



IRB APPROVAL OF MODIFICATION

May 31, 2022

Dear German G. Gornalusse:

On 5/31/2022, University of Washington IRB Committee B reviewed the following application:

Type of Review:	Modification / Update
Title of Study:	Comparing immune activation and latent HIV reservoir size between people living with HIV (PWH) on tenofovir-containing versus NRTI-sparing ART
Investigator:	German G. Gornalusse
STUDY ID:	STUDY00011699
MOD ID:	MOD00012497
Funding:	Name: National Institutes of Health (NIH), Grant Office ID: A124241, Funding Source ID: R01AI134293 Funding Title(s): "Identification of drug-targetable IFN-stimulated genes mediating immune activation during ART-treated HIV-1 infection"

IRB Approval

Under FWA #00006878, the IRB approved modifications to your research. The expiration of the current IRB approval period remains 12/13/2022.

- COVID NOTE: See the [HSD website](#) for the latest COVID guidelines for conducting human subjects research.
- This approval applies only to the activities described in your application (including any references to specific grant sections). It does not include other activities that may be described in your grant or contract.

Location of documents

Use the revised consent form that was approved by the IRB. It can be downloaded from the Final column under the **Documents tab** in Zipline.

Thank you for your commitment to ethical and responsible research. We wish you great success!

Sincerely,

Shawn Query, CIP
Senior Administrator, Committee B
squery@uw.edu
206.221.0265

The Human Subjects Division (HSD) strives to ensure that people with disabilities have access to all services and content. **If you experience any accessibility-related issues with this form or any aspect of the application process, email hsdinfo@uw.edu for assistance.**

INSTRUCTIONS

- **This form is only for studies that will be reviewed by the UW IRB.** Before completing this form, check [HSD's website](#) to confirm that this should not be reviewed by an external (non-UW) IRB.
- **If you are requesting a determination** about whether the planned activity is human subjects research or qualifies for exempt status, you may skip all questions except those marked with a . For example **1.1** must be answered.
- **Answer all questions.** If a question is not applicable to the research or if you believe you have already answered a question elsewhere in the application, state "NA" (and if applicable, refer to the question where you provided the information). If you do not answer a question, the IRB does not know whether the question was overlooked or whether it is not applicable. This may result in unnecessary "back and forth" for clarification. Use non-technical language as much as possible.
- To check a box, place an "X" in the box. To fill in a text box, make sure your cursor is within the gray text box bar before typing or pasting text.
- For collaborative or multi-site research, describe only the UW activities unless you are requesting that the UW IRB provide the review and oversight for non-UW collaborators or co-investigators as well.
- You may reference other documents (such as a grant application) if they provide the requested information in non-technical language. Be sure to provide the document name, page(s), and specific sections, and upload it to **Zipline**. Also, describe any changes that may have occurred since the document was written (for example, changes that you've made during or after the grant review process). In some cases, you may need to provide additional details in the answer space as well as referencing a document.

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1 OVERVIEW

Study Title: Comparing immune activation and latent HIV reservoir size between people living with HIV (PWH) on tenofovir-containing versus NRTI-sparing ART

1.1 Home institution. Identify the institution through which the lead researcher listed on the IRB application will conduct the research. Provide any helpful explanatory information.

In general, the home institution is the institution (1) that provides the researcher's paycheck and that considers him/her to be a paid employee, or (2) at which the researcher is a matriculated student. Scholars, faculty, fellows, and students who are visiting the UW and who are the lead researcher: identify your home institution and describe the purpose and duration of your UW visit, as well as the UW department/center with which you are affiliated while at the UW.

Note that many UW clinical faculty members are paid employees of non-UW institutions.

The UW IRB provides IRB review and oversight for only those researchers who meet the criteria described in the [SOP Use of the UW IRB](#).

University of Washington Department of Obstetrics and Gynecology

1.2 Consultation history. Has there been any consultation with someone at HSD about this study?

It is not necessary to obtain advance consultation. However, if advance consultation was obtained, answering this question will help ensure that the IRB is aware of and considers the advice and guidance provided in that consultation.

