Form B: Medical IRB Research Description

1. Background:

The Center for Clinical and Translational Sciences (CCTS) has as its overarching goal to increase the pace, effectiveness, and quality of translational research at UK and in the surrounding Appalachian community, which will ultimately result in better health for the citizens of this region. To better accomplish this mission, the CCTS, developed a biospecimens bank and research registry that will provide tissues and associated clinical information to investigators utilizing the Enterprise Data Trust (EDT) Clinical Data Warehouse.

The CCTS biobank uses specimens that are discarded as part of normal clinical care. For example, blood and DNA samples will be collected from blood samples that are discarded several days after phlebotomy. Other samples will be collected from surgery, outpatient procedures, and other clinical settings.

This is a long-term, collaborative protocol involving the CCTS and additional partner biobanks intended to build a robust bank of biospecimens and DNA with links to clinical information that can be used by investigators to answer questions about fundamental biology of human biospecimens and to study disease pathophysiology, treatment, and epidemiology. Inherent in this research process is the protection of the privacy of the potential participants.

Current hospital consent forms acknowledge that the University of Kentucky Health Care system is a research intensive institution and that there is the potential for the conduct of research on their samples. This is also described in the educational mission of UK and the fact that students and residents may be in attendance.

Under protocol 13-0219-F6A: Development of a Biobank and Research Registry at University of Kentucky, the CCTS has received IRB approval for the primary biobank and its consenting process described below:

Consenting procedures. Informed consent is obtained at the time of registration for the use of discarded samples from patients for use in a deidentified manner with the enclosed consent form. CCTS engages patients in the consenting process at registration for several reasons. All patients sign a “consent for treatment” form upon admission to the hospital as an inpatient, and once per year in the outpatient setting. This requirement provides an appropriate setting for the additional consent for sample collection without a significant interruption in work flow. The patient is less stressed at registration than later, after medical encounters, and is better prepared to make an informed decision. In addition, this consenting method fits with the strategy of obtaining discarded biospecimens. The patient is giving consent in advance to something that may/may not happen. CCTS personnel clearly do not have the resources to collect every sample from every patient, and from some patients there may not be any discarded/leftover samples. Therefore, the only practical method to obtain consent is to request it at the time of registration, prior to any medical interventions.

It is important to accurately determine which patients have/have not consented for this registry. At present, a patient signs the “consent to treat” on paper, and the registration clerk makes an electronic notification in the Enterprise Patient Index (ePI) system that is used for registration and appointments. The Enterprise Data Trust (EDT) through ePI pulls consent information into the warehouse and creates a date and timestamp. This information is used in a dashboard for the CCTS procurement specialist. In this way, the specialist can verify consent for biobanking quickly, soon after registration, which allows a method for verifying consent prior to obtaining a sample. When a patient gives consent for banking leftover samples, the CCTS considers this consent valid indefinitely unless proper withdraw procedures are initiated by the patient.

Form B: Medical IRB Research Description

In this application, we ask to link our protocol to CCTS so that we may use the existing infrastructure developed for consent, consent verification, documentation, and procurement, attached is our waiver of informed consent. Our protocol requires samples to be obtained within 24 hours so that cells can be obtained. The CCTS is unable to completely deidentify the biospecimen and its clinical data according to the HIPAA safe harbor method described in the EDT protocol 11-0750-F6A. The date the specimen was obtained will always be known since the sample must be dispersed within 24 hours; therefore, our justification for the identified data and sample is described in the protocol below, but we will utilize the CCTS consent process and procurement procedures as described in their protocol 13--0219-F6A.

[brief explanation as to why cells are needed within 24 hours]

2. **Objectives:** List your research objectives. You may reference grant application/sponsor's relevant protocol pages and attach as an appendix.

3. **Study Design:** Describe the study design (e.g., single/double blind, parallel, crossover, etc.). Indicate whether or not the subjects will receive placebo medication at some point in the research procedures. Also, indicate whether or not the subjects will be randomized in this study. You may reference sponsor's protocol pages and attach as an appendix. (Including the study design table from a sponsor's protocol is helpful to IRB members.)

