# PLCO EEMS Application Process

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## REGISTRATION

In order to apply for access to PLCO Biospecimens, you must first register with the Cancer Data Access System (CDAS). You may establish your username/password at one of the following login services:

- IMS Public Login Service
- The Cancer Imaging Archive (TCIA) Login Service

Unless you have previously established credentials at TCIA, it is suggested that you use the IMS Public Login Service.

## EEMS APPLICATION FOR BIOSPECIMENS

If you have your own source of funding and wish to obtain PLCO biospecimens, then you should register with CDAS and begin the EEMS Application for Biospecimens. This process involves submission of a preliminary and full application (including full research proposal) and peer review. It typically takes 4-6 months from application submission to review outcome. The steps are as follows:

1. **Check for Duplicative Research**

   Before submitting a preliminary application, you should first check the approved PLCO Projects to be sure that you are not proposing a project similar to one that has already been approved.

2. **Prepare and Submit a Preliminary Application**

   Once you are logged in to CDAS, you can prepare and submit a Preliminary Application. This involves the following steps:

   - **Agree to the Usage Policies**. In particular, you must agree not to identify or contact any patients or physicians whose information is contained in the data. You must also agree to publicly display the abstract of your research proposal and your contact information (provided in your application) on this website.
   - **Complete your Project and PI information**. You must provide contact information for your Principal Investigator, as well as project information such as a title, brief description, and aims.

- **Complete your Case Definitions.** You must select all case definitions that apply, and fill in any information that applies to each one, such as your requirements and distributions.
- **Define your Controls and Matchings.** You must state how many controls you need, specific requirements, and variables you plan to match on.
- **Indicate your Specimen Requirements.** You must select all types of specimens you would like. Each specimen type has other information you must provide, such as amount.

The Preliminary Application is designed to collect all relevant information that will determine which participants have adequate materials for your study. If you find there are questions that you do not understand or do not know immediately, submit the Preliminary Application completed to the best of your ability and we will work with you to better define the details.

**3. Await review of Preliminary Application**

Once your Preliminary Application is submitted, it will be reviewed based on the following criteria:

- **Feasibility.** A determination will be made regarding the project feasibility and whether specimen samples that meet your requirements are available.
- **Resubmission.** If your application is a resubmission of a previously submitted and reviewed project, it will be verified that you will address concerns from the previous reviews in your full application.
- **Duplication.** It will be determined if your proposed project duplicates effort that has been previously approved.

While you are waiting for your Preliminary Application to be evaluated, you may wish to:

- **Download the Research Plan.** If your Preliminary Application is approved, then you will be asked to complete a research plan. As part of your research plan, you must provide the specific aims of your project, your research strategy, justification for use of PLCO samples, justification for sample quantity, a quality control plan, and a list of publications pertinent to your proposed research. You may wish to get started on this prior to the preliminary application approval.
- **Obtain NIH Biosketches.** If your Preliminary Application is approved, you will be asked to upload an NIH biosketch for each member of your investigative team. It is best to have all of these documents ready for upload as soon as possible.

Estimated time: 1-2 weeks

4. **Submit a Full Application**

   If your Preliminary Application is approved, you will be asked to submit a Full Application. This is an extension of the Preliminary Application that asks you to provide:

   - **Research Plan.** You must provide the specific aims of your project, your research strategy, justification for use of PLCO samples, justification for sample quantity, a quality control plan, and a list of publications pertinent to your proposed research.
   - **Investigative Team.** You must list all members of your investigative team and upload an NIH biosketch for each member.

5. **Await review of Full Application**

   Once your Full Application is submitted, it will be reviewed to determine if it is complete and suitable for review by the EEMS Review panel. If so, it will be assigned to several peer reviewers. Following peer review, your application will either be (1) Approved, (2) Not-approved, or (3) Returned for Clarifications. If your proposal is approved, you may continue to the Post-Approval section.

   Estimated time: 2 – 4 months

6. **Submit clarifications based on EEMS Panel Review**

   Based on comments received from the EEMS reviewers, you may be asked to provide clarifications to your proposal. You may revise your Full Application to address any issues and submit your final application for a final review.

   Estimated time: 1 week

7. **Await review of Final Application**

   Once your Final Application is submitted, it will be reviewed to determine if the EEMS reviewer's concerns have been met appropriately. If your proposal is approved the Post-Approval process will begin. Details are provided in the Post-Approval section of this document.

   Estimated time: 2-4 weeks

First letters of approval typically are sent 6 months after the opening of the preliminary application.

# POST-APPROVAL

1. **Phase 1: Selection and administrative paperwork**

   In this phase, the biospecimens for your approved project will be identified and you will complete a number of required forms. This process is most efficient if you start by having an initial meeting or teleconference with CDAS staff. After that consultation, CDAS staff will begin to select study participants and appropriate biological samples. Simultaneously, you will complete the Specimen Use Request Form (SURF) and obtain all relevant regulatory documents. To increase efficiency, we strongly recommend that you complete Parts 1-3 below concurrently. Upon completion of these three tasks, CDAS staff will generate a document that summarizes the selected samples. This document will then be evaluated by NCI staff to ensure that the selection matches the approved application and adheres to PLCO biospecimen guidelines.