No

Yes → If yes, briefly describe the consultation: approximate date, with whom, and method (e.g., by email, phone call, in-person meeting).

1.3 Similar and/or related studies. Are there any related IRB applications that provide context for the proposed activities?

Examples of studies for which there is likely to be a related IRB application: Using samples or data collected by another study; recruiting subjects from a registry established by a colleague's research activity; conducting Phase 2 of a multi-part project, or conducting a continuation of another study; serving as the data coordinating center for a multi-site study that includes a UW site.

Providing this information (if relevant) may significantly improve the efficiency and consistency of the IRB's review.

No

Yes → If yes, briefly describe the other studies or applications and how they relate to the proposed activities. If the other applications were reviewed by the UW IRB, please also provide: the UW IRB number, the study title, and the lead researcher's name.

Effects of the anti-HIV pill Truvada on gene transcription in the gastrointestinal tract of HIV-uninfected individuals (ACTU 3500, IRB Number 49167). PI: Dr. Joanne D. Stekler, MD, MPH

1.4 Externally-imposed urgency or time deadlines. Are there any externally-imposed deadlines or urgency that affect the proposed activity?

HSD recognizes that everyone would like their IRB applications to be reviewed as quickly as possible. To ensure fairness, it is HSD policy to review applications in the order in which they are received. However, HSD will assign a higher priority to research with externally-imposed urgency that is beyond the control of the researcher. Researchers are encouraged to communicate as soon as possible with their HSD staff contact person when there is an urgent situation (in other words, before submitting the IRB application). Examples: a researcher plans to test an experimental vaccine that has just been developed for a newly emerging epidemic; a researcher has an unexpected opportunity to collect data from students when the end of the school year is only four weeks away.

HSD may ask for documentation of the externally-imposed urgency. A higher priority should not be requested to compensate for a researcher's failure to prepare an IRB application in a timely manner. Note that IRB review requires a certain minimum amount of time; without sufficient time, the IRB may not be able to review and approve an application by a deadline.

<input checked="" type="checkbox"/>	No
<input type="checkbox"/>	Yes

→ If yes, briefly describe the urgency or deadline as well as the reason for it.

1.5 Objectives Using lay language, describe the purpose, specific aims, or objectives that will be met by this specific project. If hypotheses are being tested, describe them. You will be asked to describe the specific procedures in a later section.

If this application involves the use of a HUD “humanitarian” device: describe whether the use is for “on-label” clinical patient care, “off-label” clinical patient care, and/or research (collecting safety and/or effectiveness data).

The goal of the project is to determine the difference in immune activation and HIV reservoir size between People living with HIV (PWH) on tenofovir-containing antiretroviral therapy (ART) versus PWH on nucleoside reverse transcriptase inhibitor (NRTI)-sparing ART. Tenofovir (TFV), a phosphonated nucleoside reverse transcriptase inhibitor (NRTI), is being used for oral pre-exposure prophylaxis (PrEP).

We will test this hypothesis: tenofovir, and perhaps NRTIs in general, stimulate a type I/III interferon also in PWH who take these drugs. Because chronic interferon stimulation may promote the survival and proliferation of cells with integrated provirus, we also hypothesize that these drugs antagonize decay of the HIV latent reservoir in PWH on ART. Consequently, we *hypothesize* that PWH who have switched from NRTI-containing ART to NRTI-sparing ART exhibit lower type I/III interferon pathway activation and lower latent HIV reservoir size.

We also *hypothesize* that independently of treatment, the extent of type I/III interferon activation correlates with latent HIV reservoir size.

Thus, the proposed study seeks to answer these two questions. Can the gastrointestinal epithelium be impacted by ART, contribute to chronic immune activation and expansion of the HIV-1 reservoir? If so, what therapeutic approaches can we implement to reduce the HIV-1 proviral load?

The data will reveal pathways that can be targeted therapeutically to treat chronic immune activation in PWH. Our findings will immediately translate to optimize the standard of care in PWH.

