application for release of Restricted Funds includes the EDRN Study Proposal Application Form and a proposal. The proposal must be single-spaced and follow NIH Format, as used in PHS Form 398. It should be organized and submitted as follows:

1. Title Page (page 1 of the PHS Form 398). Description (Abstract), Performance Sites, and Key Personnel (use page 2 of the PHS Form 398). Bibliography of key researchers involved (use page 6 of PHS Form 398).
2. Scientific Proposal and References (up to 5 pages), organized into Rationale, Goals, Sample Size, Preliminary Data (optional), Technologic Design and Approaches,

Contribution to Translational Research, and EDRN Specific Aims/Deliverables. Address review criteria as established by the EDRN Steering Committee (see Review Criteria section below).

3. Budget Page - (final page unless an Appendix section is included). Use page 4 of the PHS Form 398. Adequate budget justification for direct costs is required.
4. Appendix (optional).
5. Ten paper copies and one electronic copy of the proposal should be submitted to the NCI EDRN Program Office.

All projects must comply with institutional regulations on research involving human subjects, children, minority groups, gender, animals, recombinant DNA, and hazardous materials. Appropriate approvals from the relevant committees, including approval from institutional review boards, must be submitted to the NCI EDRN Program Office before funds can be provided for successful applications.

6.2.4. Application Requirements for Release of Developmental Funds

Applicants should clearly define the research objective for the first year, which will be peer-reviewed by the scientific review committee. Support for subsequent years will be reviewed by the EDRN SC, which will make recommendations to the NCI. Prior to proposing the developmental study, applicants are encouraged to contact the program officials listed on this RFA to discuss the needs of EDRN in the area of technology and assay refinement.

6.2.5. Review Criteria

Definition: Set-asides funds are restricted funds that are awarded to an individual grant. The primary purpose of the set-aside fund (see RFA CA-09-017, CA-09-018) is to promote the laboratory/center participation in the Network-wide Validation Studies. In absence of such a study, the funds are considered for inter-EDRN or external collaborative studies. An intra-EDRN study is of higher priority. The proposed project should capitalize and leverage on the EDRN-established infrastructure and resources. Two major criteria must be met before recommending the release of restricted funds: scientific significance and collaborative strengths.

Review criteria for release of Restricted Funds or Core Funds for Associate Membership category A or B are based on scientific merit and compatibility with EDRN objectives.(see Appendix 3 and 4) Seven formal criteria are used to assess the suitability of proposals for supplemental support and/or advancement to the large-scale validation phase:

- Scientific merit
- Study design: e.g., prospective versus cross-sectional
- Technical parameters: reproducibility, sensitivity, specificity, throughput, automation, and cost
- Clinical or scientific impact: e.g., more common cancers or a significant impact in less common neoplasia

- Portfolio balance within EDRN and NCI's need
- Practicality and feasibility: e.g., required sample size, amount of tissue
- Collaborative strength, including contribution of resources and technology. Collaboration is a central mission of EDRN.

A project does not have to be strong in all review categories to be considered highly meritorious. For example, a methodology or infrastructure-related application may not be judged to be at a high level of scientific merit yet may be a critical component in an overall plan to achieve EDRN goals and may represent a high level of cooperation and interaction among investigators toward EDRN objectives.

Additional Information on Review Criteria

Significance:

The application must clearly state the scientific merit of the proposal.

Does the proposed research convey the urgency of scientific needs in the area of biomarker-based diagnostics possible only through a collaborative approach?

Will the approaches advance the field of biomarkers/reagents development in the context of cancer detection and risk assessment?

Does the proposal uniquely discuss challenges and issues relevant to cancer detection and screening?

Does the project develop or employ novel concepts, approaches, methodologies, tools, or technologies for this area?

How would the proposed research complement or augment existing detection systems or methodologies?

Is the proposed approach or technology adaptable, or does it have the potential to analyze large samples in a population setting for screening purposes?

What is the immediacy of the research opportunity in light of the EDRN-established phases of biomarker development for early detection of cancer and potentials for moving biomarkers to Phase II or Phase III?

Does the applicant have demonstrable evidence for bringing biomarkers to Phase II or Phase III? This is particularly important for an analytical validation study.

To what extent are the specific aims integrated to address the proposed goals?

Collaborative Strengths:

The application must clearly state the need for such a collaboration and reason as to why this study requires collaborative platforms (expertise, infrastructure, resources) of the EDRN.

Are plans for collaborations provided for research objectives?

To what extent are these collaborations necessary for the successful completion of the research plan? Only projects of collaborative nature are to be supported through the restricted funds.

Do the proposed experiments take advantage of unique features of the EDRN scientific environment and incorporate the best use of collaborative arrangements?

Will this team of investigators contribute unique skills to the proposed project?

Do the investigators state their willingness to collaborate and share information?

Are there adequate plans for effective interaction and coordination with the Network components, such as the SC, the DMCC, or the NCI?

In case of genomic and proteomic profile studies, investigator will be required to post data on the EDRN Secure Portal.

Portfolio Analysis: (for program review only)

NCI program staff will evaluate each application relative to other research projects being conducted within EDRN to ensure there is a fair representation of technologies and cancer types. Under or over representations will be included in determining the final recommendation. In addition, proposal will be reviewed for:

Does the proposal compete against any already funded approach within the EDRN systems? If so, what is the added value?

Does the proposal fall under the NCI's Strategic Initiatives? To what extent is it supported by any other program, such as IMAT?

Budget:

The applicant's budget must be justified in light of the scope of the work and must not exceed the set-aside [Program is to keep track of this amount]. The reviewers may recommend a budget less than the set-aside.

6.2.6. Application Requirements for Use of Core Funds

Requests for Core Funds can be made by EDRN investigators to conduct collaborative projects involving and focusing on EDRN objectives, to advance current projects toward validation, or to conduct a Validation Study. Budgets must not exceed \$100,000 unless sufficient justification is provided, or for an approved large validation study. Adequate budgetary information should be provided to justify proposed spending. Applications for Core Funds are accepted the first week of each month and are reviewed during monthly EC calls held the last week of the month.

EDRN investigators applying for funds to conduct collaborative projects must complete both the EDRN Study Proposal Application Form and a proposal following the format of PHS Form 398 as

described in Section 6.2.3. Applicants for Associate Membership need only submit a proposal following the format of PHS Form 398 (see Section 6.2.3). All projects must comply with institutional regulations on research involving human subjects, children, minority groups, gender, animals, recombinant DNA, and hazardous materials. Appropriate approvals from the relevant committees, including approval from Institutional Review Boards, must be submitted to the NCI EDRN Program Office before funds can be provided.

6.2.7. Review Process for Type A and Type C Associate Membership Applications

The EDRN Standing Review Group will review all Type A Associate Membership applications. The EDRN EC will perform an accelerated review of applications for Associate Membership (Category C) that do not seek funds from EDRN. The specific criteria used to evaluate proposals for use of Core Funds are listed in the section above, Section 6.2.4. The review process is described below:

1. Ten copies of Associate Member applications received by the receipt date are forwarded from the NCI EDRN Program Office to the members of the EDRN Review Group within a week after the application receipt date.
2. The EDRN Standing Review Group evaluates Associate Member applications in a telephone conference call, and then scores the applications via a secure online review process on the EDRN secure website. The NCI EDRN Program Director is able to read all reviewers' comments and consolidates them. The evaluation and compilation of comments is expected to be completed within one month following the application receipt date. After compilation of comments, the EC members are notified that consolidated comments and scores are ready for their review.
3. The Executive Committee renders final approval of the reviewed proposals, informs the Steering Committee of successful applications, and submits the recommendations to the NCI EDRN Program Office.
4. The EDRN Chair's institution contacts NCI Grants Administration Branch by letter, requesting approval to release the restricted funds. Once the NCI Grants Administration Branch receives all approvals, NCI authorizes the release of funds.

6.2.8. Review Process for Validation Study Proposals

The EC will review Validation Proposals and other collaborative projects that seek Core Funds, including Type B Associate Membership applications, and may seek advisement from the relevant Collaborative Group on the merit of the proposal prior to its discussion at the EC. If necessary, it will appoint an ad hoc committee that will include at least one member from the appropriate Collaborative Group.

Progress of a biomarker to a validation study is a critical step in the development of a biomarker and is, therefore, a critical part of EDRN. Applicants are encouraged to submit their validation study proposal to the relevant collaborative group and seek their concurrence before the EC reviews their proposal.

1. Pre-proposal:

A pre-proposal/letter-of-intent, limited to 5 pages, must be submitted to the appropriate Collaborative Group Chair or directly to the EC. Validation Studies are collaborative, therefore, the pre-proposal must name the EDRN sites which will be included as part of the collaboration. A Biomarker Reference Lab and the Data Management and Coordinating Center must be consulted for all Validation Studies. A Clinical Validation Center should be included as needed.

The Collaborative Group Chair will disseminate the pre-proposal amongst Collaborative Group members for discussion and recommendation. Applications submitted directly to the EC may be reviewed by the EC or referred to the appropriate Collaborative Group for review. If approved by the EC, the submitting investigator will be asked to complete a full proposal as described below and submit it to the NCI EDRN Program Office.

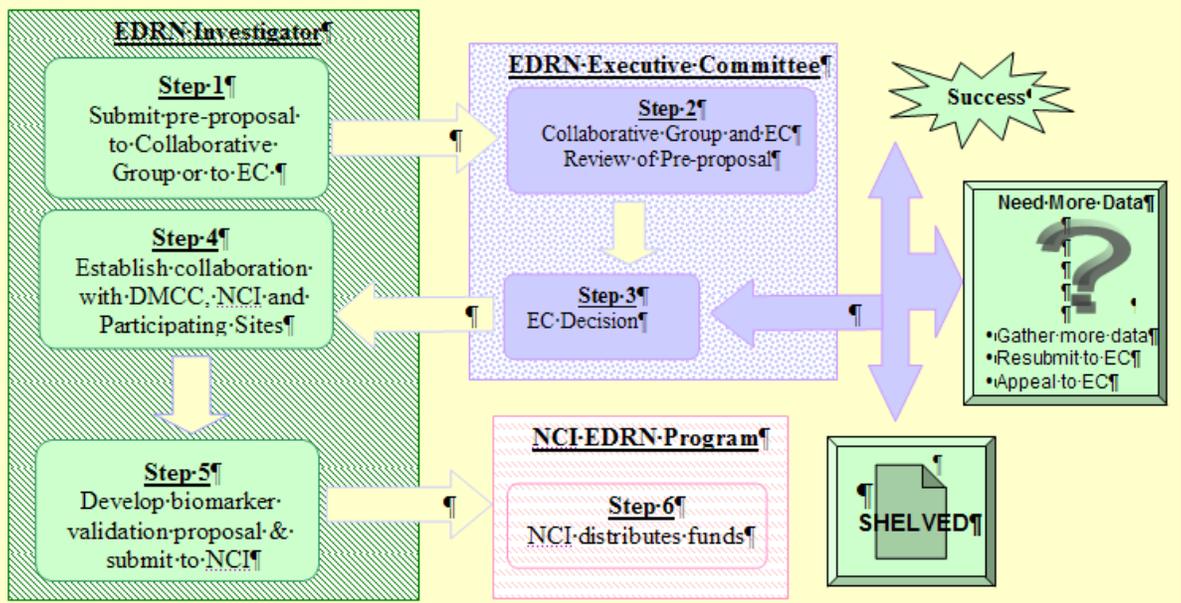
2. Proposal:

Once the pre-proposal is approved by the EC, the investigator contacts a Biomarker Reference Lab, Data Management and Coordinating Center, and/or Clinical Validation Centers, as appropriate for collaboration, and develops a full proposal with them. The full proposal should be prepared as described in Section 6.2.3 with the exception that it should not exceed 20 pages rather than 3 pages. A detailed background and rationale are not necessary but presentation of preliminary data is required.

