Instructions for Completing the PRO SmartForm with Biospecimen/Tissue Bank Requests

This document was developed to assist the MCW/FH research community in completing the IRB application for protocols utilizing de-identified human tissue.

Guide includes screenshots, question explanations, and commentary. Please contact the IRB Office (414-955-8422) with any specific questions about your project.

Jan. 12, 2017

1. Project Identification

1.0 * **Does this project involve any minor subjects, or use of records or biospecimens related to minors?** Minor status is defined by the legal age of consent for the state or country where the research activity takes place; e.g., under 18 years of age in Wisconsin.

(select one)
- ○ All minors
- ○ Some adults and some minors
- ◉ **All adults of legal age**

☐ **If you selected "All minors" or "Some adults and some minors" above, you must consult with the MCW/FH IRB Office (414-955-8422). Check the box to confirm that you have done so and have been advised to submit this project to the MCW/FH IRB.**

Policies, procedures, forms and additional information are available on the IRB/HRPP website.

For assistance in completing the PRO SmartForm, please see the Instructions for Completion of the Study SmartForm.

1.0 Self-explanatory

1.1 * **Short Title:**

Functional analysis of HHV-6 gene products

***1.1** This title should contain key words used to identify your study.*

1.2 * **Full Title of Project:**

Functional analysis of HHV-6 gene products

***1.2** The formal title. This is the title that will appear on correspondence from the IRB.*

1.3 * **Principal Investigator (PI):**

1.3.1 * **Does the Principal Investigator, their immediate family members (spouse and dependent children) or their significant other have a "Significant Financial Interest" with the sponsors of this research or that might affect the result of this research?**
○ Yes ◉ **No**

If Yes:
☐ **1.3.1.1 Has this interest already been fully reported to MCW Grants and Contracts Office or MCW Corporate Compliance?**

If not, immediately update this financial interest information using the MCW Corporate Compliance form for this purpose.

***1.3** How to add a PI*
Must be an MCW faculty member, a person designated as "CTSI scientist", or a Froedtert nurse. See IRB SOP on Requirements and Qualifications to serve as a PI.
An investigator may not be a Principal Investigator until training is completed.

***1.3.1 IRB SOP:** Conflict of Interest for Investigators and Study Team Members*

1.4 * **Provide phone/pager number in case of an emergency and/or if the IRB Committee has questions during the Committee meeting:**
414-510-8280

1.5 * **Will there be other project team members in addition to the Principal Investigator (PI)?**
○ Yes ◉ **No**

***1.5** Other Project Team Members include those defined as:*
- *Key Personnel*
- *Other Administrative or Project Staff*
- *Community Partners*

3. Project Category

3.1 * **Which category best describes the type of project you are submitting for review?**

(select one)

- (•) **a) Research study - including clinical trials, retrospective record reviews, specimen reviews, surveys, etc.**
- ( ) b) Research study plus distant bank. No banking at a local study site
- ( ) c) Research study plus creating a new local bank; at least one at a local study site *Note: see 3.1.1 below
- ( ) d) Creating a new Local Bank - no research study being proposed in this submission
- ( ) e) Treatment Use: Use of investigational drugs, medical devices, biologics or Humanitarian Use Devices (HUDs) solely for clinical purposes with no elements of research or research data collection
- ( ) f) Emergency Use: use of an investigational drug, medical device, biologic or Humanitarian Use Device (HUD) – after-the-fact report to the IRB
- ( ) g) Deferral to NCI CIRB - for Cancer Cooperative Group (RTOG, ECOG, SWOG, etc.) studies in which the NCI CIRB will be the IRB of record

3.1 *A protocol is required to be uploaded in section 52.*

3.1 *Local study sites are defined as MCW, FH, CHW, or BCW.*

3.1b & c *If the research project includes a study, a distant bank, and a local bank, check c) study plus new local bank.*

3.1d *Project is collecting data and/or specimens for future unspecified research.*

3.1e *Treatment Use is also often called "Compassionate Use".*

3.1e *If the investigator plans to collect data according to a Sponsor's protocol, for example, the IRB considers the activity to be a "research project."*

3.1f *Emergency use must be reported to IRB within 5 days.*

3.1.2 * **Is this research study designed to evaluate the safety or effectiveness of some form of research TREATMENT/intervention?**

(select one)

- ( ) YES
- (•) **NO**

3.1.2 *Research Treatment is defined here as any intervention for an illness, disorder, or unwanted behavior or condition. Educational, psychosocial, or community interventions designed to make changes e.g., improve knowledge, change attitudes, or lead to better access to care are also considered "research treatments."*

3.2 **Does the research involve:**

(select all that apply)

- [ ] Drug: FDA-approved, investigational, or other
- [ ] Device: FDA-approved, 510(k), investigational, HUD, or other
- [ ] Biologic: FDA-approved, investigational, or other
- [ ] Botanical, medical food, or dietary supplement
- [ ] None of the above

3.2 *Definitions:*
Investigational Device
Investigational Drugs/ Investigational Biologics (Test Articles)
Botanical

3.1. (a) is the correct choice if obtaining specimens from the MCW tissue bank or surgical discards.