1.6 Study design. Provide a one-sentence description of the general study design and/or type of methodology.

Your answer will help HSD in assigning applications to reviewers and in managing workload. Examples: a longitudinal observational study; a double-blind, placebo-controlled randomized study; ethnographic interviews; web scraping from a convenience sample of blogs; medical record review; coordinating center for a multi-site study.

Open-label, cross-sectional, two-cohort study.

Cohort 1: Tenofovir-containing ART (tenofovir disoproxil fumarate [TDF] OR tenofovir alafenamide [TAF] PLUS any other ART drugs) prescribed for daily use by participants' primary care providers

Cohort 2: NRTI-sparing ART (specifically: rilpivirine PLUS dolutegravir OR rilpivirine PLUS cabotegravir) prescribed for daily use by participants' primary care providers

1.7 Intent. Check all the descriptors that apply to your activity. You must place an "X" in at least one box.

This question is essential for ensuring that your application is correctly reviewed. Please read each option carefully.

Descriptor

- 1. Class project or other activity whose purpose is to provide an educational experience for the researcher (for example, to learn about the process or methods of doing research).
- 2. Part of an institution, organization, or program's own internal operational monitoring.
- 3. Improve the quality of service provided by a specific institution, organization, or program.
- 4. Designed to expand the knowledge base of a scientific discipline or other scholarly field of study, and produce results that:
 - Are expected to be applicable to a larger population beyond the site of data collection or the specific subjects studied, or
 - Are intended to be used to develop, test, or support theories, principles, and statements of relationships, or to inform policy beyond the study.
- 5. Focus directly on the specific individuals about whom the information or biospecimens are collected through oral history, journalism, biography, or historical scholarship activities, to provide an accurate and evidence-based portrayal of the individuals.
- 6. A quality improvement or program improvement activity conducted to improve the implementation (delivery or quality) of an accepted practice, or to collect data about the implementation of the practice for clinical, practical, or administrative purposes. This does not include the evaluation of the efficacy of different accepted practices, or a comparison of their efficacy.
- 7. Public health surveillance activities conducted, requested, or authorized by a public health authority for the sole purpose of identifying or investigating potential public health signals or timely awareness and priority setting during a situation that threatens public health.
- 8. Preliminary, exploratory, or research development activities (such as pilot and feasibility studies, or reliability/validation testing of a questionnaire)
- 9. Expanded access use of a drug or device not yet approved for this purpose
- 10. Use of a Humanitarian Use Device
- 11. Other. Explain:

1.8 Background, experience, and preliminary work. Answer this question only if the proposed activity has one or more of the following characteristics. The purpose of this question is to provide the IRB with information that is relevant to its risk/benefit analysis.

- Involves more than minimal risk (physical or non-physical)
- Is a clinical trial, or
- Involves having the subjects use a drug, biological, botanical, nutritional supplement, or medical device.

"Minimal risk" means that the probability and magnitude of harm or discomfort anticipated in the research are not greater than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

a. Background. Provide the rationale and the scientific or scholarly background for the proposed activity, based on existing literature (or clinical knowledge). Describe the gaps in current knowledge that the project is intended to address.

This should be a plain language description. Do not provide scholarly citations. Limit your answer to less than one page, or refer to an attached document with background information that is no more than three pages long.

Current antiretroviral treatment (ART) is extremely effective in controlling HIV replication and in many patients suppresses the number of virions measurable in peripheral blood to undetectable levels. Nevertheless, whenever ART is stopped, HIV levels rebound due to the reactivation of integrated HIV proviruses in resting CD4+ T lymphocytes. During effective ART, it would theoretically require 60 years of treatment to eliminate the latent reservoir in T cells.

Maintenance of the latent viral reservoir depends on viral silence and cellular proliferation. Some latently-infected cells do not express viral proteins and because of this silence escape immune system detection. Proliferation of virally-silent cells then increases the host pool of viral DNA. It is typically assumed that the maintenance of infection is entirely determined by characteristics of HIV itself and its effects on immune activation, so little attention has been given to the possibility that ART drugs could contribute to viral latency.