Full proposals are submitted to the NCI EDRN Program Office. The full proposal is evaluated by EC or appointed ad hoc committee and external reviewers (non-EDRN members). The remaining steps for the Validation Study review process are the same as steps 3 & 4 in Section 6.2.6.

See Appendix 5 for the policy regarding blinding of specimens for collaborative studies.

EDRN Validation Studies and Use of Validation Labs



Application Process

- Step 1:** An EDRN Principal Investigator (PI) shall notify relevant Collaborative Group or EC of biomarkers that may be ready for validation studies through a pre-proposal or letter of intent (LOI).
- Step 2:** The Collaborative Group or EC reviews proposal.
- Step 3:** If the EC recommends a proposal be submitted, the PI shall establish collaboration with DMCC and Participating Sites. If more data is needed, gather more data and resubmit or appeal.
- Step 4:** The PI, DMCC, NCI and Participating Sites develop and finalize proposal.
- Step 5:** NCI receives final proposal and Review by EC
- Step 6:** NCI distributes funds

6.3 EDRN Standard Specimen Reference Set Guidelines

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 (see Appendix 6) 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.

See Appendix 7 for EDRN Pre/Validation Reference Set Specimen Sharing Guidelines)

6.4 EDRN Informatics

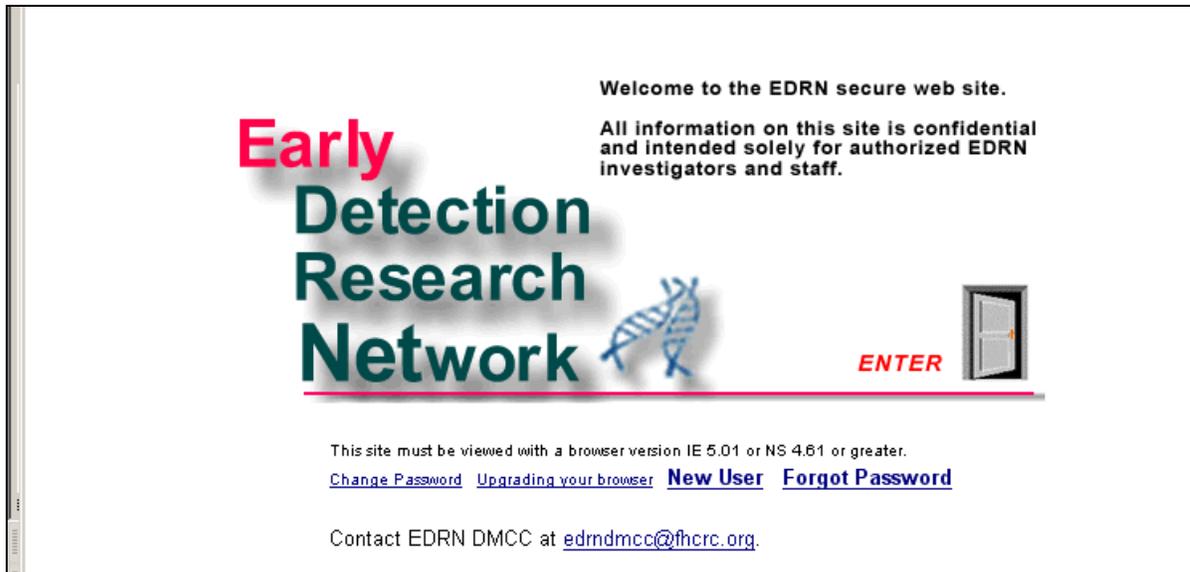
6.4.1. EDRN Secure Website

6.3.1.1 Overview

The Data Management and Coordinating Center (DMCC) is responsible for developing and maintaining a secure website for EDRN. The website contains general EDRN information such as contact information for all participating institutions, committee and subcommittee membership, upcoming events, etc., as well as items that are less public such as data from collaborative studies, approved validation proposals, paper drafts, etc. Due to the sensitive nature of some of the information available on the secure website, only people approved by an EDRN member have access to the website. Access to the website requires a log-in and password distributed by the DMCC.

A website user's guide is provided in Appendix 9.

6.3.1.1 Obtaining A Log-In And Password



In order to obtain access to the secure website, one must complete the Application for EDRN Secure Web Site Access (see <http://www.compass.fhcrc.org/enterEDRN/>) and FAX the completed form to the DMCC Project Manager at 206-667-5964. The application form must be signed by an EDRN Principal Investigator. Once the application is processed at the DMCC, the applicant is sent a log-in via email and a password via post mail. The log-in name generally consists of the applicant's first name initial and entire last name.

6.3.1.1 Passwords and Security Issues

Once an applicant receives their password, the website will prompt the user to change their password at first login. A user can change their password at any time by clicking on "Change Password" at the bottom of any page on the website. For security reasons, passwords for the EDRN secure website must adhere to the following guidelines:

1. May not contain all or a part of the username
2. Must be at least 8 characters in length
3. Must contain characters from three of the following categories: Uppercase letters, Lowercase letters, numbers, non-alphanumeric characters (like # and !)
4. Cannot reuse the last 5 passwords
5. Cannot change a password more than 5 times per day

After the user has changed their password, they will be asked 2 personal questions which, when answered correctly, will retrieve their password in case they forget it or need to confirm it.

The DMCC also recommends that public personal data (e.g. name, birthday) should not be used in passwords. Log-in IDs and passwords should also be kept in a safe place. To maintain compliance with the DMCC's IRB, you may not share your password or log-in.

Each user's password will expire every four months. If a person enters his/her log-in and the password has expired, s/he is prompted to change the password at that time. A log-in will lock after three failed attempts and then reset itself in 30 minutes. If this happens, please wait 30 minutes and then try to log into the web site again.

6.4.2. Common Data Elements (CDEs)

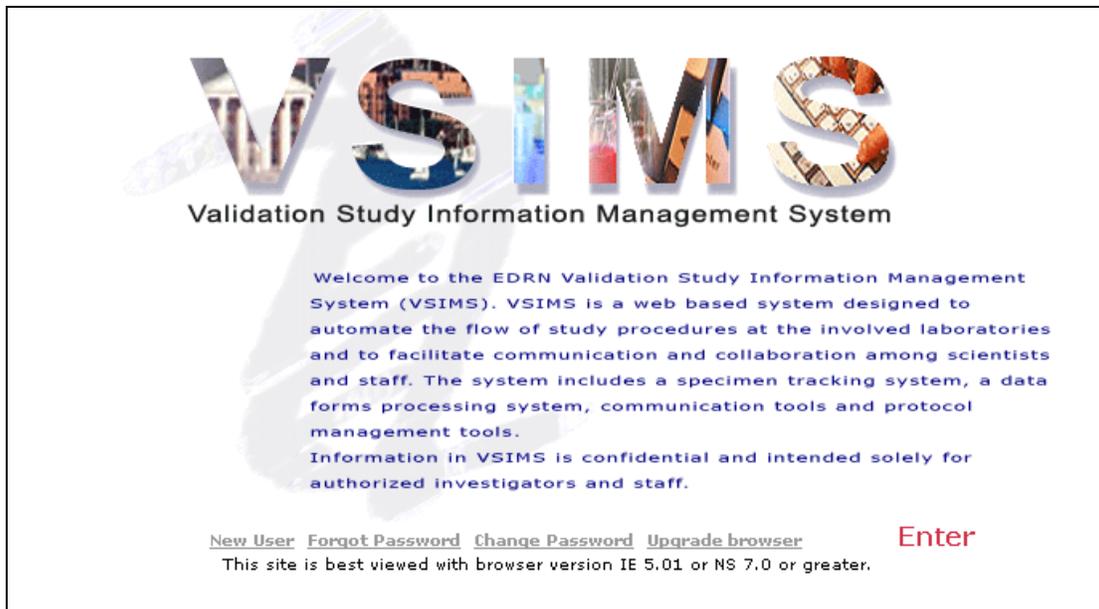
The EDRN Common Data Elements (CDEs) are composed of three main components: the exact wording of the questions used to collect data, all possible responses to the questions, and the data format for sharing and/or transmission of the data within EDRN. The CDEs will standardize data that is collected and stored at all sites to ensure consistency in data and specimen sharing.

Any EDRN sites collecting new prospective data for EDRN studies are required to use the EDRN CDEs.

Currently there are three categories of CDEs that have been developed to varying extents for EDRN. The first is the Core CDEs. The Baseline and Follow-up Core CDEs are comprised of a participant ID, protocol ID, site IDs and basic epidemiologic data relevant to EDRN. The Core Specimen CDEs include the specimens that are collected from a participant at each specimen collection date. The next category of CDEs is the Specimen type-specific CDEs and includes information on the processing and storing of the specimens that were collected. The last category is Organ-specific CDEs and consists of data elements important for organ-specific studies. The development of the Organ-specific CDEs requires the participation of the Collaborative Groups.

The CDE tools created by the Data Management and Coordinating Center (DMCC) enable sites to view all existing groupings of CDEs on forms, create and modify their own groupings on forms, and view all the information associated with the EDRN CDEs.

6.4.3. Validation Study Information Management System (VSIMS)



Validation Study Information Management System (VSIMS) allows for the efficient and secure collection and management of information for all EDRN Validation Studies. VSIMS is a secure web-based system that is designed to automate evaluation of eligibility criteria and data collection, transfer data, track specimens, serve as a resource for study-specific information, facilitate communication across multi-center studies, track data queries and resolutions, and allow administrative management of studies. The ability of the system to adapt to different sets of business criteria and workflows allows information to be stored separately for each study allowing multiple studies to be coordinated centrally through the same data management system framework. The greatest strength of the system lies in its flexibility and ease in making changes, enabling several Validation Studies to be simultaneously or consecutively implemented and managed in a timely manner. See Appendix 8 for the policy regarding the use of VSIMS for EDRN Collaborative Studies.

6.4.4. EDRN Catalog and Archive Service (eCAS)

The EDRN Catalog and Archive Service (eCAS) supports the capture and distribution of the published science data acquired during a validation study. The eCAS infrastructure will satisfy several EDRN informatics goals, including:

- Acquisition of published science data from multiple EDRN validation studies
- Software interfaces for sharing of data across biomedical applications
- Secure transfer and distribution of data to the science community
- A common information model for describing EDRN science data
- A web-based interface to search and download EDRN science data

The EDRN Informatics Working Group is currently prototyping the eCAS to validate these goals. The prototype demonstrates how data acquired locally at institutions can be archived using the EDRN common information model and then distributed to scientists nationally through the EDRN Public Portal. Participating EDRN sites will also be able to catalog their science results remotely with the eCAS system via the Public Portal. The common science portal will provide access to all published EDRN science data enabling distribution to a broad range of users using a well-defined security access policy.