3.1.2 and 3.1.3 No and None of the above

3. Elements and Review Category

3.3 * **Does this project involve any of the following elements?**

(select all that apply)

- [ ] 100% of subjects are known to be deceased, e.g., work with cadavers or biospecimens of deceased persons; record reviews where all subjects are demonstrably deceased
- [ ] In-vitro or laboratory diagnostic tests in the absence of FDA approval and/or CLIA certification: chemistry, drug monitoring, immunological/hematologic, tumor marker, genetic disorder, infectious disease, microorganism, bio-threat tests
- [ ] More than one site. Study activity will take place at other institutions or locations that are not under the supervision of the PI listed on this IRB application.
- [ ] Subjects are recruited by home location or neighborhood; key project procedures take place in the subjects' homes or neighborhoods e.g., churches, bars, public places
- [ ] Any part of the project takes place in another country. Check here if the PI is the lead PI for a multi-site study where one or more sites are in another country or if any project related work or oversight work is being done in another country.
- [ ] Application to waive informed consent requirements for certain types of planned emergency medicine research [(21 CFR 50.24 or 45 CFR 46 Waiver of Informed Consent Requirements in Certain Emergency Research) or (FR doc. 96.24968)]
- [ ] Research using the internet as a source of information or a survey tool
- [ ] None of the above

***3.3** In vitro Diagnostic: Any clinical laboratory test that is not CLIA-certified or FDA approved.*

***3.3** More than one site: A project involving more than one performance site (i.e. at MCW/FH and non-MCW/FH Sites) engaged in research.*

***3.3** Do not check "Any part of the project takes place in another country" if the MCW PI has no involvement with activities at any international site.*

3.4 * **What type of review is being requested?**

(select one)

- ○ Full Committee
- ◉ Expedited
- ○ Exempt

Clear

***3.4** Definition: Minimal Risk*

***3.4** Expedited Research Review Criteria*

***3.4** Exempt Research Criteria*

If Expedited or Exempt Review:

3.4.1 If all the proposed activities fall within one or more of the categories described below, it is possible that your proposal will meet criteria for "exemption" or "expedited review" by the IRB.

(select all that apply)

- [ ] Surveys, questionnaires, interviews, focus groups, or observation of behavior
- [ ] Evaluations or comparisons of effectiveness among instructional techniques or curricula within an accredited educational setting
- [ ] Analysis of records (e.g., medical records, other databases) not created for the purpose of this study
- [x] Use or analysis of biospecimens not created for the purpose of this study
- [ ] Minimal risk, minimally-invasive or non-invasive procedures routinely employed in clinical practice, e.g., blood draws, urine samples, buccal swabs, EKGs, ultrasound procedures
- [ ] Analysis of existing data if the sources are publicly available.
- [ ] None of the above-listed categories apply

***3.4.1** For example, a project involving surveys plus analysis of biospecimens could be expedited, but not a project involving surveys within a clinical trial of a new drug.*

3.3 For MCW banked specimens or surgical discards, None of the above
3.4. Expedited
3.4.1. Checked box is correct.

3.5 * **Use of Identifiers - indicate the level of "subject identification" you require to BEGIN this work.**

- If any element of your records, data files, or administrative records contains an identifier, you should select Identified Data.
- If you plan to de-identifiy data at any time other than the first day you access the information, you should select Identified Data.
- If different levels apply, choose the "most identified" one, e.g., if level A and level B apply, choose level A.

(select one)

- **A - IDENTIFIED DATA**: Utilizes one or more identifiers, including those defined by HIPAA Privacy Rule but not using a "limited data set." See help text for complete listing.
- **B - CODED DATA, KEY held by study team**: Data is coded; **and** key code held by any person at MCW, Froedtert Hospital, Children's Hospital of Wisconsin, or BCW whether or not they are part of the project team.
- **C - CODED DATA, KEY not held by study team**: Data is coded; key code not held by any MCW/Froedtert faculty member, employee, fellow, resident, or student; key code not held by any member of the project team; **and** the key code will never be accessible to any member of the project team.
- **D - LIMITED DATA SET**: The only HIPAA identifiers utilized are dates or certain allowable geographic subdivisions; an IRB "limited data set" data use agreement has been executed by the PI; and is uploaded into this IRB application.
- **E - DE-IDENTIFICATION PROCESS**: The IRB application describes how the project team will de-identify data in one of two approvable methods: 1) reliance on an MCW/FH IRB-sanctioned "honest broker" or 2) receiving coded data/specimens without identifiers and without a key code. For details see *"Two ways to de-identify data or biospecimens for IRB purposes."* To use these options, no code keys may be created or saved and the resulting dataset can never be re-identified. In addition, a complete list of project variables must be uploaded in Section 52.
- **F - ANONYMIZED**: The investigator receives data in anonymized form and no other party has the potential to re-identify data (i.e. no code key exists anywhere in the world). In this case, the IRB application must include a detailed description of how the data was collected, e.g., anonymous surveys, or who provided the anonymized data or biospecimens, so the IRB can verify the source and the irreversibility of anonymization. In addition, a complete list of variables, e.g., data recording sheet, Case Report Form, anything that summarizes all the information that will be recorded, must be included in Section52 Attached Documents.

Clear

***3.5** This question must be answered by all studies / projects, even those not using any Protected Health Information under HIPAA rules.*

***3.5** Examples of Identifiers*

***3.5** De-identifcation Agreement*

***3.5** For questions regarding encryption requirements please reference: MCW Corporate Policy #AD.HS.130 - Workstation Use and Security and MCW Encryption Security Guidelines*

***3.5** De-identification of data: Under MCW/FH IRB policy, there are only two ways that data can be "de-identified" (e.g., for purposes of Exemption category # 4). Note that if the information or specimens are collected directly from subjects for the study, this exemption cannot be applied – the exemption may only be applied to data already existing – i.e., created for purposes other than the study in question.*

- *The study team proposes to receive data/specimens in truly anonymized form (without any codes, without any HIPAA identifiers) from an MCW IRB-sanctioned "honest broker." To exercise this option, the IRB must verify the study plan and the identity of the broker.*
- *The study team proposes to receive coded*

3.5. This depends on the information that you need in addition to the specimens. Best to describe your needs to the tissue bank or IRB personnel for their advice on how to answer this question.