Tenofovir (TFV), a phosphonated nucleoside reverse transcriptase inhibitor (NRTI), is being used for oral pre-exposure prophylaxis (PrEP). We conducted a comprehensive systems biology assessment of its impact on the mucosa in several clinical trials. Surprisingly, we found that TFV in combination with emtricitabine, another drug of the NRTI class, stimulated a type I/III interferon signature throughout the gut, specifically in the duodenum and the rectum, the two anatomical sites we studied. We were able to clearly discern this as a feature of the drugs because of the unique opportunity to study them in the setting of PrEP taken by healthy, HIV-uninfected individuals.

These findings prompted our hypothesis that tenofovir, and perhaps NRTIs in general, stimulate a type I/III interferon also in PWH who take these drugs. Because chronic interferon stimulation may promote the survival and proliferation of cells with integrated provirus, we also hypothesize that these drugs antagonize decay of the HIV latent reservoir in PWH on ART. Consequently, we hypothesize that PWH who have switched from NRTI-containing ART to NRTI-sparing ART exhibit lower type I/III interferon pathway activation and lower latent HIV reservoir size.

We also hypothesize that independently of treatment, the extent of type I/III interferon activation correlates with latent HIV reservoir size. Recent studies in humanized mice, showing that blocking IFN-I/III pathways led not only to less immune activation but also to a lower HIV reservoir, support this. If these hypotheses are true, effectively suppressing HIV with an NRTI-free regimen could benefit PWH in two ways: First, less immune activation will overtime translate to lower co-morbidities, such as cardiovascular and gastrointestinal inflammatory diseases. Second, less immune activation will allow for faster decay of the latent HIV reservoir.

Thus, using NRTI-sparing regimens in conjunction with specific new curative approaches may increase the likelihood of achieving HIV cure.

We plan to test type I/II IFN pathway activation using droplet digital PCR (ddPCR) to quantify mRNA copy numbers of ISG15 (ISG15 ubiquitin-like modifier), MX1 (MX dynamin like GTPase 1) and IFI6 (interferon alpha inducible protein 6). RNA will be isolated from the rectal and duodenal biopsies stored in RNALater using the RNeasy Fibrous Tissue Mini Kit (Qiagen) and from the PBMC using the RNeasy Plus Mini Kit (Qiagen). ddPCR will be performed on a 6-color Naica droplet digital PCR instrument (Stilla Technologies).

The latent HIV reservoir will be tested using a novel intact/defective proviral HIV DNA ddPCR assay developed jointly by the Hladik and Jerome groups in Seattle

b. Experience and preliminary work. Briefly describe experience or preliminary work or data (if any) that you, your team, or your collaborators/co-investigators have that supports the feasibility and/or safety of this study.

It is not necessary to summarize all discussion that has led to the development of the study protocol. The IRB is interested only in short summaries about experiences or preliminary work that suggest the study is feasible and that risks are reasonable relative to the benefits. Examples: Your team has already conducted a Phase 1 study of an experimental drug which supports the Phase 2 study being proposed in this application; your team has already done a small pilot study showing that the reading skills intervention described in this application is feasible in an after-school program with classroom aides; your team has experience with the type of surgery that is required to implant the study device; the study coordinator is experienced in working with subjects who have significant cognitive impairment.

We have extensive experience in assessing immune responses in human blood cells and in mucosa as well as in characterizing the HIV reservoir. We have numerous publications using these methods. For example, our group has recently reported that the two nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs) tenofovir disoproxil fumarate (TDF) and emtricitabine (FTC), which are commonly used as part of cART (e.g., Truvada®), stimulate a type I/III interferon signature throughout the gut (Hughes et al, September 22, 2020, Cells Reports Medicine). This study was done in the setting of oral pre-exposure prophylaxis (PrEP) in healthy, HIV-uninfected individuals. By using transcriptomics (microarray and RNA-Seq) and proteomics (mass spectrometry), we defined a short list of interferon-stimulated genes (ISGs) that are induced by TDF/FTC. ACTU-3500 was reviewed through the University of Washington Institutional Review Board, number 49167. Likewise, we have just published a paper in which we developed a digital droplet PCR assay to determine the size of intact/defective proviral HIV reservoir in genomic DNA (Levy et al, Cell Reports Medicine, April 2021)

1.9 Supplements. Check all boxes that apply, to identify relevant Supplements that should be completed and uploaded to **Zipline**.