6.4.5. Biomarker Database

The EDRN Biomarker Database (BMDB) is currently being constructed to capture and catalog biomarker annotations and related ancillary data from biomarkers pursued within EDRN and elsewhere. Biomarker data and results will be curated into the BMDB including links to study protocols, publications and other related information and resources from multiple EDRN and non-EDRN databases. BMDB will also support access to raw biomarker data for the purposes of statistical analysis and meta-analyses.

6.4.6. Public Portal

The principal focus on the EDRN Public Portal is to raise the awareness of the EDRN by the public through a web portal. It provides an online mechanism to distribute information and results from the EDRN to the public. This includes news, announcements of opportunities, availability of online data sets, information about EDRN studies, access to various EDRN resources, and overall information about the EDRN program. The Public Portal also serves as a gateway to other EDRN tools including eCAS and ERNE. It provides a publishing capability so that new information can be easily reviewed and published to the portal.

6.4.7. EDRN Resource Network Exchange (ERNE)

EDRN has deployed the EDRN Resource Network Exchange (ERNE) to ten institutions providing a common web-based client interface. ERNE unifies search and retrieval of biospecimen data from all institutions regardless of where it is located, how it is stored, or the differences in the underlying data models. This enables a scientist, for example, to locate tissue specimens for breast cancer by searching data catalogs at participating institutions across the country.

As the knowledge system evolves, the governing CDE model and the use-cases derived in the working groups will be used to drive the relationships between the data sets enabling discovery through data mining. Scientists, for example, will be able to query an assay result from a validation study and then find the associated specimens that were collected as part of that assay.

6.4.8. EDRN Study Information System (eSIS)

eSIS is a subsection of the EDRN Secure Website that is used to monitor progress of all EDRN projects (single site, collaborative and network collaborative). It is the responsibility of the Principal Investigator(s) to maintain accurate content as well as track milestones.

SECTION 7 EDRN PROGRAM EVALUATION

7.1 Metrics for Evaluation

7.1.1. Objectives

It is the responsibility of the awarding agency, in this case the National Cancer Institute (NCI), National Institutes of Health, to review progress achieved towards scientific goals in original grant applications over specified grant periods and to provide scientific and logistical input to grantees to enhance the quality of their scientific efforts. For details, see HHS 45 CFR, Part 74. To review progress towards achieving the objectives of the Early Detection Research Network (EDRN) and its investigators, it is imperative for EDRN program officials to gather information on the functioning of the network in order to update the NCI leadership. This document describes metrics, rationale, and standards for evaluating the overall success of the EDRN.

7.1.2. Introduction

Fair, rigorous peer review of investigator-initiated scientific applications remains the cornerstone of scientific progress in the United States. Peer review has ensured that the best science is supported. The EDRN was initiated with this concept in mind. By selecting scientific collaborators for the EDRN on the basis of rigorous peer review and fully funding the best applications, the NCI has successfully obtained strong participation from the scientific community.

The EDRN represents a major pioneering effort in collaborative translational research. It departs from prior Cancer Cooperative Group models in many important ways - through empowering investigators by funding their Centers directly and by placing the burden of scientific leadership, research agenda, and collaboration upon these directly funded Centers. Basic scientists with robust bench research records have been funded to pool their ideas, resources, and tools. Translational and epidemiologic investigators with strong tools and publication track records are directly funded with a mandate to translate concepts arising from basic science labs. Analytical tools, laboratories, statistical methods, and informatics are also supported directly with a collaborative mandate. Leadership of this collaborative must emanate from the grass-root investigators, and the Executive Leadership must communicate with a highly knowledgeable group of scientists in a manner that enhances collaboration and productivity. This Network represents a new paradigm of Cooperative research.

7.1.3. NCI Charge to the EDRN

NCI leadership and Program Staff have provided the following charge for this collaborative enterprise:

- Establish criteria for the discovery and validation of biomarkers at all points of the integrated research scheme;
- Establish a rigorous quality assurance/quality control program for biomarkers;
- Establish and deal with issues of biorepositories -- how the samples will be obtained, stored and most importantly, allocated;

- Support Translational Research Projects-both within and outside the EDRN - and establish policies and procedures that are inclusive of investigators who wish to utilize the infrastructure and facilities of the EDRN;
- Establish and foster industrial collaborations which will be crucial to the ability to rapidly translate the research effort into products and to test innovative biomarkers being developed by industry;
- Establish and maintain effective and efficient communications, including the use of EDRN websites (public and private), listservs, email, and regularly scheduled meetings;
- Develop and maintain an effective, efficient, and productive management domain with minimal committee structure and maximal collaboration, with financial rewards for collaboration;
- Encourage inclusiveness by ensuring that scientists with promising research ideas get the opportunity to collaborate constructively with the EDRN.

7.2 Evaluation Metrics

Since there are no prior models of such a cooperative research enterprise, it is very important to carefully monitor and assess progress from both macro and micro perspectives. Substantial administrative effort will be expended in order to build and expand this infrastructure. The following evaluation metrics are suggested.

7.2.1. For the Individual Laboratory and Center

1. Scientific Excellence

Quality of Questions: Has the EDRN site clearly defined their objectives, hypotheses, and scientific plan?

Scientific Progress to Date: Has the EDRN site made progress towards meeting these objectives as specified in their originally funded research plan? What pitfalls have been encountered and how have they been managed?

Innovation: How has the EDRN site used innovation to overcome obstacles? Is the site aware of new methods or approaches that might be useful to or portable into the EDRN environment?

Future Plans: What does the site plan to do over the coming two years? How will these plans meet the original grant objectives?

2. Productivity Metrics

Publication productivity: Has the site published papers on the objectives funded by the EDRN? How many and in what Journals? If not, are there problems that need to be addressed or require assistance?

Grant funding: Has the site applied for additional grant or contract funding? Has the site team been successful in gaining additional funds? Has the EDRN been helpful to the success of funding these new grants or contracts?

Biomarkers identified (BDLs): Number of new biomarkers pursued for evaluation? Number of biomarkers sent forward to CVCs or BRLs for validation? Number of biomarkers added to early detection or risk assessment panels? Number of biomarkers used in chemoprevention clinical trials?

Assays performed (BRLs): Numbers of assays developed for EDRN projects? Numbers of samples processed? Types of samples processed? Results reported? Quality control of samples assayed? Number and type of development projects approved? Use of CDEs?

DMCC: Standards of informatics support? Type of informatics, QC procedures, patient privacy protection measures, data storage, and retrieval systems for Validation Studies? Development of Network-wide communication systems? Development of Network-wide systems to promote data and specimen sharing? Development of statistical methodology to meet the needs of EDRN?

Samples collected and provided (CVCs): Numbers of samples collected? Types of samples collected? Sources of samples collected? Numbers of samples provided to EDRN BDLs or BRLs? Use of CDEs? How many CVCs have had their set-aside funds released? How many CVCs have requested the release of Developmental funds?

3. Collaborative Metrics

EDRN collaborations: With whom is the EDRN site collaborating? How many projects are collaborative? How many joint papers have been published? Use of EDRN resources: Has the EDRN site collaborated with CVCs, a BRL or BDL site? If so, how many? Joint publications? Joint grants? How many BDLs have requested release of their restricted funds for Network Collaborative Studies?

Participation in EDRN Activities: Attendance from the site at EDRN meetings. Participation on Committees, working groups, and task forces? Special EDRN projects completed. Did EDRN site participate in developing the CDEs? Did EDRN site help to standardize/streamline the IRB approval process? Did EDRN site help develop systems for streamlining data sharing and/or specimen sharing? Did EDRN site help develop systems to standardize/streamline technology transfer issues?

EDRN outreach: Number of new Associate Members from the outside? Amount of core funds allocated to new Associate Members? The number of applications for core funding? Other outreach activities?

7.2.2. Process for Evaluating Metrics

1. Annual written progress report

Reviews should be based upon the yearly progress report required for non-competitive renewal. Instructions for preparation of the non-competitive renewal should be specific

and emphasize progress towards scientific goals of the original grant application and progress towards addressing EDRN's mission. While scientific quality and progress need to be recorded and addressed, primarily, metrics should be required to allow NCI staff to report data to NCI leadership.

The review process should assess the progress of each of the funded units towards meeting the specific aims of their funded grant application and their progress and contributions in meeting the above-described charges for the entire group. While the review is structured to provide NCI leadership and staff with data to track the progress of the EDRN and its components, equally important goals are to provide constructive feedback to EDRN Principal Investigators and their collaborators. Reviews may be used by EDRN leadership, NCI staff, and the Network Consulting Team to make mid-course changes or to encourage constructive changes in individual scientific direction or focus. Initial reviews might assist in building collaborations among investigators and their groups. Reviews may also be used to assess administrative progress, to quantify publications and grants, and to quantify numbers of subjects studied.

2. Site Visits

Each Center/Laboratory should be site visited by a panel comprised of external consultants (including individual members of the Network Consulting Team), NCI staff and other experts on an as needed basis. The site visit should be brief (preferably a half day or less) but enable a thorough review of scientific progress, future scientific plans, performance metrics, facilities and staff in support of the EDRN charge. The site Principal Investigator(s) should provide a 2-3 hour presentation period to review scientific progress, spell out new scientific initiatives for EDRN research, and address required metrics. The Principal Investigator(s) are encouraged to share problems, concerns, and questions to the site visit team so that the process is interactive and collegial. While an agenda and presentation should be necessary, no scoring should be used.

3. Frequency of Site Visits

The frequency of the site visits will be determined by the NCI. However, it is anticipated that one initial site visit by NCI program officials will occur in year one, and one mid-grant site visit (for a five-year grant) will occur between year 2 and year 3. Additional site visits may be required when deemed necessary by the NCI.

Deficient performance and remedies will be conducted in accordance with HHS 45 CFR, Part 74 and other pertinent regulations.

4. At time of Type 5 renewal each site must submit their Site Task Reminder list generated from the EDRN Secure Website. In addition each site must submit a copy of each of their individual reports (publications, specimen survey, research interests, and registered protocols).

7.3 Overall Evaluation of Early Detection Research Network

It is the intention of the NCI that the members of the Network Consulting Team and Chairs and Co-Chairs of the EDRN Steering Committee will discuss the overall performance of the EDRN using the metrics presented in this document and suggest changes/modifications in the working structure of EDRN.

SECTION 8 APPENDICES

8.1 Appendix 1 – Format for Preparing the Last Page of the Application for Use of EDRN Set Aside Funds by Biomarker Developmental Laboratories and Clinical Validation and Epidemiology Centers

It is mandatory that the last page of the application be in the following format:

List separately each collaborating EDRN investigator; specify the specific work they will contribute to the collaboration and where their work will be done (e.g., their laboratory, another laboratory). Also indicate how this work is separate from core work of the investigator already funded by the EDRN; if there is overlap with core funds, please describe the overlap. Note that contributing tissues alone, especially by the CVCs, does not constitute a collaboration with respect to justifying the use of aside funds.