3G. Biospecimens of Any Type - Part I

You received this section because in 3 Elements and Review Category, Question Section 3.4.1, you checked "Use or analysis of biospecimens …"

3G.1 * **For what purpose were the biospecimens originally collected?**

(Check all that apply)

- ☐ Clinical pathology specimens
- ☑ **Discard material**
- ☐ Different research study
- ☑ **Other**

3G.1.1 Specify other:

bank-PRO 17015

3G.2 * **Are some or all of the biospecimens publicly available?**

○ Yes ◉ **No**

If Yes,
Instruction: Upload published description of the public-access database and its access criteria for IRB documentation to Section 52.

3G.2 *"Publicly available" means that the records are unidentified and available to the general research community without conditions*

3G.1. If obtaining tissue from the tissue bank, you should check other and specify “From MCW tissue bank” in 3G.1.1.

Don’t specify PRO number of the tissue bank here, because if you ever change tissue banks, you will be required to change this number. There is a dropdown menu later where you will specify the Tissue Bank PRO number.

3G. Type: Biospecimens of Any Type - Part II

3G.3 * **Do you plan to use/analyze biospecimens and related clinical records created before the date of IRB submission (retrospective specimens)?** (i.e., NO additional cases created after that date, and NO opportunity to include follow-up information created after that date)

○ Yes ◉ **No**

If Yes,
3G.3.1 What is the date for the earliest biospecimens you will access?

3G.4 * **Do you plan to access biospecimens created after the date of IRB submission (prospective biospecimens)?**

◉ **Yes** ○ No

If Yes,
3G.4.1 How will these biospecimens be obtained?

- ☐ Using informed consent
- ☑ **From an IRB approved bank**
- ☐ Other

3G.4.1.1 Specify other:

3G.5 * **Estimate the total number of biospecimens (number of persons and number of specimens) that you intend to access for this project.**

120

3G.6 * **Explain how you determined the number of biospecimens to include in the project at this site.**

This is very difficult to estimate, since the frequency with which we will need biospecimens depends on the outcome of our experiments. If our experiments work, we will need more. If they don't work, we will need less. Anticipating that they work, we estimate that mice will be generated every month for 2 years. For each set of 10 mice, we will need to prepare virus in cord blood mononuclear cells. To prepare virus, we will need 1-3 donor cords. We wont know how many donor cords we need for each experiment until we can perform pilot experiments to assess viral titers in these cord blood mononuclear cells. An estimate, if we need 3, is 3 X 12 = 36. Before the mice become available, we will need to perform pilot experiments to assess virus production and titer in CBMCs, as well to as assess infectivity of genetically modified virus. We anticipate another 24 cords for these purposes.
Maybe 60 cords over the next 2-3 years.

3G.7 * **What kind of clinical information will you have about the specimens?**

(check all that apply)

- ☐ Patient diagnosis
- ☐ Patient symptoms or signs
- ☐ Patient lab values
- ☐ Patient course of illness
- ☑ **No clinical or health information corresponding to the biospecimen**
- ☐ Other

3G.7.1 Specify other:

3G.3. Important to check with the tissue bank. If you will use frozen or fixed samples, then the answer could be yes. For fresh, it will be No.

3G.4. Same as above, for fresh samples, you will certainly answer Yes. Check as shown.

3G.5. It is best here to overestimate the number you need so that you do not need to amend later.

3G.6. Describe how you came to the estimate, even if it was a guess as in this case.

3G.7. Your answer here will depend on what additional information you need.

4. Additional Features

4.1 * **Does the proposed project involve any of the following features?**

(select all that apply)

- [ ] Deception studies
- [ ] Direct contact with subjects
- [ ] Genetic Research/ Gene Therapy
- [x] **None of the above**

4.2 **If drug or biologic clinical trial, what is the phase of this clinical trial? For combined phase studies - e.g., Phase II/III - select only the smaller number**

-

- [ ] Phase I
- [ ] Phase II
- [ ] Phase III
- [ ] Phase IV
- [ ] N/A

4.1 *More about research project features*

Definition of Deception Study

Direct contact includes interaction or intervention of any kind, such as obervation, contact by mail, phone, or internet, or biospecimen-taking

4.2 *Definition of Phases and more about clinical trial design*

Check N/A

6. Project Locations

6.1 ***Under the direction/supervision of this Principal Investigator, project activities will take place at the following locations:**

- [x] Froedtert & the Medical College of Wisconsin Hospitals and Health Partners
  - Froedtert Hospital Campus (including all specialty clinics, the Cancer Center and the Eye Institute)
- [x] **Medical College of Wisconsin**
- [ ] Center for AIDS Intervention Research (CAIR)
- [ ] Adult Translational Research Unit (TRU - formerly GCRC)
- [ ] BloodCenter of Wisconsin and Blood Research Institute
- [ ] Children's Hospital of Wisconsin†
- [ ] Clement J. Zablocki Veteran's Affairs Medical Center†
- [ ] UW-Milwaukee†
- [ ] Marquette University†
- [ ] Milwaukee School of Engineering†
- [ ] Other

6.1.1 For all locations other than MCW, Froedtert Hospital, or BloodCenter of Wisconsin list the lead collaborator at each institution, their role at each institution, and the name of the institution.