   Estimated time for phase 1: 2-4 months

   - **Part 1: Population Selection:** You will work with CDAS staff to identify the particular study participants for inclusion in your study (your study population). Selection will usually include identifying cases as well as a matching set of controls that are selected using the criteria proposed in your approved application. CDAS staff will create a detailed report of the selection that will require your approval before moving forward. Once the population is finalized, specific vials of biospecimen will be identified for each included participant. (estimated time: 1-3 months)

   - **Part 2: Specimen Use Request Form (SURF):** While the population selection programming is ongoing, you will be provided and asked to complete the SURF form that details your sample handling requirements, such as batching, requirements for specific tubes, QC requirements and other sample handling requests. (estimated time: 1 week)

   - **Part 3: Regulatory Documents:** In addition, there are a number of regulatory documents that must be obtained and uploaded to CDAS prior to sample requisition and shipment. All extramural investigators are required to obtain approval from their local IRB. NCI staff will use this approval to then gain required approval from NCI's Special Studies IRB (SSIRB). Furthermore, a Material Transfer Agreement (MTA) must be completed. Extramural investigators will be contacted by a member of the NCI Technology Transfer Center (TTC) to start this process. MTAs are not needed for projects conducted by NIH employees, including intramural Investigators, who will establish federal contracts with assaying labs. However, SSIRB and MTAs are needed for

collaborations in which there is not a specified contract. (estimated time: 1-2 months)

- **Part 4: Impact Analysis:** Once the vials are selected, CDAS staff will run a final Impact Analysis that will summarize the selection. The final impact analysis allows the NCI to ensure that selections match the approved application, and that all EEMS biospecimen use guidelines have been followed. The final impact analysis will be reviewed and approved by the NCI before your project can move forward. CDAS staff will also verify that all necessary regulatory documents have been obtained. (estimated time: 2 weeks)

2. **Phase 2: Sample Handling** (**requisition, aliquoting, and shipment)** – The amount of time required for sample requisition and processing varies substantially by project. Factors that influence this phase include, but are not limited to, the number of samples, the complexity of processing requirements, and the existing queue of jobs at PLCO core laboratories. (estimated time: at least 2 months, may take significantly longer)

    - **Sample Requisition:** CDAS staff will submit sample requisitions that direct the NCI biorepository to pull the samples for your study, and have them shipped to the processing lab. (estimated time: at least 1 months, again may take longer)

    - **Sample Processing:** Next, the samples in your study will be processed according to your instructions on the SURF form and PLCO guidelines, e.g. serum aliquoted, DNA extracted, samples blinded and batched, etc…. The information contained in the SURF form will be used to direct the processing labs and you will be informed as each step is completed. Once processed, the blinded samples will be sent to your analytic lab. (estimated time: at least 1 month, again may take longer.)

3. **Phase 3: Analysis** – After generating your data, you will submit your results back to CDAS staff through the CDAS website. They will then unblind them and provide you with an analytic dataset that includes appropriate covariate data. To expedite this process, please complete a DTA agreement, if needed, prior to submitting your data. Having a DTA agreement in hand will allow you to receive your analytic file as soon as it's prepared. (estimated time: 2-4 weeks)

    - **Data Transfer Agreement (DTA):** For extramural investigators, you and an authorized signatory from your institution must sign a DTA prior to the release of PLCO covariate data. DTAs must be completed to ensure the confidentiality of study participants. NIH personnel are not required to complete a DTA but must

instead agree electronically to the CDAS Data Use Policies if they have not done so already. If there are collaborators at other institutions, a DTA will need to be completed for each institution requiring access to the data. DTAs must be submitted to CDAS staff and will ultimately be signed by an NCI representative. DTAs may be submitted at any time post-approval. However, since they expire after three years, it is recommended that you wait until you are ready to receive the data to submit them. (estimated time: 1-4 weeks)

- **Data Submission:** Once your assays have been run and your data has been generated, you must submit the raw data to CDAS staff in order for them to un-blind your samples. In addition to raw numbers, you must supply all other information necessary for other researchers to understand and correctly interpret the results, such as units of measurement, platform, etc. For more information, please see the EEMS Data Return and Data Sharing Policy section of the EEMS Policies and Procedures. An exception is made for Genome Wide Association Studies (GWAS) and other types of large-scale genomic studies (e.g. whole exome sequencing) where such datasets must be submitted to the NIH database of Genotypes and Phenotypes (dbGaP). (estimated time: 1 week)

- **Analysis File Delivery:** CDAS staff will merge lab results with PLCO covariate data and deliver a SAS dataset (or other specified format) to you to conduct your analysis. Results from QC assays will be delivered in a separate adjoining dataset. These datasets will be delivered via a secure data portal. (estimated time: 1 week)

## ADDENDUMS

You may submit addendums to request small changes to the specifications of your project, or for related pilot or small-scale follow-up analyses. All submissions will be reviewed by the EEMS Steering Committee and, depending on your changes, may require submission of a new full application. Addendums submitted after the original study samples have been selected and requisitioned may require new or updated regulatory documents (see above).

## PROGRESS REPORTS

Once a year, the CDAS system will prompt you to complete a progress report in CDAS in which you will update NCI staff about the status of your project. Progress reports are not required for completed or withdrawn projects. In order to ensure compliance, you will receive regular emails from CDAS until you submit your progress report. Repeated failure to respond in a timely fashion will adversely affect your ability to use the PLCO resource.

## SUNSETTING

In order to ensure that PLCO samples benefit the scientific community in a timely fashion, PIs are required to initiate Phase 1 of their project within three years of approval. Investigators will therefore be reminded of this requirement at year two, year two and a half, and year three after study approval. If the PI has not initiated their study by year three, then their project will be administratively withdrawn.