List separately each collaborating non-EDRN investigator; specify their specific contribution to the project and where their work will be done, and how it will be funded.

Describe how this project advances early detection or risk assessment. Also describe how it forwards translational research in general and specifically in areas of diagnosis, prognosis or surrogate endpoints.

8.2 Appendix 2: Format for Application for Developmental Funds by a Biomarker Reference Laboratory

The application for the use of developmental funds should mirror a U01 application with a limit of 25 pages.

The application should focus on the purpose and the mission of the BRLs as described in RFA-CA-09-019. This includes, but is not limited to, analytical validation of published candidate biomarkers; analytical validation of high throughput platforms and methods for efficient, accurate and economical testing of biomarkers using small volumes of samples; pre-validation and validation studies of biomarkers with EDRN BDLs and CVCs; analytical validation of platforms and methods in support of EDRN BDLs and CVCs; development of standard operating procedures, as directed by the EDRN steering committee or by the EDRN executive committee. The BRL may also conduct studies to improve collection, processing and storage of samples and sample sets. Finally, collaboration between BRLs and other EDRN components are encouraged. It is recognized that developmental funds may be used to support several small projects.

The application should be organized in similar manner to traditional grant applications and include, background; hypothesis (if applicable) and specific aims, progress made and or preliminary data; study design, alternative approaches, and methods; timeline and millstones. The last page should follow the format used in the application for set aside funds.

It is mandatory that the last page of the application be in the following format:

List separately each collaborating EDRN investigator, specify the specific work they will contribute to the collaboration and where their work will be done; (e.g., their laboratory, another laboratory). Also indicate how this work is separate from core work of the investigator already funded by the EDRN; if there is overlap with core funds, please describe the overlap. Note that contributing tissues alone, especially by the CVCs, does not constitute a collaboration with respect to justifying the use of aside funds.

List separately each collaborating non-EDRN investigator; specify their specific contribution to the project and where their work will be done, and how it will be funded.

Describe how this project advances early detection or risk assessment. Also describe how it forwards translational research in general and specifically in areas of diagnosis, prognosis or surrogate endpoints.

8.3 Appendix 3 – Guidelines for Reviewing Requests for Release of Set-aside Funds

1. EDRN PI sends request to the appropriate NCI Program Director (PD) within 90 days of award date. PD checks application of completeness. If incomplete, PD requests additional information from the PI. Applications received in the first week of the month should be reviewed during that month's EDRN EC call.
2. PD identifies an EDRN PI, who is not on the EDRN EC, to provide a written review prior to the EDRN EC call. If EDRN PIs lack the necessary expertise, an Associate Member or Co-PI can be used as the reviewer. PD sends the application and review guidelines at least two weeks prior to EDRN EC call.
3. PD assigns two EC members as primary and secondary reviewers for each application. Applications should be sent directly to the assigned EC members two weeks before the EC call. Request that written comments be provided prior to the call. Coordinate EC and non-EC assignments with other PD to distribute the review workload evenly. A spreadsheet works well for this.
4. During the EC call, the PD introduces the request, briefly describing the specific aims, approach, and collaborators. This should only take 2 or 3 minutes. Both EC reviewers provide their comments. PD presents the outside reviewers comments and if necessary his/her own comments. Open discussion of the application by whole EC. Chair of EC asks for recommendations and EC votes. Possible recommendations:
 - Approve
 - Conditionally approve - PI must revise and/or respond in writing to EC questions and concerns. NCI staff evaluates the response and makes decision about release of set aside funds.
 - Revise- PI must revise and resubmit the request which will be reevaluated by the EC.
 - Disapprove - PI may submit a new set-aside request but it must be for a different project.
5. If the request is not approved by the EC, the PD communicates the result to the PI, providing the written comments of all the reviewers, and if appropriate, a list of questions the EC would like addressed. Depending on the recommendation of the EC, the PI sends a written response, a revised application, or a new application to the PD.
6. Once the request has been approved either by the EC or by NCI staff after an appropriate response, PD writes a letter to the PI informing him/her that the EC recommended approval of the release of the restricted, set-aside funds and advising them that the official notification of the release of restricted funds will come via a revised Notice of Grant Award issued by the NCI Office of Grants Administration.

7. PD sends a memo to the appropriate grants specialist in OGA and to the person in OGA who coordinates the EDRN informing them that NCI program staff recommends the release of the restricted set-aside funds and stating the total costs to be released. The PD also sends a copy of the letter sent to the PI and a signed copy of the application. Send a copy of the memo to the program specialist.
8. PD retains a copy of these communications in their records.

8.4 Appendix 4 – Guidelines for Reviewing Applications for Core Funds

Core Funds are used to support three types of activities - Associate Members, prevalidation or PRIDE studies, and validation trials. These guidelines are for the process of reviewing prevalidation or PRIDE studies and validation trials. The process for reviewing Associate Membership applications is different and is described elsewhere.

According to the EDRN Manual of Operations, applications for Core Funds are accepted the first week of each month and are reviewed during monthly EC calls held the last week of the month.

Reviewing prevalidation and PRIDE applications: (note guidelines for validation studies differ and are given in the next section)

1. The investigator sends the application directly to the NCI Program Director (PD) or to either the chair of the Collaborative Group (CG) or Chair of the EC who will then send it to the appropriate PD.
2. PD checks application to ensure that it complies with the EDRN requirements as specified in the EDRN Manual of Operations. If the application is not compliant, the PD returns it to the investigator for revision.
3. If the application is compliant, the PD sends the application, review guidelines, and the conflict of interest, confidentiality and non-disclosure form to the EDRN PIs who are members of the appropriate CG. The PIs should send reviews back to the PD within two weeks.

Alternatively, the application for a prevalidation may be sent directly to the EC for evaluation. This decision is based on the size and scope of the application and the PD should discuss this with Sudhir Srivastava. The EC can either proceed as in step 5 or send to the appropriate CG for review.

4. If there is a strong consensus, the outcome of the review (summary of all of the individual comments), the CG's recommendation, and the application are sent to the EDRN EC for discussion at the next conference call.

If there is no consensus or if the Chair of the CG thinks it necessary, the PD will set up a conference call with the PIs to discuss the application. The application and outcome of the review (summary of all of the individual comments) and conclusion of the conference call are sent to EDRN EC for discussion at the next conference call. The CG may send the application back to the investigator for minor revisions prior to going to EC.

5. During the EC call, the PD introduces the application, briefly describing the specific aims, approach, and collaborators. The Chair of the CG and the PD then summarize the outcome of the review and their recommendations. Open discussion of the application by whole EC. Chair of EC asks for recommendations and EC votes. Possible recommendations:

- Approve – recommend any changes to budget

- Conditionally approve - PI must revise and/or respond in writing to CG and EC questions and concerns. NCI staff (assigned PD and other CBRG PDs) evaluates the response and makes decision whether to fund. If PD can not decide, consult Chair of CG and if necessary resend to CG or EC for re-review.
 - Revise - PI must revise and resubmit the request which will be reevaluated by the CG and EC.
 - Disapprove
6. After the EC makes its recommendations, the PD communicates the results to the investigator in writing.
 - If approved, PD sends written comments and any recommended changes to budgets to the investigator. PI may need to submit a revised budget before PD approves funding.
 - If conditionally approved, PDs sends written comments and results of EC discussion to the investigator. PI must revise and/or respond in writing to CG and EC questions and concerns. NCI staff (assigned PD and other CBRG PDs) evaluates the response and makes decision whether to fund. If PD can not decide, consult Chair of CG and if necessary resend to CG or EC for re-review.
 - If the EC requests a revised application, PDs sends written comments and results of EC discussion to the investigator. PI must revise and resubmit the request which will be reevaluated by the CG and EC.
 - If the EC disapproves, the PD sends the sends written comments and results of EC discussion to the investigator. The PD must edit the written comments such that they accurately reflect the EC discussion.
 7. Once the request has been approved either by the EC or by NCI staff after an appropriate response, PD writes a letter to the PI informing him/her that the EC and NCI staff have recommend funding the application. This letter should contain an explanation about the funding mechanism and who will be contacting their business office. The program specialist (currently Don Johnsey) will provide a sample letter.
 8. PD gives completed and signed application to the program specialist (currently Don Johnsey) to send to Johns Hopkins University of Texas, San Antonio for funding. These awards are subcontracts to the grant of the Chair of the EDRN Steering Committee (currently David Sidransky/Dr. Ian Thompson).
 9. PD retains a copy of the application, the reviews and all communications.

Reviewing applications for validation trials

Due to the importance of a validation trial, larger costs, more complex organization, and significant involvement of the EDRN DMCC and NCI staff, the application process has some additional requirements. It is a two step process – a short 3 5page preproposal that is evaluated by the same

process as used for prevalidation and pride proposals and a full proposal. The content and requirements for both the proposal and full proposal are given in the EDRN Manual of Operations.

A full validation proposal can only be submitted if the preproposal has been approved the EDRN EC.

1. The investigator sends the full proposal to the PD who then checks to make sure that it follows the guidelines as given in Manual of Operations. There are specific requirement about the involvement of the DMCC, EDRN BRLs and CEVCCVCs
2. If the proposal is compliant, the PD identifies two experts who are not part of the EDRN to provide a written review of the proposal. The PD sends the application, review guidelines, and the conflict of interest, confidentiality and non-disclosure form to these external reviewers at least two weeks prior to EDRN EC call. The reviews of the external reviewers must be sent to the EC at least three days prior to the EC call.
3. PD also sends the full proposal to the EDRN EC at least two weeks prior to EDRN EC call. The PD should assign three EC members to be primary reviewers. The EC may decide to have an ad hoc committee composed of other EDRN PIs also review the proposal. If this decision is made, it is the responsibility of the PD to administer the review by this committee. The review should be run as described above for prevalidation proposals reviewed by the CGs.
4. During the EC call, the PD introduces the proposal, briefly describing the specific aims, approach, and collaborators. The assigned EC reviewers provide their comments, and if there was an ad hoc committee, its recommendation should be presented by a member of that committee or the PD. This is followed by open discussion of the proposal by whole EC. Chair of EC asks for recommendations and EC votes. Possible recommendations:
 - Approve – recommend any changes to budget
 - Conditionally approve - PI must revise and/or respond in writing to CG and EC questions and concerns. NCI staff (assigned PD and other CBRG PDs) evaluates the response and makes decision whether to fund. If PD can not decide, consult Chair of CG and if necessary resend to EC for re-review.
 - Revise - PI must revise and resubmit the request which will be reevaluated by the EC.
 - Disapprove
5. After the EC makes it recommendations, the PD communicates the results to the investigator in writing.
 - If approved, PD sends written comments and any recommended changes to the budget to the investigator. PI may need to submit a revised budget and work with the DMCC and other components of the EDRN before PD approves funding.
 - If conditionally approved, PD sends written comments and results of EC discussion to the investigator. PI must revise and/or respond in writing to CG and EC questions and concerns. NCI staff (assigned PD and other CBRG PDs)

evaluates the response and makes decision whether to fund. If PD can not decide, consult Chair of CG and if necessary resend to CG or EC for re-review.