Note that this section refers to those studies under the direction of an MCW Principal Investigator only, no matter where activities are occurring.

***6.1** Project activities include data analysis or data storage.*

***6.1** †For some studies, the MCW/FH IRB may coordinate its review with IRBs at these sites to allow a single IRB review for the total project. Please review the information here to determine if your study may quality for Coordinated IRB Review.*

***6.1** For International Projects, please always check your home institution (e.g. MCW, FH, etc.) as well as any other international sites by checking "other" and specifying those sites.*

6.2 * **Will any subject recruitment activities or research procedures under the responsibility of this Principal Investigator take place outside of Wisconsin but within the US?**

( ) Yes (•) **No**

If Yes,
6.2.1 Identify those states (within the US) where project activities will take place; and describe the activities that will take place in those jurisdictions.

***6.2** If Internet research only, this question is not applicable, please respond "No".*

***6.2** If some sites are international, only describe U.S. activities in the response.*

6.1. Check all institutions involved. If getting tissues from Froedtert operating rooms or MCW tissue bank, need to check Froedtert as well as MCW.

8. Cancer Cooperative Groups

8.1 * **Is this project part of a cancer cooperative group?** (University of Chicago and Northwestern Consortium projects are not considered "Cancer Cooperative Group" projects)

○ Yes ◉ **No**

8.1 Cooperative groups are generally a large network of researchers, physicians, and health care professionals at public and private institutions across the country.

If Yes:
8.1.1 Which group?

(select all that apply)
☐ Alliance
☐ COG
☐ ECOG-ACRIN
☐ NRG
☐ SWOG
☐ Other (SPECIFY)

If Other:
8.1.2 Specify below:

Note: If your project is sponsored by a cooperative group listed above, the Medical College of Wisconsin and Froedtert Hospital IRBs will accept the **cooperative group consent template with the modifications permitted by the IRB policy on Cancer Cooperative Group consent templates.**

- IRB checklist for modifications to the NCI Cooperative Group Informed Consent on Cooperative Group consent templates

Upload completed cooperative group consents in Section 52.

11. Funding Source

11.1 * **Do you have funding to support any of the activities for this project:**
(•) **Yes** ( ) No

If Yes,
11.1.1 List all current MCW department funding for this study:

Title	Cost Center	Fund	Project Number
Program Development			

11.1.2 List all current and pending funding sources for this study (excluding department funds listed in 11.1.1):

	Validated	Type	Short Title	Funding Source	Prime Grantor	Grant Award Number	FP ID	FP Current State	Budget ID	FP Parent State
View	Yes	Federal		NIH Allergy and Infectious Diseases				Active		

11.1.2 *How to create a link to an eBridge Budget / Funding Proposal.*

11.1.2 *FP refers to the eBridge Funding Proposal*

11.1.2 *Changes to information about the eBridge Funding Proposal displayed here must be made on the Funding Proposal SmartForm in the eBridge Grants module.*

11.1.3 Do you have funding that is not managed through MCW:
( ) Yes (•) **No**

If Yes:
11.1.3.1 Provide the name of the funding source(s):

11. It is fine to say that you do not have funding.

12. Project Subject Types

12.1 * **What type of subjects will be included?**
(check all that apply)

- [x] **a.** Healthy subjects, i.e. subjects NOT selected because they have a particular medical condition or history
- [x] **b.** Inpatients
- [ ] **c.** Outpatients
- [ ] **e.** Other

12.2 * **Will subjects in any of the following groups be a focus of the project?** Do not check a box only because it is possible you might enroll one or a few subjects.

check all that apply
[ ] Persons with alcohol or drug use disorders
[ ] Traumatized, sedated, or comatose patients
[ ] Issues of cognitive or decisional impairment
[ ] Persons with developmental disabilities - neurologic or psychiatric
[ ] Persons with mental illness
[ ] Elderly - age 70 and over
[ ] Employees including faculty, staff, residents or fellows
[ ] Neonates
[ ] Fetuses or fetal tissue
[ ] Pregnant women
[ ] Limited or non-reader
[ ] Non-English speaking
[ ] Nursing home residents
[ ] Poor and/or uninsured
[ ] Prisoners - see help text
[ ] MCW students
[ ] Terminally ill patients
[ ] Visually / hearing impaired
[ ] Other (SPECIFY)
[x] **None of the above**

If Other,12.2.1 Specify:

12.2 *Click here to view regulations regarding vulnerable subjects*

If your project will include subjects with issues of cognitive or decisional impairment, developmental disabilities (neurologic or psychiatric), or mental illness, these subjects may only consent for research for 15 months by Wisconsin state law. At that time, the informed consent must be repeated.

You cannot include a prisoner or pregnant woman without prior approval from the IRB. If a subject becomes pregnant or becomes a prisoner at any time during the project, the IRB must be notified. You cannot continue following such a subject without IRB approval.

Not sure when you should check "Neonates"? Check "Neonates" when neonates of uncertain viability and nonviable neonates are to be involved in research. Newborns are only considered neonates until they are determined to be viable. Once they are determined to be viable, they are considered children; then, you would select the appropriate "minors" option in Section 1, question 1.0 and do not select Neonates here.

12.3 * **Are the exclusion criteria for this project likely to exclude groups or categories of subjects based on race, socioeconomic status, or insurance coverage?**

( ) Yes (•) **No**

If Yes,
12.3.1 Please specify and provide the rationale for excluding these subjects. Selection of subjects must be fair and equitable. Explain how the subject selection process in this research is fair and equitable, taking into account eligibility criteria, vulnerability and recruitment process.