   Community-Based Participatory Research: If you are conducting community-based participatory research (CBPR), describe strategies for involvement of community members in the design and implementation of the study, and dissemination of results from the study.

   Research Repositories: If the purpose of this submission is to establish a research repository describe the repository design and operating procedures. For relevant information to include, see question 22 of the UK IRB "Frequently Asked Questions (FAQs) on the Return of Research Results or Incidental Research Findings" [PDF].

4. **Study Population:** Describe the characteristics of the subject population, such as anticipated number, age range, gender, ethnic background and health status. Identify the criteria for inclusion and exclusion. Explain the rationale for the use of special classes such as fetuses, pregnant women, children, institutionalized, adults with impaired consent capacity, prisoners or others who are likely to be vulnerable. If women or minorities are included, please address how the inclusion of women and members of minority groups and their subpopulations will help you meet your scientific objectives. Exclusion of these groups requires clear and compelling rationale that shows inclusion is inappropriate with respect to the health of the subjects or that inclusion is inappropriate for the purpose of the study. Cost is not an acceptable reason for exclusion except when the study would duplicate data from other sources. Women of childbearing potential should not be excluded routinely from participation in clinical research.

   Provide the following information:

   - A description of the subject selection criteria and rationale for selection in terms of the scientific objectives and proposed study design;
   - A compelling rationale for proposed exclusion of any sex/gender or racial/ethnic group;
   - The proposed dates of enrollment (beginning and end);
   - The proposed sample composition of subjects.
   - You may reference grant application/sponsor's relevant protocol pages and attach as an appendix.

5. **Subject Recruitment Methods and Privacy**:

As described above, patients will be enrolled at the time of registration and at the time they also sign the consent for treatment. The consent for biobanking will be valid indefinitely, unless the patient requests withdrawal.

6. **Informed Consent**

Waiver of informed Consent Request

Since the research team will not have contact with the patient and the CCTS biobank has already obtained consent through the registration process, we are requesting a waiver of informed consent. CCTS consent process is listed below.

CCTS consent process

The goal of the informed consent process is to provide people with sufficient information so they can make informed choices about whether to participate in this biobank registry. The informed consent document provides a summary of the biobank registry and the individual's rights as a research participant. Also, research participants and their families may use the consent document as an information resource and reference throughout participation in this biobank registry. The subject should read and consider the statement before signing and dating it, and should be given a copy of the signed document. If the subject cannot read or sign the documents, oral presentation may be made or signature given by the subject's legally appointed representative, if witnessed by a person not involved in the study, mentioning that the patient could not read or sign the documents.

Because the consenting process will be handled by registration clerks, who have no specific role in the research, there will be no risk of undue influence or coercion. The registration clerks will be educated about the biobank/registry and the use of the biospecimens such that they will be able to answer simple questions from patients. In addition, a brochure will be available in waiting rooms for patients to read, and these brochures will be offered to patients to take home. On the brochure, a toll-free phone number will be provided for the patient to call with questions. This number will be staffed by personnel of the CCTS and Markey Cancer Center.

Consent forms will be available in English and Spanish. Illiterate potential participants will have the document read to them in its entirety and have their questions answered prior to consent.

7. **Research Procedures:**

No procedures will be performed that are not a normal part of clinical care. Only discarded biospecimens will be collected.

[Describe why cell collection is needed with 24 hours and what will be completed.]

8. **Resources:**

Project Resources

[Describe project specific resources/facilities that are available to perform the research (i.e., staff, space, equipment)]

CCTS Resources

The CCTS and Markey Cancer Center devote significant personnel and equipment to this effort. Several freezers were purchased for sample storage and these freezers are located in the CCTS laboratory. Significant Biomedical Informatics and Markey Cancer Center Informatics expertise and software was implemented to manage the data. Personnel from both Centers are devoted to retrieving and storing samples.

EDT honest broker(s) are not part of the clinical or research team. The IRB recognizes the EDT as a third party "honest broker" and has approved the EDT deidentification scheme in UK IRB protocol 11-0750-F6A, entitled, "Umbrella IRB for Use of Health Information in the CCTS Enterprise Data Trust- UK HealthCare dataset."