- If the EC requests a revised application, PD sends written comments and results of EC discussion to the investigator. PI must revise and resubmit the request which will be reevaluated by the CG and EC.
 - If the EC disapproves, the PD sends the sends written comments and results of EC discussion to the investigator. The PD must edit the written comments such that they accurately reflect the EC discussion.
6. Once the request has been approved either by the EC or by NCI staff after an appropriate response, PD writes a letter to the PI informing him/her that the EC and NCI staff have recommend funding the application. This letter should contain an explanation about the funding mechanism and who will be contacting their business office. The precise funding mechanism will depend on how the validation study is organized. There may be a single primary contract from Hopkins to the PI's university with subcontracts to the other participating sites or there maybe individual contracts from Hopkins to each site. The PD must work with the program specialist and the PI of the validation study to work out the details.
 7. PD gives completed and signed application to the program specialist (currently Don Johnsey) to send to Johns HopkinsUniversity of Texas San Antonio for funding. These awards are subcontracts to the grant of the Chair of the EDRN Steering Committee (currently David SidranskyDr. Ian Thompson).
 8. PD retains a copy of the application, the reviews and all communications.

8.5 Appendix 5 – Policy on Blinding Specimens for EDRN Collaborative Studies

Definition of blinding:

Any information associated with the specimens remains unknown to the blinded party. Usually the blinded party is only given the labels (coded numbers) associated with the specimens. Some assays requires that cases and controls specimens are allocated with a certain ratio within the assay device. In that case, the blinded party may know the ratio of the mixing if necessary.

Unblinding may occur after the blinded party has completed the assay, completed the quality check of their data, and submitted data to DMCC, and the study group decided decides that the blinding is no longer necessary. Blinding may continue for other reasons (e.g. the reference set specimens that will be used for more than one study).

Studies using prospectively collected specimens:

Prospective study sites should use VSIMS and use the labels provided by DMCC. The labels provided by DMCC ensure the blinding in the subsequent uses of the specimens.

Studies using existing repository specimens:

1. Principal Investigator and any personnel of in his/her lab should be blinded, regardless of whether the actual assay for the study is conducted at PI lab or at another lab. The lab performing study assays should also be blinded.
2. Sites contributing Specimen specimen contributing sites should contact the DMCC for blinding guidance prior to sending out specimens to a study PI lab or assay lab, and should only send out the specimens after obtaining a written permission from the DMCC.
3. The study group (including DMCC) will determine whether the specimen contributing site could directly send the specimens directly to assay lab without relabeling. Factors to considers includes, but not restricted to, ratio of cases and controls contributed by this the site, the nature of the study (assay done at an independent lab or each lab will perform their candidate marker assays, etc). If the study group decides it is necessary, relabeling will be performed prior to the shipment of specimens to assay labs.

Single Site or Collaborative Studies not Coordinated by the DMCC:

EDRN investigators are encouraged to do as much as blinding when as possible even at the discovery phase. For EDRN network collaborative studies, DMCC will perform blinding. For site specific studies or collaborations between sites, the blinding is done locally but investigators are encouraged to consult DMCC regarding blinding procedures.

8.6 Appendix 6 - Request for Specimen Reference Sets

<i>Early Detection Research Network</i>		
Part 1: Request For Specimen Reference Sets		
Date of Submission:		
Investigator: Name: Institution: Address:	Phone: Fax: E-mail	
Specimen Reference Set(s) Requested		
Collaborative Group Oversight <input type="checkbox"/> Breast & Gynecological <input type="checkbox"/> Colorectal & Other GI <input type="checkbox"/> Lung & Upper Aerodigestive <input type="checkbox"/> Prostate & Other Urologic	Organ Site _____ (e.g. lung, ovary, colon, etc)	Specimen Type <input type="checkbox"/> Serum <input type="checkbox"/> Plasma <input type="checkbox"/> Other: Specify _____
Minimum volume of each sample required: (microliters)	Expected Length of Study: months	
Institutional Approval		
Do you have IRB approval to work with the requested samples?	<input type="checkbox"/> Yes: Institution: Approval Number: <input type="checkbox"/> No <input type="checkbox"/> Pending: Expected Date:	
Funding		
How will testing of the reference set(s) be funded?	<input type="checkbox"/> Current NIH-funded grant: Grant No. Annual Direct Costs: Funding Period: <input type="checkbox"/> Other Sponsorship: Please provide a letter of commitment from the sponsoring agency, company, or foundation. <input type="checkbox"/> Other: Specify:	

Part II: Scientific Proposal

Using the standard PHS 398 Continuation Page (<http://grants.nih.gov/grants/funding/phs398/continuation.doc>) address the following items as outlined. (3-5 pages recommended)

- I. **Clinical Relationship:** Clearly state the clinical question that you are trying to address: risk assessment, early detection, diagnosis or prognosis. How would the reference samples expedite addressing the intended clinical question?
- II. **Background and Significance:** Clearly state the scientific rationale of the proposal for using the requested specimen reference set(s). Describe your biomarker/platform and how you came upon its discovery/development for potential application in cancer detection.
- III. **Preliminary Data & Methods:** Provide sufficient information describing how experiments were performed, details on convenience samples used, and presentation of data in terms of specificity, sensitivity, and variance of your measurements. Explicit description of your studies will facilitate review considerations. Figures and other supporting documentation can be appended after your proposal.
- IV. **Data Analysis Plan:** Specify whether you will need a training set in addition to a blinded test set. Provide adequate detail concerning how statistical analysis of your data coming from these samples will be performed and a justification that the requested references set(s) is/are large enough to demonstrate the utility of the biomarker. Describe the statistical resources at your disposal. If you require statistical support, EDRN can assist you with this.
- V. **Collaboration:** In this section state your willingness to deposit all raw data obtained using the reference set(s) with the EDRN Data Management and Coordinating Center (DMCC). EDRN may compare this data as a reference with other biomarkers applied to the same sets.
- VI. **Future Plans:** If the biomarker is found to have promising performance characteristics, the EDRN might be interested in working with you to proceed to Phase II clinical validations. Address each specific scenario below according to your intentions:
 - a. Do you plan to approach EDRN for funding and collaboration in proceeding to a Phase II validation study? If not, do you have other resources where validation can be accomplished? Describe clearly other resources at your disposal and how they are sufficient to complete a larger Phase II validation study if you will not seek help from the EDRN.
 - b. Are you amenable to working within the collaborative framework of EDRN in proceeding to Phase II studies?
 - c. If deemed beneficial, will you be amenable to including your biomarker into a larger panel of biomarkers for Phase II validation?
 - d. If refinements will improve the performance of the biomarker test, will you concur with further development of the test? Will it be advantageous to include resources of EDRN for this purpose?

8.7 Appendix 7 – EDRN Pre/Validation Reference Set Specimen Sharing Guidelines

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.

8.8 Appendix 8 – Policy on Use of VSIMS for EDRN Network Approved Collaborative Studies

Studies using prospectively collected specimens:

Prospective study sites should use VSIMS and use the labels provided by DMCC. The labels provided by DMCC ensure the blinding in the subsequent use of the specimens. The use of VSIMS means that all clinical and epidemiological data pertaining to a specimen be key-entered into the data entry tool, as well as all information about collection, processing and shipping of specimens. Using VSIMS for prospective studies enables the DMCC to query data for accrual, accuracy and eligibility at any time. When sites collecting specimens prospectively continue to use their existing data systems the work involved in exporting and mapping data from the site to the DMCC is extensive. In addition, several of the sites that need to export data to the DMCC do not have the staffing or experience to conduct this request in a timely fashion.

8.9 Appendix 9 – Secure Website Users Guide

SECTION 1 HOMEPAGE

1.1 Overview

This section describes the overall set up of the EDRN Secure Website that is used by all EDRN Sites (BDLs, BRLs, CVCs, Associate Members, NCI and DMCC). The URL used to access the website is <https://www.compass.fhcrc.org/enteredrn/> and only those users with approval to access the site can get past the “Enter Page” (See Section 6.3 of the EDRN Manual of Operations for obtaining access to the EDRN Secure Website.)

Figure 1.1 – Home Page

The screenshot shows the EDRN Home Page with the following layout:

- Header:** "Early Detection Research Network" logo, tagline "An infrastructure for supporting collaborative research on molecular, genetic and other biomarkers in early cancer detection and risk assessment", and "NATIONAL CANCER INSTITUTE DIVISION OF CANCER PREVENTION".
- Navigation Bar:** SEARCH, FEEDBACK, SITE MAP, EDRN PUBLIC, LISTSERV. A pull-down menu for "Relevant Sites:" is on the right.
- Left Sidebar (Navigation):** Administration (Members, Committees, Collaborative Groups, Resources, Informatics, Protocols, Policies, Publications), Home.
- Main Content Area:**
 - EDRN Strategic Plan:** Draft Strategic Plan
 - Meetings:** EC Meeting on June 30, 2010
 - Documents:** Meeting Summary: Research Strategies, Study Designs, and Statistical Approaches to Biomarker Validation for Cancer Diagnosis and Detection; The Statistical Evaluation of Medical Tests for Classification and Prediction, by Margaret Pepe. Oxford University Press, 2003; Status of Requests for Release of Set-Aside Funds; Manual of Operations; Application Requirements for Release of Restricted Funds; Application Requirements for Release of Core Funds
 - Announcements:** The next EDRN Steering Committee Meeting will take place November 15-16, 2010, in Dallas, TX. Details about this event will be posted soon.
 - Frequently Used:** Site Task Reminder; Publication Report; Collaborative Activity Report; Find Research Partners | Post Research Interests; Find Investigators & Staff | Update Contact Information; Find Registered Protocols | Find Specimen Reference Sets; Find Specimens From the Surveys | Submit Specimen Survey; EDRN Resource Network Exchange; Validation Study Information Management System (VSIMS); Submit/View EDRN Surveys
- Footer:** About the EDRN, About the EDRN Secure Web Site

A navigation bar is located at the top of every screen. The navigation bar consists of the following features: [Search](#), [Feedback](#), [Site Map](#), [EDRN Public](#) and [Listserv](#). There is also a pull-down list of other Relevant Sites that users may be interested in.

The main menu consists of nine components: [Members](#), [Committees](#), [Collaborative Groups](#), [Resources](#), [Informatics](#), [Protocols](#), [Policies](#) and [Publications](#). The [Administration](#) menu is only for the DMCC.

The Home Page also consists of information pertaining to upcoming Meetings, regularly accessed Documents and Frequently Used tasks and links.

The following section contains instructions for completing the tasks and/or maintenance for which each EDRN site is responsible. It is up to each site to ensure that the Contact Information, Protocol Registration(s), Specimen information, Research interests, and publication list are up-to-date and accurate.