This section is here instead of at the end of the form to reduce the risk of duplicating information in this IRB Protocol form that you will need to provide in these Supplements.

Check all That Apply	Type of Research	Supplement Name
<input type="checkbox"/>	Department of Defense The research involves Department of Defense funding, facilities, data, or personnel.	SUPPLEMENT Department of Defense
<input type="checkbox"/>	Department of Energy The research involves Department of Energy funding, facilities, data, or personnel.	SUPPLEMENT Department of Energy

<input checked="" type="checkbox"/>	Drug, biologic, botanical, supplement Procedures involve the use of <u>any</u> drug, biologic, botanical or supplement, even if the item is not the focus of the proposed research	SUPPLEMENT Drugs
<input type="checkbox"/>	Emergency exception to informed consent Research that requires this special consent waiver for research involving more than minimal risk	SUPPLEMENT Exception from Informed Consent for Emergency Research (EFIC)
<input checked="" type="checkbox"/>	Genomic data sharing Genomic data are being collected and will be deposited in an external database (such as the NIH dbGaP database) for sharing with other researchers, and the UW is being asked to provide the required certification or to ensure that the consent forms can be certified	SUPPLEMENT Genomic Data Sharing
<input type="checkbox"/>	Medical device Procedures involve the use of <u>any</u> medical device, even if the device is not the focus of the proposed research, except when the device is FDA-approved and is being used through a clinical facility in the manner for which it is approved	SUPPLEMENT Devices
<input type="checkbox"/>	Multi-site or collaborative study The UW IRB is being asked to review on behalf of one or more non-UW institutions in a multi-site or collaborative study.	SUPPLEMENT Multi-site or Collaborative Research
<input type="checkbox"/>	Non-UW Individual Investigators The UW IRB is being asked to review on behalf of one or more non-UW individuals who are not affiliated with another organization for the purpose of the research.	SUPPLEMENT Non-UW Individual Investigators
<input type="checkbox"/>	Other REDCap Installation Attestation for Electronic Consent The research will use a non-UW installation of REDCap for conducting and/or documenting informed consent.	SUPPLEMENT Other REDCap Installation
<input type="checkbox"/>	None of the above	

1.10 Confirm by checking the box below that you will comply with these basic COVID infection and risk control measures, OR that you have an exception granted by the HSD Director: (a) the only in-person interactions are essential for the study; (b) study team members and participants will wear face coverings throughout all procedures; (c) all study staff and participants will be screened for COVID-19 just prior to each research visit; and (d) no participants over the age of 85 years will be enrolled if their in-person participation is not connected with a clinical visit. See this [webpage](#) for details, including what “screening” means.

Review the HSD [website](#) for current guidelines about which in-person research activities are allowable.

Confirmed

2 PARTICIPANTS

2.1 Participants. Describe the general characteristics of the subject populations or groups, including age range, gender, health status, and any other relevant characteristics.

People living with HIV (PWH) on stable use of antiretroviral therapy (ART). They will be between 18 and 65 years of age. Children less than 18 years of age are excluded. Women of childbearing potential should not be pregnant to participate.

Cohort 1: Tenofovir-containing ART (tenofovir disoproxil fumarate [TDF] OR tenofovir alafenamide [TAF] PLUS any other ART drugs) prescribed for daily use by participants' primary care providers.
Cohort 2: NRTI-sparing ART (specifically: rilpivirine PLUS dolutegravir) prescribed for daily use by participants' primary care providers.

2.2 Inclusion and exclusion criteria.

a. Inclusion criteria. Describe the specific criteria that will be used to decide who will be included in the research from among interested or potential subjects. Define any technical terms in lay language.