Instruction: Please upload any project materials in other languages in section 52.

12.1 If using discarded surgical tissues, choose b. If coming from the tissue bank, it is best to ask the bank what to choose here.

12.2 Usually will be no. Note that obtaining cord blood following a delivery is not considered using pregnant women as subjects.

12.3 No for tissue banked samples. Likely also no for surgical discards.

14. Biospecimen Collection

14.1 * **In this project, will the study team (or their agents – lab technicians or cooperative surgeons) collect biospecimens from human subjects for RESEARCH purposes?**

○ Yes ◉ **No**

14.1 *Your response here should be relevant to biospecimens collected for this research project, not for banking.*

14.1 If all specimens will be collected for routine care purposes, and in the usual

14.1 The answer here should be no. The specimens were collected by someone other than your own study staff.

15. Inclusion/Exclusion Criteria

15.1 * **List inclusion criteria (e.g., age, gender, ethnicity):**

This is performed by the MCW Tissue Bank

Placental cord blood collected by the MCW Tissue Bank

15.1 *Participant-entry criteria should be as detailed as necessary to define the participant population. Criteria for inclusion can be but are not limited to: age, gender, ethnicity, physical and mental conditions.*

How to Cut & Paste from a Word Document

15.2 * **List exclusion criteria (e.g., age, gender, ethnicity):**

This is performed by the MCW Tissue Bank.

Placental cord blood collected by the MCW Tissue Bank

15.2 *State criteria that would exclude an individual from the research study. Generally this would include age, gender, physical or mental conditions.*

15.1 For banked specimens and surgical discards, the answers are None unless you do have exclusionary criteria. Note that the specimens will be collected by the Bank.

16. Recruitment Waivers for Using Subject Records

16.1 * **Will potential subjects be identified or screened by searching any kind of pre-existing MEDICAL records before consent is obtained?** (e.g., medical records, hospital census or procedure logs, emergency room visit rosters)

○ Yes ◉ **No**

If Yes,

16.1.1. Does this research team request permission to screen existing medical records for potentially eligible subjects before consent is obtained? Do not check "Yes" unless you intend to obtain informed consent for subjects who decide to enroll in the project.

○ Yes ◉ **No**

If No, only the physician or nurses caring directly for the patient are allowed to review the patient's records.

16.1.2 Does this research team request permission to retain screening logs as part of the investigator files?

○ Yes ◉ **No**

If Yes,

Justify retaining Protected Health Information without consent:

16.2 * **Will potential subjects be identified or screened by searching records of any source outside MCW/FH /CHW/BCW?** (e.g., motor vehicle records, military service records, state registries, Medicare files, other hospitals including International hospitals)

○ Yes ◉ **No**

If Yes,

16.2.1 What are the sources of these records? Describe the types of records, the sources, and explain or document the access you have to each one.

16.1 *For many clinical trials and other research studies, the investigator plans to obtain informed consent from willing subjects, but would like research team members to: (a) search medical records to obtain the names, contact information, or next clinic visit date for likely eligible subjects; or (b) review medical records to evaluate the eligibility of potential subjects before they have been approached about consent. These two plans of action require prior IRB review and approval because subjects have not yet given consent or HIPAA authorization for these types of research record reviews. The IRB will make its determination to grant WAIVER OF INFORMED CONSENT AND WAIVER OF HIPAA AUTHORIZATION FOR RECRUITMENT based upon information provided here and throughout this submission.*

16. All of these answers will be no unless you or your staff are doing the consenting.

17. Recruitment Strategies

17.1 * **To recruit potential subjects, will you use any of the following:**

- ☐ **Print advertisements (e.g. newspapers, magazines, flyers, posters, brochures)**

  Specify where the print advertisements will be posted:

  IRB SOP: *Recruitment Methods and Compensation*
  IRB SOP: *Advertisements*

- ☐ **Letters/emails**

  Identify who will sign the letters/send the emails and indicate the relationship between the sender and recipient(s):

- ☐ **Radio or television advertisements**

  Specify the radio or television station(s):

- ☐ **Web solicitations**

  Specify the website address(es):

  17.1 *Examples of web solicitations include posting on Craig's list, sponsor hosted study specific website, advertisements on internet search engines and social media websites.*

- ☐ **Telephone**

  Identify who will telephone the subjects and indicate the relationship between the caller and the recipient(s):

- ☐ **Recruiting company**

  Specify the organization and the services they will be providing:

- ☐ **Physician referrals (includes in-house and/or outside referrals)**

  Describe the process:

  17.1 *Please be aware that according to HIPAA regulations, patients must first be informed of a trial and contact the study team on their own, or complete a HIPAA authorization agreement before any healthcare providers can pass the identity of potential subject over to the research team.*

- ☐ **Approach subjects in-person** (Example: a public place or knocking door-to-door)

  Briefly describe the process and specify if any MCW or Froedtert patients will be approached in-person:

- ☐ **Other strategies (not already covered) to identify, screen, or recruit subjects**

  Specify those strategies in detail:

  17.1 *Other professional referral sources (PhD clinicians, nurses, other investigators) should be classified as "other".*

- ☑ **No recruitment activities**

Instruction: Upload all recruitment materials in Section 52.