SECTION 2 MEMBERS

The [Members](#) component allows a user to view the entire Members List or view by type of EDRN site ([BDL](#), [BRL](#), [CVC](#), [DMCC](#), [JPL](#), [NCI](#)). It also provides the following functions:

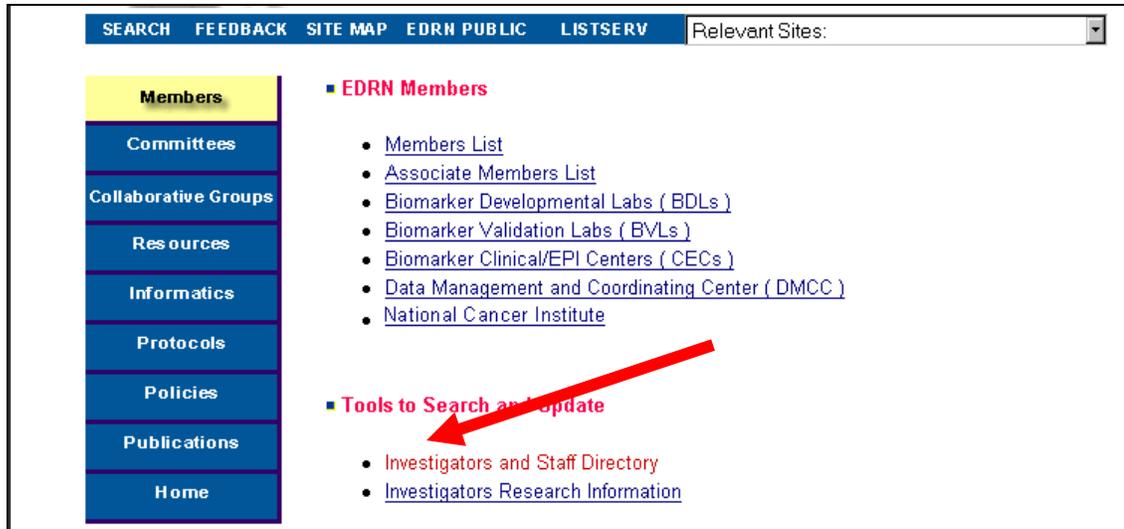
- Add, update or remove/reactivate contact information for anyone at your site.
- Search for contact information for any EDRN member.
- Add, update, remove or search for Investigator Research Information.

2.1 Contact Information

To **ADD**, **UPDATE** or **REMOVE/REACTIVATE** contact information from your EDRN site complete the following steps:

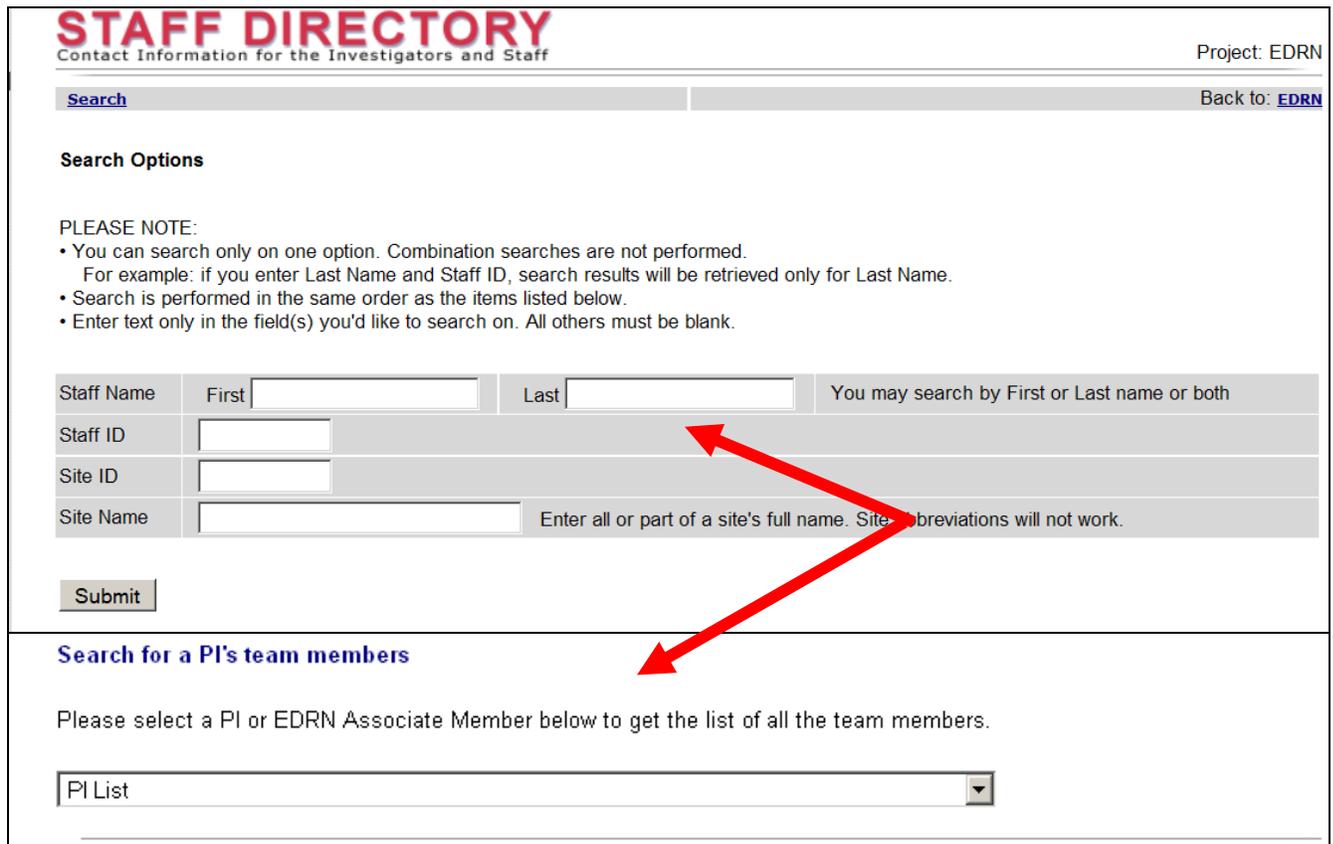
- On the homepage  click on the blue [Members](#) button on the left hand side of the page.
-  Click on the [Investigators and Staff Directory](#) link.
-  Click on the **[ADD](#)**, **[UPDATE](#)**, or **[REMOVE/REACTIVATE](#)** link on the left side
- Select your PI's name from the drop-down list
- To **ADD** contact information, enter all required information then  click on the [Submit](#) button at the bottom of the page.
- To **UPDATE** information, choose the person's name and click on the [Search](#) button at the bottom of the page. Update any information necessary then  click [Submit](#).
- To **REMOVE/REACTIVATE** contact information, select the person's name and choose either Active or Remove from the drop-down list and then  click [Submit](#).

Figure 2.1 – Investigators and Staff Directory



To **SEARCH** for contact information for any EDRN Site,  click the Investigators and Staff Directory then enter the name of the person you are searching for, or select PI's name from the drop-down list to search information for his/her entire site.

Figure 2.2 - Search



2.2 Investigators' Research Information

The Investigators' Research Information section of the website was created for EDRN investigators to enter information about their research interests so that they can be identified by other EDRN members looking for potential collaborators.

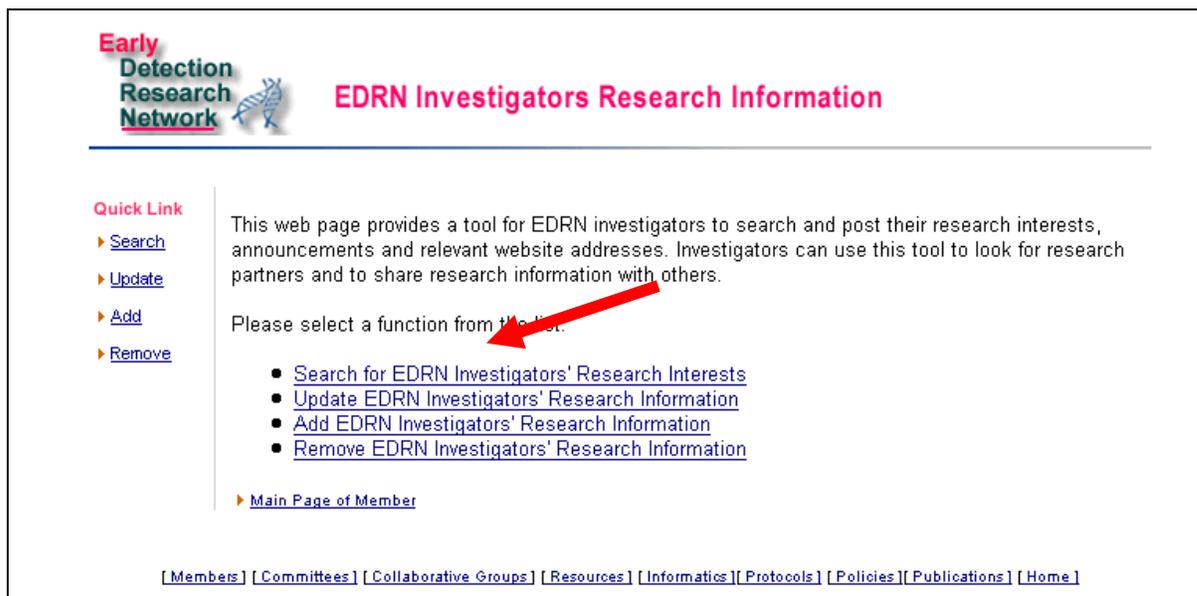
To **SEARCH** for Investigators' Research Information:

- On the homepage click on the blue **Members** button on the left of the page
- Click on the [Investigators Research Information](#) link
- Click on the [Search for EDRN Investigators' Research Interests](#) link
- Search by EDRN site, Information Subject, or Keyword.

To **ADD**, **UPDATE**, or **REMOVE** research information for an investigator from your site:

- On the homepage, click on the blue **Members** button on the left of the page
 - Click on the [Investigators Research Information](#) link
 - Click on **ADD**, **UPDATE**, or **REMOVE** [Investigators' Research Information](#)
 - Select the PI's name from the drop-down list
 - Choose the person's name then click on **Submit**.
- Use the **ADD** function to enter an Interest Topic that has not been entered before; for each Topic entered you must enter a corresponding Description.
- Use the **UPDATE** function to modify an Interest Topic that has already been entered into the system.

Figure 2.3 – Investigators Research Information



SECTION 3 COMMITTEES

EDRN is comprised of three main committees (Steering Committee, Executive Committee and the Network Consulting Team). In addition, EDRN has several Subcommittees and Working Groups.

To obtain an overview of each committee and to view the members of each committee select **Committees** from the main menu bar then click on the committee of interest.

Figure 3.1 – Committees



SECTION 4 COLLABORATIVE GROUPS

Collaborative Groups are informal, organ site-oriented groups designed to exchange information on organ related biomarkers. EDRN has four Collaborative Groups:

1. Breast and Gynecologic Cancers
2. GI and Other Associated Cancers
3. Lung and Upper Aerodigestive Cancers
4. Prostate and Urologic Cancers

To view the members of each Collaborative Group select **Collaborative Groups** from the main menu bar then click on the group of interest.

Figure 4.1 – Collaborative Groups

Early Detection Research Network
An infrastructure for supporting collaborative research on molecular, genetic and other biomarkers in early cancer detection and risk assessment

NATIONAL CANCER INSTITUTE
 DIVISION OF CANCER PREVENTION

SEARCH FEEDBACK SITE MAP EDRN PUBLIC LISTSERV Relevant Sites:

Members

Committees

Collaborative Groups

Resources

Informatics

Protocols

Policies

Publications

Home

EDRN Collaborative Groups

- Collaborative Groups are informal, organ site-oriented groups designed to exchange information on organ related biomarkers. An EDRN Principal Investigator serves as the Chair elected by Collaborative Group members. Collaborative Group membership is open to any investigator.