1. Confirmed HIV infection, by two different positive antibody tests and/or detectable plasma HIV RNA on two different dates
2. ≥ 18 and ≤ 65 years of age
3. Stable use of ART medication for ≥ 1 year
4. No switch of ART regimen within the past 180 days
5. CD4 $> 350/\text{mm}^3$ within the past 180 days
6. HIV RNA < 40 copies / mL on ≥ 2 occasions during continuous ART of ≥ 1 years, with no blip of > 1000 HIV RNA copies / mL
7. Karnofsky score ≥ 80
8. Willingness and ability to provide informed consent for study participation
9. Willingness to undergo all required study procedures

b. Exclusion criteria. Describe the specific criteria that will be used to decide who will be excluded from the research from subjects who meet the inclusion criteria listed above. Define any technical terms in lay language.

1. Active malignancy including myelodysplastic syndrome, or myeloproliferative disease within 24 weeks prior to study entry
2. Prior organ or bone marrow transplantation
3. Diagnosed autoimmune disease
4. Medical need for ongoing treatment with an immunosuppressive drug
5. Diagnosis of AIDS (defined as any AIDS-defining opportunistic infection or cancer, or a history of blood CD4+ T cell count $< 200/\mu\text{L}$)
6. Active opportunistic infection
7. Vomiting or diarrhea which prohibits consistent use of ART
8. Pregnant or breastfeeding
9. Excessive ingestion of ethanol determined by an AUDIT score of > 8
10. Substance abuse
11. History of medical non-compliance
12. The following laboratory values (< 30 days before enrollment):
 - Hemoglobin < 8.5 mg/dL
 - Platelet count $< 100,000/\mu\text{L}$
 - Coagulation (PT/PTT) tests above the normal reference
 - Creatinine clearance < 60 mL/min
13. Using disallowed medications:
 - Systemic corticosteroids
 - Other immunosuppressive medications (e.g., cyclosporine, sirolimus, tacrolimus, pimecrolimus, tofacitinibe)
14. BMI > 40
15. Pulmonary dysfunction.
16. Use of narcotics.

2.3 Prisoners. IRB approval is required in order to include prisoners in research, even when prisoners are not an intended target population.

Is the research likely to have subjects who become prisoners while participating in the study?

For example, a longitudinal study of youth with drug problems is likely to have subjects who will be prisoners at some point during the study.

<input checked="" type="checkbox"/>	No
<input type="checkbox"/>	Yes

→ If yes, if a subject becomes a prisoner while participating in the study, will any study procedures and/or data collection related to the subject be continued while the subject is a prisoner?

<input type="checkbox"/>	No
<input type="checkbox"/>	Yes

→ If yes, describe the procedures and/or data collection that will continue with prisoner subjects

2.4 Will the proposed research recruit or obtain data from individuals that are known to be prisoners?

For records reviews: if the records do not indicate prisoner status and prisoners are not a target population, select "No". See the [WORKSHEET Prisoners](#) for the definition of "prisoner".

<input checked="" type="checkbox"/>	No
<input type="checkbox"/>	Yes

→ If yes, answer the following questions (i – iv).

i. Describe the type of prisoners, and which prisons/jails:

ii. One concern about prisoner research is whether the effect of participation on prisoners' general living conditions, medical care, quality of food, amenities, and/or opportunity for earnings in prison will be so great that it will make it difficult for prisoners to adequately consider the research risks. How will the chances of this be reduced?

iii. Describe what will be done to make sure that (a) recruitment and subject selection procedures will be fair to all eligible prisoners and (b) prison authorities or other prisoners will not be able to arbitrarily prevent or require particular prisoners from participating.

iv. If the research will involve prisoners in federal facilities or in state/local facilities outside of Washington State: check the box below to provide assurance that study team members will (a) not encourage or facilitate the use of a prisoner's participation in the research to influence parole decisions, and (b) clearly inform each prisoner in advance (for example, in a consent form) that participation in the research will have no effect on his or her parole.