17. At the very bottom is the box you want: No recruitment activities.

18. Subject Compensation/Reimbursement

18.1 * **Will you offer subjects stipends, gifts or compensation for their participation, or reimbursement for project-related expenses, e.g., transportation, baby-sitting, parking?**

- ○ Yes
- ◉ **No**

If Yes,

18.1.1 Describe what will be offered and why this was determined to be appropriate:

18.1 *This also includes non-monetary forms of compensation such as pens, blankets, and other forms of gifts.*

18.1.1 *For example, $30.00 per hour while in MRI, $10.00 for travel expenses.*

18.1 No is correct here.

26. Connecting with a Bank

26.1 * **Will this project contribute data to a local bank or access data from a local bank? (Data includes records and biospecimens)**

- ◉ **Yes**
- ○ No

26.1.1 Cite the PRO for the local bank to which this project will contribute data (records or biospecimens):

Bank ID	Bank Title	Principal Investigator	Bank State	Contributing Records	Contributing Biospecimens
There are no items to display					

26.1.2 Cite the PRO for the local bank from which you will access data (records or biospecimens) for this project:

Bank ID	Bank Title	Principal Investigator	Bank State	Accessing Records	Accessing Biospecimens
PRO00017015	Tissue Bank	Saul Suster	Approved	☐	☑

26.1.1 & 26.1.2 *MCW/Froedtert Hospital IRB-approved banks have their own PRO # and exist independently of any study that may have created or collected the records in the first place.*

Can't find a Bank? Contact the IRB Office at 955-8422 or IRBManager@mcw.edu.

26.1. Answer Yes if you are using any of the MCW tissue banks. The PRO numbers will be in the drop down menu.

27. Safety and Research Review Committees

27.1 * **What other MCW safety or research review committee should review this project, per MCW Office of Research policies?** The IRB review process will begin as soon as all these other reviews have been completed.

(select all that apply)

- [ ] Project proposing to use Adult Translational Research Unit (TRU) facility or resources
- [x] **Safety Committees (Institutional BioSafety Committee, HazChem Committee, MRI Committee) or Office of Radiation Safety**
- [ ] Human Stem Cell Committee
- [ ] None of the above

If Safety Committee:

27.1.1 Check the relevant committees or safety offices that address the issues raised in your project. The IRB review process will begin as soon as all these other reviews have been completed.

(select all that apply)

- [ ] Office of Radiation Safety (Irradiators, CT, X-ray, Fluoroscopy and Unsealed Radioactive Materials)
- [ ] HazChem Committee (Carcinogens, Acutely Toxic, Reproductive Hazard, Highly Reactive, Homeland Security Chemical of Interest, Untested Substance, Other) View a detailed list of Particularly Hazardous Substances: PHS List (MCW network access is required to view this link.)
- [ ] MRI Safety Committee
- [x] **Institutional BioSafety Committee**

  - [X] Human Source Material (human blood, tissues, cell lines)
  - [ ] Toxins
  - [ ] Pathogens
  - [ ] rDNA
  - [ ] Synthetic nucleic acids

Note: If you have checked one of the Committees listed above, use the link(s) below to access and complete the application for that Committee. The IRB has no mechanism for tracking the review progress of these Committees. If you have questions, please contact that Committee directly.

Additional Information:

- **Adult Translational Research Unit** (TRU):
  - Click **here** to complete the online request form. Before you can submit your request, please complete a one-time registration to join CTSI.
- **HazChem Committee** :
  - **Website** (MCW network access is required to view this link.)
- **Institutional BioSafety Committee** :
  - **Website** (MCW network access is required to view this link.)
- **Office of Radiation Safety:**
  - **Website**
- **MRI Safety Committee:**
  - **Website**
  - Complete form and attach in Section 52.
- **Human Stem Cell Committee:**
  - **Website**

27.1 *Select 'Project proposing…' checkbox if you are using any CTSI-TRU core facility, resource, or service.*

27.1 *Selecting any of the Safety and Research Review Committees will route this application to the applicable Committee. The IRB review process will NOT begin until the Committee has forwarded its determination to the IRB. Investigators are advised to track the progress of the review; the IRB does not have any information about review progress until it receives the Committee determination.*

27.1.1 *Select Office of Radiation Safety if project research procedures include Irradiators, CT, X-ray, Fluoroscopy or Unsealed Radioactive Material.*

27.1.1 *If every one of the MRI procedures in the protocol are:*

- *routinely performed for similar patients NOT enrolled in a study AND*
- *performed for this study at FH Radiology AND*
- *billed to the patient/patient's insurance as routine care cost*

-- then do NOT check the MRI Safety Committee box in 27.1.1 and do NOT complete the "MRI Research Using Human Subjects" form. Studies meeting these criteria do not require MRI Safety Review.

27.1.1 Use should check Institutional Biosafety committee as here, but then the human source material box. Do not need to check pathogens unless you know that the tissue is pathogenic.

28. Purpose

28.1 * **Why is it significant or important to conduct this project?**
We want to produce high-titer HHV-6 and HHV-7 in culture.

It is reported that the best way to do this is in fresh human cord blood mononuclear cells. It is possible that the best host for HHV-6 and -7 is human immature thymocytes, which are most abundant in cord blood mononuclear cells.

Moreover, since 100% of the human population acquires HHV-6 and 7 by the age of 5, adult mononuclear cells are not usable, since we need to be sure that we are working with the strain of virus that we think we are working with.

Eventually, we will want to infect humanized mice with the virus that we propagate in human cord blood mononuclear cells.

We will also want to propagate recombinant green-fluorescent protein-containing HHV-6 in cord blood mononuclear cells.