Collaborative Groups List

- [Breast and Gynecologic Cancers](#)
- [GI and Other Associated Cancers](#)
- [Lung and Upper Aerodigestive Cancers](#)
- [Prostate and Urologic Cancers](#)

[\[Members\]](#) [\[Committees\]](#) [\[Collaborative Groups\]](#) [\[Resources\]](#) [\[Informatics\]](#) [\[Protocols\]](#) [\[Policies\]](#) [\[Publications\]](#) [\[Home\]](#)

SECTION 5 RESOURCES

EDRN provides mechanisms for investigators to access information about Standard Specimen Reference Sets, SOPs for collection and processing of serum/plasma and search for Biological Specimens, Search for Content of Biological Specimen Survey, Submit Biological Specimen Survey, Update Biological Specimen Survey and provides a list of potential cohorts that have specimen banks. Every EDRN site is required to submit a Biological Specimen Survey and update the survey at least once per year.

Figure 5.1- Resources

Early Detection Research Network
An infrastructure for supporting collaborative research on molecular, genetic and other biomarkers in early cancer detection and risk assessment

NATIONAL CANCER INSTITUTE
DIVISION OF CANCER PREVENTION

SEARCH FEEDBACK SITE MAP EDRN PUBLIC LISTSERV Relevant Sites: [dropdown]

Members

Committees

Collaborative Groups

Resources

Informatics

Protocols

Policies

Publications

Home

EDRN Resources

- The EDRN provides the expertise and resources of individual laboratories and centers for collaborative studies. These web pages provide tools for EDRN investigators to submit the Specimen Survey, search EDRN specimen resources, and search and update the facility information of EDRN labs.

Reference Sets & Specimen SOPs

- [Specimen Reference Sets](#)
- [Serum SOP](#)
- [Plasma SOP](#)

List of Resources

- [The Diagnostics and Biomarkers Statistical \(DABS\) Center](#). This website assembles resources for education about, application of, and new research on, statistical methods for evaluating diagnostics and biomarkers. The focus is on validation rather than on discovery.
- [David Chia Lab Tissue Microarrays](#)
- [MALDI DilutionData EDRN.zip](#) (147 MB). These data come from a dilution experiment aimed at elucidating which features in MALDI-TOF mass spectrometry data are informative for quantifying peptide content. The details of the experiment are described in Ref[1].pdf.
- [Program for Rapid Independent Diagnostic Evaluation \(PRIDE\)](#)
- [Search for Biological Specimens](#)

5.1 Biological Specimen Survey Information

To **SUBMIT** a Biological Specimen Survey online:

- On the homepage, click on the blue **Resources** button on the left of the page
- To **SUBMIT** a survey, click on the [Submit Biological Specimen Survey online](#) link
- Click on either [Tissue Repository Survey Form](#) or [Prospective Cohort Survey Form](#) at the top of the page
- Enter all information for your site's specimens and click **Submit** at the bottom of the form

Figure 5.2 – Biological Specimen Survey

Tissue Repository Survey Form
Prospective Cohort Survey Form

Tissue Repository

Please complete one tissue repository form for **each organ site** which specimens might potentially be available for EDRN projects.
Please note that you can only submit this form for your own EDRN site.

Name of Study: (required)

Study Principal Investigator 1: (other than EDRN PI)

To **UPDATE** a survey:

-  Click on the [Update Biological Specimen Survey](#) link
- Choose the type of survey to update and the PI's name
-  Click on the button at the bottom of the page
- Choose the study name and  click
- Update information as necessary then  click

Figure 5.3 – Update Biological Specimen Survey

Update the Specimen Survey



Please note that you only can update specimen survey for a EDRN PI who signed your EDRN secure Web Site Access Application.

Choose what type of specimen survey you would like to update.

Tissue Repositories and Prospective Cohort

Tissue Repositories

Prospective Cohort

Choose Which EDRN member's specimen surveys you would like to update.

To **SEARCH** for information contained in the Biological Specimen Surveys:

- On the homepage,  click on the blue **Resources** button on the left of the page
-  Click on the Search for Content of Biological Specimen Survey link
- Choose the type of survey to search and the PI's name
-  Click on the **Search** button at the bottom of the page
- Choose the study name and  click **Search**

The information contained in the survey selected will be displayed.

Figure 5.4 –Biological Specimen Content Results



Content of Specimen Survey

Biological Specimen Survey - Prospective Cohort

Name of Study: GRPR/EGFR and Lung Cancer Risk
 Study Principal Investigator: Jill M. Siegfried, Ph.D.
 EDRN PI: William Bigbee

Do you obtain participant consent for research use of biological specimens? Yes
 Does your consent allow for the use of specimens by a third party? No

What Information is available about the subjects with specimens in the collection?

- ◆ Demographic (e.g., age, sex, race, ethnicity)
- ◆ Vital status
- ◆ Diagnosis

EDRN Specimen Storage



Click on EDRN PI's name for the contact information:

EDRN PI	Institute	Study Name	Specimen	Organ	Exist Cases	Controls Availability
William Bigbee	University of Pittsburgh Cancer Institute (BDL)	GRPR/EGFR and Lung Cancer Risk	Buccal scrapings	Lung	25	Possible
William Bigbee	University of	GRPR/EGFR and	Malignant primary	Lung	10	Possible

5.2 Search Specimen Surveys for Available Biological Specimens

To **SEARCH** for Biological Specimens:

On the homepage,  click on the blue **Resources** button on the left of the page.

 click on the Search for Biological Specimens link.

Select the organ site, specimen type, and EDRN PI you want to search on, or broaden your search by selecting “All” for a specified category, then  click on **Search**.

Figure 5.5 –Biological Specimen Search

SECTION 6 INFORMATICS

EDRN provides mechanisms for investigators to Search the EDRN Research Network Exchange for Biological Specimens, view Common Data Elements, access Study Design Guidance Tools and determine Check Digit Algorithms.

Figure 6.1 –Informatics

6.1 ERNE

The EDRN Resource Network Exchange (ERNE) is an initial informatics tools to promote the sharing of specimens to the EDRN community and outside researchers. Ultimately it is the intent of EDRN to use the data architecture more generally to access other types of data that are of interest to EDRN investigators, for instance imaging data, validation data etc... Currently eight EDRN sites are linked to ERNE. ERNE allows users to perform a Quick Search or an Advanced Search for potentially available specimens.

Figure 6.2 –ERNE



6.2 Common Data Elements

Common data elements (CDEs) have been, and are being developed for studies conducted by EDRN sites. The Core EDRN CDEs represent the minimum information that should be collected in all EDRN studies. The CDEs will standardize data that is collected and stored at all EDRN sites to ensure consistency in data and specimen sharing. The CDE tools enable sites to view all existing groupings of CDEs on forms, create and modify their own forms, and view all information associated with the EDRN CDEs.

Figure 6.3 –CDE Tool

■ **Data Element Mapping Tool**

This site allow user to create Common Data Elements and map their data element with created common data element. The DMCC will maintain this online information for all interested sites.

[DE Forms](#): allows all sites to view current or retired forms from all sites, create and modify their own forms

[DE Search](#): search common data elemnts

6.3 Study Design Guidance Tools

EDRN provides sites with various Study Design Guidance Tools to assist investigators in designing studies. The Tool lists various publications that have been written on Study Design mechanisms, a Sample Size Formula and Look-up Table and Relevant Links.

Figure 6.4 –Study Design Guidance Tools

Study Design Guidance Tools

Publications

- Pepe MS, Etzioni R, Feng Z, Potter JD, Thompson ML, Thornquist M, Winget M, Yasui Y. Phases of biomarker development for early detection of cancer. [Journal of the National Cancer Institute](#) 2001; 93(14):1054-61 (July 18).
- Baker SG, Kramer BS, Srivastava S. Markers for early detection of cancer: Statistical guidelines for nested case-control studies. [BMC Medical Research Methodology](#) 2002;2(1):4 (February 28).

Comment from DMCC statisticians: The sample size in Baker et al. is based on controlling the precision of sensitivity and specificity measures, not based on statistical power. The DMCC statisticians suggest sample sizes based on both precision and adequate statistical power. See [Thompson et al.](#) for further explanations and comparisons.

Sample Size Formula and Look-up Tables

- [Sample Size Calculations for Phase 2 Studies](#), 326 KB (26 pages) in pdf format. From the book: Pepe MS. The Statistical Evaluation of Medical Tests for Classification and Prediction. New York: Oxford University Press - USA (in press). (Citation last updated March 11, 2003)

Related Link

[Bioconductor packages for the analysis of genomic data.](#) Bioconductor is an open source bioinformatics software project based on R.

6.4 EDRN Informatics Survey

EDRN recommends that all sites provide the DMCC with information pertaining to their hardware platforms and operating systems used locally, as well as contact information for their IT support staff.

Figure 6.5 –Web Survey

EDRN WEB SURVEY
A Web Survey Tool for EDRN Investigators and Staff

Menu ▶ Submit Survey ▼ Back to: Web Site List ▼

[Survey List](#)

EDRN Informatics Survey (DRAFT)
The fields with * sign are required.

EDRN Members * ▼

Informatics Contact Person

Contact Email

Contact Phone Number

Title

Hardware Platforms

Operating Systems

SECTION 7 PROTOCOLS

7.1 General Questions

1. Why obtain an EDRN Protocol ID?

- Registration of your EDRN protocols provides NCI (and EDRN members) with an easy way of finding out about activities that are going on within EDRN. NCI will use this system to make a report of both individual site studies as well as collaborative studies that are being conducted within EDRN. These reports will be used to evaluate sites for renewal as well as to evaluate EDRN overall. To register a protocol please contact the DMCC at edrndmcc@fhcrc.org or at 206-667-6972.
- You can print or download the reports to include in your annual renewal to inform NCI of your collaborative activities.
- Protocol registration results in a unique ID being assigned to each protocol. The protocol ID is one of three CDEs that are essential for uniquely linking study participant data with their specimens.
- All protocols that you are conducting either as a single EDRN site or jointly with other EDRN sites should be registered. If you want NCI and other EDRN investigators to know about the activity, register it.

2. What information is needed to obtain an EDRN Protocol ID?

- You will need your IRB approval number, date of approval, and information about the specimens you will collect (if applicable).
- Other information such as study design and study abstract is optional for single-site studies, but required for collaboration and validation studies. The abstract can be copied from a Word document and pasted into this field.