EDT honest broker services for researchers include:

- Work with the Biobanking Executive Steering Committee to receive research requests for access to data held in the EDT
- Determine feasibility for research access requests
- Provide advice to EDT Access Applicants on the necessary approvals prior to release of data
- Extract data required for the approved research request
- Removes all protected health information denoted in the HIPAA regulations, to provide the researcher with a deidentified data set for analysis
- Retain a crosswalk table for linkage of data, but does not release this information to the researcher
- Reverse linkage of data with proper approvals
- Provide linkage of data and assure the integrity of the linkage
- Perform data quality assessments when necessary
- Distribute data to users on an ad-hoc basis or as an automated regular basis
- Manage data transfer between clinical and research systems
- Maintain reference data for researcher to support future analysis of data provided
- Audit compliance of researcher recipients with terms and conditions associated with EDT Access Application approvals

Oncore, a software Inventory management program, is used for the biospecimen registry inventory management. The registry is not maintained by the EDT; however, to link clinical data with biospecimen information, the EDT will transfer data from the Oncore database to determine feasibility of research studies.

9. **Potential Risks:**

There is no risk from the procedures, since all biospecimens are obtained for routine clinical purposes.

Our research team will sign the CCTS biobank data use agreement (DUA). We are bound by the signed data use agreement on usage of the data being viewed. Researchers attest to not disclosing, loaning, duplicating, or sharing with individuals or institutions information without the written permission of the EDT.

With any kind of biobank/registry, new research findings could provoke the question of whether or not a patient/family member should be contacted. This is a controversial subject that is not

readily resolved by current guidelines. In most instances, investigators are studying diseases or physiological processes, using non-CLIA certified lab techniques, and the research findings will not be of clinical relevance to the patient or his family. However, a situation could arise where potentially actionable research findings could present an ethical challenge. In the CCTS consent form, the patient is specifically told that they **will not be recontacted**. However, if an investigator presents the Biobanking Executive Steering Committee with data which suggests that a humanitarian intervention may be warranted, then the CCTS Research subject advocate will present this information to the IRB for adjudication.

10. **Safety Precautions:**

The safety precautions for protecting privacy and confidentiality are described above.

11. **Benefit vs. Risk:**

There are no direct benefits to the subjects. There are tremendous potential benefits for advancement of knowledge from developing a biospecimens bank linked to clinical information. This proposal will greatly accelerate the pace of translational research at UK. The risks to the subjects are minimal because the probability there could be a breach is very small and all patients will sign consent for use of their samples.

11. **Available Alternative Treatment(s):**

The alternatives to this study are to not participate. The care of the patient will never be compromised by non-participation.

12. **Research Materials, Records, and Privacy**

The CCTS/Markey biobanking program maintains the right to keep, preserve, use and dispose of the findings of this protocol in accordance with institutional guidelines. The appropriate offices of the federal government (e.g. OHRP) maintain the right to inspect the records of the study at any time. Investigational records from this study will be maintained in a confidential manner; subject names will not be associated with any published results.

13. **Confidentiality:**

During and after this study, the participants' identities will be kept confidential to the extent permitted by law. Patients will be identified by a code, and, except as set forth below, personal information from subjects' records will not be released to any third party without written permission. Subjects will not be personally identified in any publication or presentation about this study. However, the records may be reviewed, under the guidelines of the Health Insurance Portability and Accountability Act (HIPAA), by the FDA, United States Department of Health and Human Services. Additionally, local site personnel, agents of the University of Kentucky, the Institutional Review Board may review the biobank records including those with identifying information. The information may be disclosed if the recipients described above are not required by law to protect the privacy of the information.

14. **Payment**:

There will be no charge to the patients for their participation, and they will receive no compensation.

Form B: Medical IRB Research Description

15. **Costs to Subjects**:

There will be no costs to the subject. Samples are collected as part of normal clinical care, so injury to the subjects from clinical care will not affect this research study. In the event of complications, injury or illness requiring emergency medical treatment resulting from participation in this study, appropriate acute medical care will be provided, however, the Principal Investigator and this institution have made no provision to reimburse the subject for the cost of medical care beyond emergency medical treatment or to pay for any lost wages, pain and suffering, hospitalization, or other expenses may occur as the result of any such complication, injury or illness.