These two end-goals are significant because there is no animal model for HHV-6 and -7. Establishement of a humanized mouse model for HHV-6/7 infection would allow us to answer questions that have previously been unanswerable, such as, what is the natural reservoir for HHV-6/7, and, do these viruses undergo latencye, and if so, in what cell population do these viruses remain latent?

28.1 *This narrative should be written so that committee members outside the investigator's area of expertise can understand the issues involved.*

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28.2 * **Briefly summarize findings from previously published data or pilot studies that substantiate the soundness of protocol being proposed; or describe formulation of research questions:**

28.2 *This summary should be written so that committee members outside the investigator's area of expertise can understand the issues involved.*

The propagation of a GFP-containing BAC-derived HHV-6 virus in cord blood is described in:

Tang, Huamin, Akiko Kawabata, Mayumi Yoshida, Hiroko Oyaizu, Takahiro Maeki, Koichi Yamanishi, and Yasuko Mori. 2010. "Human Herpesvirus 6 Encoded Glycoprotein Q1 Gene Is Essential for Virus Growth.." Virology 407 (2) (November 25): 360–367. doi:10.1016/j.virol.2010.08.018.

28.1 This description doesn't need to be too extensive. I probably went overboard.

29. Hypotheses and Objectives

Some projects are designed around explicit scientific hypotheses. Others (chart reviews, pilot studies) may be better described in terms of Aims or Objectives. Answer the question (29.1 or 29.2) that suits your project best.

29.1 **State the hypotheses:**

29.1 *If this study involves community-based research, indicate so and explain the project goals.*

29.2 **Describe the Aims and Objectives of this project:**

29.2 *The objectives should be stated in such a way that the reader can determine the appropriateness of the study design.*

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Answer either 29.1 **or** 29.2. If the tissue is not a part of your hypothesized research, then use the aims and objectives box.

30. Procedures and Analysis

30.1 * **Narrate project procedures listing in sequential order the steps that will be followed to conduct the protocol:**

1. obtain coded deidentified cord blood from the **MCW Tissue Bank, PRO 17015.** We, the investigative team, will not hold the key to the code and will not ever be able to trace the specimen back to an individual.

2. pipet blood onto ficoll gradeint, centrifuge, and obtain buffy coat (CBMCs)

3. Incubate HHV-6 or -7 infected cells with mononuclear cells from the ficoll gradient

4. examine cells every day to see if they become infected with HHV-6/7 - we will assess cells for CPE, or label the cells with HHV-6 or -7-specific antibodies and examine in a fluorescence microscope or using a flow cytometer.

Initially, we just want to experiment to see how we can best obtain a high percentage of cells infected.

If so, later, we will infect cells with recombinant GFP-expressing BAC-derived HHV-6 and examine infectivity by assessing GFP fluorescence.

** An amendment will be submitted to the IRB if rDNA studies become feasible, with application to the IBC for approval to conduct rDNA work.

If infections work well, eventually, we will prepare high titer virus in CBMC to infect humanized mice or to prepare RNA from infected cells, or to assess the infected cells for protein content using mass spec.

Note: If desired, upload an activity table into Section 52 listing tests that will be conducted (e.g., lab draws, EKG, chest x-ray, genetics, proteomics, H&P, survey) as well as the frequency of these tests.

30.1 *This section should state in order the procedures which the subject must undergo. The investigational treatment or procedures must be clearly detailed as to how and when they will be performed. Include information regarding "end of study procedures" for individuals who withdraw or are withdrawn before completion of study activities.*

If this site is the central coordinating site, list the activities that occur at each project location.

30.2 * **Explain how you intend to analyze the data:**

We will use the cord blood to propagate recombinant HHV-6 virus and will also determine which mononuclear cells are infected by the rHHV-6A virus.

30.2 *These methods must be appropriate for the design of the project and the nature of the data being collected. These methods must compliment the design of the trial and the nature of the data which is being collected.*

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30. Enter a short description of what you are going to do with the specimen.
If the specimen is not subject to data analysis, you can state that the data will not be analyzed or that no data will be obtained.

31. Procedures and Expenses for Subjects

31.1 * **Explain which procedures are research-related:**
All procedures using this discarded material are research related.

31.1 *For example: An MRI is standard of care, but a second MRI is required for research purposes.*

31.2 * **Explain what expenses are NOT covered in the project, i.e., the expenses the subject is expected to pay:**

There are no physical subjects involved in this project, only human biospecimens. Therefore, there are no costs.

31.2 *For example: "The following are costs that are not covered in the study and therefore you or your insurance provider will be billed: MRI Scan, Blood Draws." List the expenses and a justification (if applicable) for why the participant is responsible (e.g., The MRI Scan is part of your routine care...).*

31.3 * **Explain what expenses ARE covered in the project, i.e., the expenses the subject is not expected to pay:**

There are no physical subjects involved in this project, only human biospecimens. Therefore, there are no costs.

31.3 *For example: "The following are costs that are covered in the study and you will not be expected to pay: MRI Scan, Blood Draws." List the expenses and a justification (if applicable).*

31. These answers were recommended by the IRB.

32. Risks and Safeguarding Against Risks

32.1 * **List all reasonably foreseeable risks or discomforts. Consider physical, psychosocial, confidentiality, and privacy risks. List in order of frequency (likelihood), but be sure to include uncommon risks that might influence a person's decision to participate.**
The material will have been deidentified at the MCW Tissue Bank.
PRO 17015. We will not have any contact with subjects.

Loss of confidentiality is a risk, but we will not oversee the donor records.