3. What information about the specimens is needed?

- You will need to know whether the specimens are newly collected or previously collected.
- 4. What is meant by “newly collected” vs. “previously collected?”**
- Newly collected specimens are those that are actively being collected under the protocol. Previously collected specimens are those that were collected under a previous protocol and are being used for the current protocol.
 - If the protocol involves collecting new specimens, then the EDRN specimen processing questions must be answered:
 - ✓ Type of specimen collected (e.g. Blood, Bone marrow, Urine, Tissue, etc.)
 - ✓ Type of specimen stored (e.g. Whole blood, DNA, RNA, Plasma, etc.)
 - ✓ Temperature of original sample prior to processing:
 - ✓ Approximately how long was the original sample maintained at the above temperature:
 - ✓ Temperature of specimen during processing:
 - ✓ Elapsed time from collection to final storage:
- 5. What if I don’t know how the specimens are/were processed?**
- The answers to these questions must be written in the study protocol. If the protocol involves the use of previously collected specimens, the answers to the specimen processing questions are optional, but if the information is known, please provide it.
- 6. What is a Single Site Study?**
- A Single Site Study is a study that is conducted with EDRN funds and involves only one EDRN site. Non-EDRN sites may or may not be involved in the study.
- 7. What is a Collaborative Study?**
- A Collaborative Study is a study conducted with EDRN funds in which more than one EDRN site is involved. Non-EDRN sites may or may not be involved. Collaborative studies include studies conducted for the purpose of assay validation. There are two types of Protocol Registration for Collaborative Studies. Pre-Registration and Registration.
- 8. What is a Network Approved Collaborative Study (eg., Validation Study, Standard Specimen Reference Set)**
- A Network Approved Collaborative Study is a study conducted with EDRN funds for the purpose of clinical validation of a biomarker. By definition, the study will include more than one EDRN site. At a minimum a Validation Study must include the DMCC and at least one BDL.

7.2 Search Protocols

To **SEARCH** for information on a registered protocol:

🔗 Click on the [Search EDRN Protocols](#) link, then select the EDRN Site, Study Type, Specimen Collection or Study Cancer Type from the appropriate drop-down list and the search results will display.

Figure 7.1 – Search EDRN Protocols

7.3 Lead PI Updates

Figure 7.2 – Lead PI Updates

To UPDATE a protocol that you are the Lead PI for, Click “Leading PI Updates” then select your protocol from the drop down list and supply answers to the following questions:

- Protocol/Project Design Type
- Protocol/Project Study Design Description

- Protocol/Project Timing
- Objective
- Specific Aims
- Eligibility Criteria
- Abstract
- Is there a Data Sharing Plan? Explain
- Blinding Policy? Explain
- Field of Research
- Analytic Method
- Biomarkers Evaluated (list)
- Finish Date
- Final Sample Size
- Results Outcome

7.4 Involved/Lead PI Updates

Figure 7.3 – Involved/Lead PI Updates

The screenshot shows the EDRN Protocol website interface. At the top, there is a header with the EDRN logo and the text 'Search, Register, Update and Report EDRN Protocol'. Below the header, there are two dropdown menus: 'Collaborative Activity Report' (set to 'EDRN PI List') and 'Back to:' (set to 'Web Site List'). A navigation bar contains links for 'Quick Search EDRN Protocols', 'Detail Search EDRN Protocols', 'Leading PI Updates', and 'Lead & Involved Investigator Updates'. A message says 'Please select a function from the menu.' Below this is a table of menu items:

Quick Search EDRN Protocols	Select from four fields to quickly find basic Protocol & Project information.
Detail Search EDRN Protocols	Create custom searches to find exactly the Protocols and Projects of interest.
Leading PI Updates	Update the Protocol or Project information abstracted from documentation supplied to the DMCC.
Lead & Involved Investigator Updates	Update the Protocol or Project information for each involved investigator's site & supply milestones, comments, dates and other specifics of your research.
Request initialization of new protocol	The DMCC initializes all EDRN Protocols and Projects by entering some "shell" information obtained from approved proposals. The lead PI is able to view the information and request changes if needed.

A red arrow points to the 'Lead & Involved Investigator Updates' link. At the bottom of the page, there is a footer with the text: 'Secure site maintained by COMPASS, Fred Hutchinson Cancer Research Center ©. Last updated on 3/2/2011' and 'Contact: edrmdmcc@fhcrc.org'.

To UPDATE a protocol that you are involved with, regardless of whether or not you are the Lead PI, ☞ Click “Lead & Involved Investigator Updates” then select your protocol from the drop down list, then select your site and supply answers to the following questions:

- IRB Approval Information
- Contact Information
- Select the “Roles” your site will have in the protocol
 - Funding Source
 - Discovery

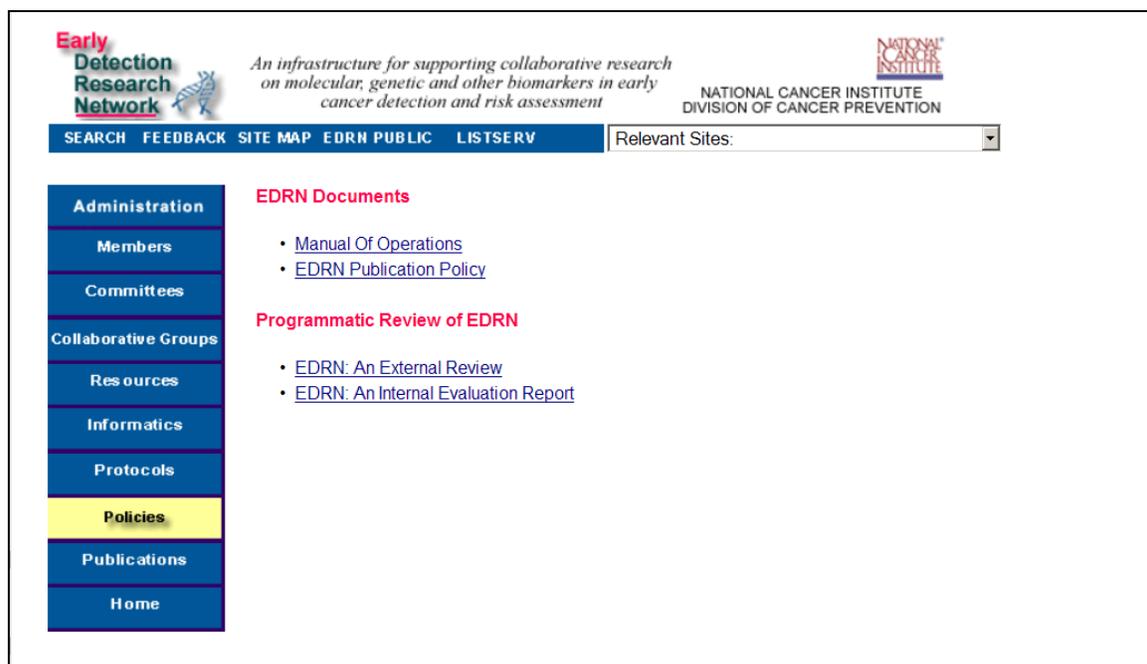
- Reference
- Coordinating Center
- Specimen Contributing Site
- Specimen Storage
- Analysis Lab
- Statistical Services
- Consultant
- Specimen the stages your site will be involved in throughout the protocol
 - Development Stage
 - Funding Stage
 - Protocol Development Stage
 - Procedure Development Stage
 - Retrospective Sample Identification Stage
 - Recruitment Stage
 - Lab Processing Stage
 - Blinding Stage
 - Lab Analysis Stage
 - Statistical Analysis Stage
 - Publication Stage
 - Completed

Subsequently, for each role/stage supply milestones for estimated start/finish dates and actual start/finish dates.

SECTION 8 POLICIES

The EDRN Policies section of the website displays the EDRN Manual of Operations and the EDRN Publication Policy.

Figure 8.1 – Policies



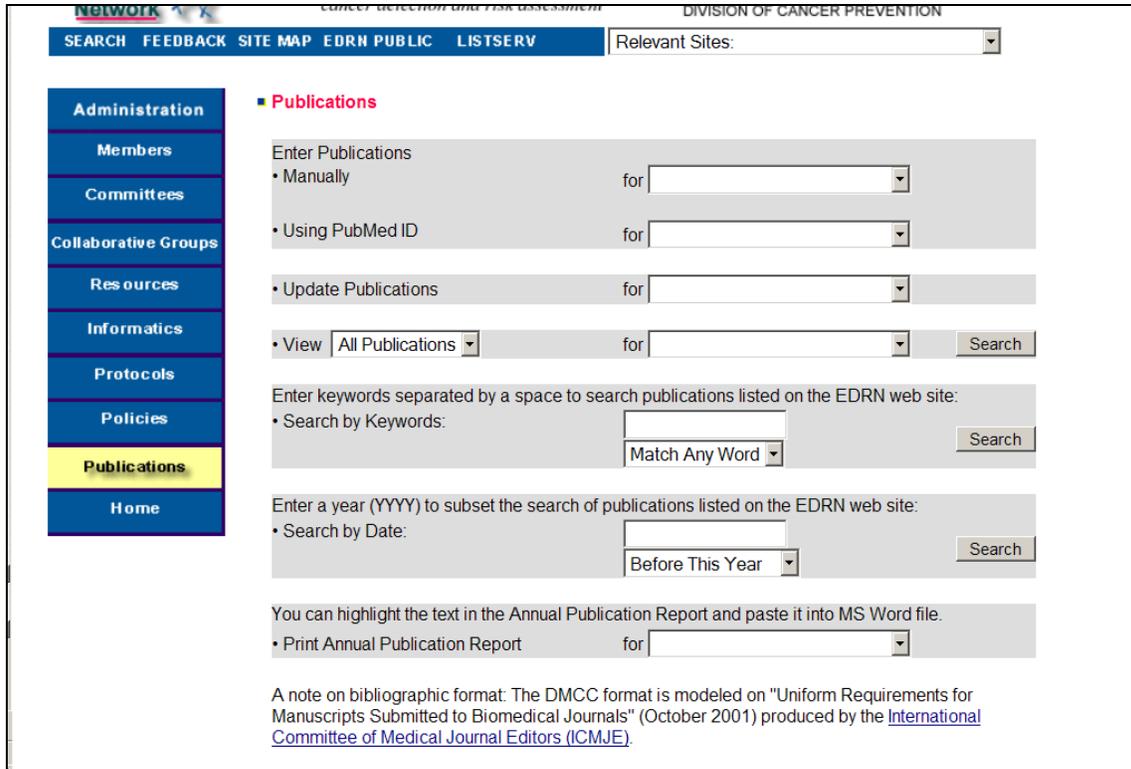
SECTION 9 PUBLICATIONS

The EDRN Publications section of the website allows EDRN members and NCI to easily find out about published activities in EDRN. Sites can also print or download their information into a Word document to include in their annual Progress Report to NCI.

Each site is responsible for entering and maintaining their EDRN publication information.

To **ENTER, UPDATE or VIEW** publications  click on the blue **Publications** button on the left of the page. You may enter your publications by PubMed ID or manually.

Figure 9.1 – Publications



SEARCH FEEDBACK SITE MAP EDRN PUBLIC LISTSERV Relevant Sites:

Publications

Enter Publications

- Manually for
- Using PubMed ID for
- Update Publications for
- View for

Enter keywords separated by a space to search publications listed on the EDRN web site:

- Search by Keywords:

Enter a year (YYYY) to subset the search of publications listed on the EDRN web site:

- Search by Date:

You can highlight the text in the Annual Publication Report and paste it into MS Word file.

- Print Annual Publication Report for

A note on bibliographic format: The DMCC format is modeled on "Uniform Requirements for Manuscripts Submitted to Biomedical Journals" (October 2001) produced by the [International Committee of Medical Journal Editors \(ICMJE\)](#).