16. **Data and Safety Monitoring:**

As described above, the CCTS/Markey Biobanking Executive Steering committee will provide overall guidance for the Core, interact with the IRB and handle problems that may arise. One member of this committee will be the CCTS Research Subject advocate, one will be a statistician, and one will be a member of the IRB. This committee will be charged with ensuring that policies and procedures are in place to protect patient interests and to review the requests for biospecimens.

This committee has reviewed our protocol and has advised that our study needs its own IRB approval, however, we may use the CCTS infrastructure and consenting process if agreeable to the IRB.

17. **Subject Complaints:**

In addition to the procedures described in the consent form, subjects will be encouraged to voice complaints. Contact information for the CCTS Research participant advocate will be given to anyone with a complaint. If the patient's questions/complaints cannot be satisfied, the patient will be asked to contact the IRB.

18. **Research Involving Non-English Speaking Subjects or Subjects from a Foreign Culture:**

Only individuals who have adequate English/Spanish speaking/readings skills will be studied.

19. **HIV/AIDS Research:**

Universal precautions will be used with all samples. Samples from patients with HIV will be collected along with samples from patients with other illnesses.

20. **PI-Sponsored FDA-Regulated Research:**

N/A

Form B: Medical IRB Research Description

Principal Investigator:	Date:
Study Title:	[13-0219-F6A: Development of a Biobank and Research Registry at University of Kentucky] **[insert project name]**

Form E
Include in IRB Application to
Waive Requirement for Informed Consent

If you are requesting IRB approval for waiver of the requirement for the informed consent process, or alteration of some or all of the elements of informed consent (i.e. medical record review, deception research, or collection of biological specimens), complete Section 1 and Section 2 of this form and include it with your IRB application submission.

Note: The IRB does not approve waiver or alteration of the consent process for research that is subject to FDA regulations, except for planned emergency/acute care research as provided under FDA regulations. Contact ORI for regulations that apply to single emergency use waiver or acute care research waiver (859-257-9428).

SECTION 1

Check the appropriate item:

✠	1) I am requesting waiver of the requirement for the informed consent process. For **[insert project name]** utilizing the CCTS biobank
☐	2) I am requesting alteration of the informed consent process. *If you checked the box for this item, describe which elements of consent will be altered, and/or omitted, and justify the alteration.*

SECTION 2

The IRB may consider your request provided that **all** of the following conditions apply to your research and are appropriately justified. Explain in the space provided for each condition how it applies to your research.

a) The research involves no more than minimal risk to the subject.

The waiver of informed consent is for **[insert project name]** utilizing the CCTS biobank. Since the CCTS Biobank already exists, and no interactions or interventions are being conducted under the researcher's protocols accessing the biobank, the individual research projects accessing the data ***does not rise to the federal definition for human subject research.***

There are no foreseeable risks as these are retrospective studies using existing data and discarded clinical samples. No patient interaction will occur by the researchers and they will be unable to consent patients for participation.

b) The rights and welfare of subjects will not be adversely affected.

There are no foreseeable risks as these are retrospective studies of existing data.

c) The research could not practicably be carried out with out the waiver or alteration.

The waiver of informed consent is for building the **[insert project name]** utilizing the CCTS biobank. Since the CCTS Biobank data already exists, and no interactions or interventions are being conducted under the researcher's protocols accessing the registry, the individual research

projects accessing the data ***does not rise to the federal definition for human subject research.***

There are no foreseeable risks as these are retrospective studies using existing data and discarded clinical samples. No patient interaction will occur by the researchers and they will be unable to consent patients for participation.

d) Whenever possible, the subject will be provided with additional pertinent information after they have participated in the study.

In the CCTS consent form, the patient is specifically told that they **will not be recontacted**. However, if an investigator presents the Biobanking Executive Steering Committee with data which suggests that a humanitarian intervention may be warranted, then the CCTS Research subject advocate will present this information to the IRB for adjudication.