32.1 *If your project involves a high volume of risks and/or includes a document that is specially formatted, i.e. tables and charts, please upload the document into Section 52. In 32.1, enter a comment referencing the name of the uploaded document.*

32.2 * **Identify features of the project, e.g., recruitment practices, project design, procedural plans, intended to minimize safety risks to subjects**:

Recruitment will be performed by the MCW Tissue Bank.

We will not have any contact with cord donors.

The material will have been deidentified at the MCW Tissue Bank by the time we receive it.

32. The major risk to identify is potential loss of confidentiality.

The IRB would also like you to outline how you will protect the biospecimen itself. This is not explicitly stated but is part of the process.

35. Benefits

35.1 ***Identify and list separately the potential benefits:**

- **to subjects participating in this project or state "none", if appropriate**
- **to science or society from this project**

No benefit to subjects.

There may be eventual potential benefits to science and society as we strive to understand the biology of HHV-6A infection.

***35.1** The following are not considered to be benefits: compensation, access to medical care, more frequent access to medical care.*

35. Self explanatory. Does not need to be extensive.

38. Informed Consent

38.1 * **Indicate your approach to the informed consent process requirement for this project:**

(select all that apply)

- ☐ Subjects or parents of minor subjects participate in an informed consent process and sign an informed consent document
- ☐ Waiver of the Informed Consent Process is granted by the IRB. This option is not permitted for most FDA regulated research.
- ☐ Subjects participate in an informed consent process, but a Waiver of Documentation of Informed Consent is granted by the IRB
- ☑ **None of the above**

***38** General requirements for informed consent.*

***38.1** You must select at least one.*

More about the Waiver of the Informed Consent Process.

More about the Waiver of Documentation of Informed Consent.

***38.1** "None of the above" may be used for projects using data from IRB-approved banks where informed consent has already been addressed.*

36. As checked.

39. No Informed Consent

39.1 * **If consent forms will not be used, and you are not requesting a Waiver of the Informed Consent Process, explain why:**

Informed consent will be obtained by the MCW Tissue Bank.

39.1 *Projects using data from IRB-approved banks may be allowed to proceed without informed consent. Otherwise go back and select "Requesting a Waiver of Informed Consent" and/or "Requesting a Waiver to Document Informed Consent."*

39. Biobank has obtained consent.

42. HIPAA: Protected Health Information

42.1 * **Indicate the HIPAA authorization pathway applicable to this project.** Generally, the Health Insurance Portability and Accountability Act (HIPAA) prohibits collecting, accessing, using or disclosing a person's protected health information (PHI) for research without valid authorization. Under some circumstances, a waiver of authorization may be granted by the IRB:

(select all that apply)

- [x] **No Private Medical Information Will Be Accessed or Used For This Project**
- [ ] **An IRB-Approved Consent Process and Document will be Used** that incorporates the required HIPAA authorization
- [ ] **Waiver of HIPAA Authorization Is Requested.** Generally, this request should accompany the "Waiver of the Informed Consent Process" at 38.1.
- [ ] **Research using only information on deceased persons**
- [ ] **Limited Data Set**, as defined by HIPAA regulations (download "Data Use Agreement" form located on InfoScope HIPAA website, complete it or an equivalent, and upload in Section 52)
- [ ] **De-identification of data** subject to the IRB's definition and verification of de-identification
- [X] **None of the above**

42.1 *"Records Review for Potential Subjects" to determine eligibility is now addressed in Question 16.1 and 16.2.*

No protected health information will be accessed or used" is also allowed for sites that are not covered entities, e.g., the MCW Center for AIDS Intervention Research.

More about the Waiver of HIPAA Authorization

Use "None of the above" for projects using data from IRB-approved banks, where HIPAA has already been addressed, or for non-research use of an investigational article where there are no plans to collect data according to a sponsor's protocol.

42. Check "None" if the above if specimens come from IRB approved bank.

52. Attached Documents

52.1 * **Select all items that will be included for IRB review:**

(select all that apply and upload documents in Section 52.1.2, using the prefix in the title of the document. For example, ICF-PRO1234 (document name), IB-PRO1234(document name))

- [x] **PRO - Sponsor's protocol, protocol summary or narrative**
- [ ] IB - Investigator Brochure
- [ ] ADV - Advertisement
- [ ] ICF - Informed Consent form
- [ ] SMP - Safety Monitoring Plan
- [ ] DM - Device Manual
- [ ] SUR - Surveys / Questionnaires
- [ ] DCF - Data Collection forms/tools
- [ ] INF - Informational material for subjects
- [ ] TBL – Activity table, schedule of assessments
- [ ] BNK – Bank documents and forms
- [ ] SAF – Ancillary Safety Committee or Human Stem Cell Committee approvals, Adult Treatment Research Unit (TRU) approvals
- [ ] LET - IND/IDE/HDE or 510(k) documentation, communication from/with the sponsor, IRB approvals or administrative letters from other institutions
- [ ] DA - Data agreements or contracts
- [ ] Other(s) (SPECIFY)

52.1 *For all projects, except Banks, the IRB requires the investigator to include a formal written overview of the entire study (e.g. Sponsor's protocol, a protocol summary or narrative). Please select PRO in 52.1 and upload the document into 52.1.2.*

52.1 *Select all that apply.*

Other items may include: questionnaires; study journals; forms.

Remember: *All items must be submitted and receive IRB approval before use.*

MCW/FH Consent Form Templates can be found at IRB/HRPP website.

52.1 You will likely need :
PRO
DCF
SAF
Call the IRB to discuss your individual situation.

The PRO involves writing a brief outline describing what you will do with the tissue you obtain.