<input type="checkbox"/>	Confirmed
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2.5 Protected populations. IRB approval is required for the use of the subject populations listed here. Check the boxes for any of these populations that will be purposefully included. (In other words, being a part of the population is an inclusion criterion for the study.)

The WORKSHEETS describe the criteria for approval but do not need to be completed and should not be submitted.

Population	Worksheet
<input type="checkbox"/> Fetuses in utero	WORKSHEET Pregnant Women
<input type="checkbox"/> Neonates of uncertain viability	WORKSHEET Neonates
<input type="checkbox"/> Non-viable neonates	WORKSHEET Neonates
<input type="checkbox"/> Pregnant women	WORKSHEET Pregnant Women

a. If you check any of the boxes above, use this space to provide any information that may be relevant for the IRB to consider.

2.6 Native Americans or non-U.S. indigenous populations. Will Native American or non-U.S. indigenous populations be actively recruited through a tribe, tribe-focused organization, or similar community-based organization?

Indigenous people are defined in international or national legislation as having a set of specific rights based on their historical ties to a particular territory and their cultural or historical distinctiveness from other populations that are often politically dominant.

Examples: a reservation school or health clinic; recruiting during a tribal community gathering

- No**
- Yes** → If yes, name the tribe, tribal-focused organization, or similar community-based organization. The UW IRB expects that tribal/indigenous approval will be obtained before beginning the research. This may or may not involve approval from a tribal IRB. The study team and any collaborators/investigators are also responsible for identifying any tribal laws that may affect the research.

2.7 Third party subjects. Will the research collect private identifiable information about *other individuals* from the study subjects? Common examples include: collecting medical history information or contact information about family members, friends, co-workers.

“Identifiable” means any direct or indirect identifier that, alone or in combination, would allow you or another member of the research team to readily identify the person. For example, suppose that the research is about immigration history. If subjects are asked questions about their grandparents but are not asked for names or other information that would allow easy identification of the grandparents, then private identifiable information is not being collected about the grandparents and the grandparents are not subjects.

- No**

Yes → If yes, these individuals are considered human subjects in the study. Describe them and what data will be collected about them.

2.8 Number of subjects. Is it possible to predict or describe the maximum number of subjects (or subject units) needed to complete the study, for each subject group?

Subject units mean units within a group. For most research studies, a group will consist of individuals. However, the unit of interest in some research is not the individual. Examples:

- Dyads such as caregiver-and-Alzheimer’s patient, or parent and child
- Families
- Other units, such as student-parent-teacher

Subject group means categories of subjects that are meaningful for the specific study. Some research has only one subject group – for example, all UW students taking Introductory Psychology. Some common ways in which subjects are grouped include:

- By intervention – for example, an intervention group and a control group.
- By subject population or setting – for example, urban versus rural families
- By age – for example, children who are 6, 10, or 14 years old.

The IRB reviews the number of subjects in the context of risks and benefits. Unless otherwise specified, if the IRB determines that the research involves no more than minimal risk: there are no restrictions on the total number of subjects that may be enrolled. If the research involves more than minimal risk: The number of enrolled subjects must be limited to the number described in this application. If it is necessary later to increase the number of subjects, submit a Modification. Exceeding the IRB-approved number ([over-enrollment](#)) will be considered non-compliance.

No → If no, provide the rationale in the box below. Also, provide any other available information about the scope/size of the research. You do not need to complete the table.

Example: It may not be possible to predict the number of subjects who will complete an online survey advertised through Craigslist, but you can state that the survey will be posted for two weeks and the number who respond is the number who will be in the study.

Yes → If yes, for each subject group, use the table below to provide the estimate of the maximum desired number of individuals (or other subject unit, such as families) who will complete the research.

Group name/description	Maximum desired number of individuals (or other subject unit, such as families) who will complete the research
	<i>Provide numbers for the site(s) reviewed by the UW IRB and for the study-wide total number; example: 20/100</i>
Cohort 1: Tenofovir-containing ART (tenofovir disoproxil fumarate [TDF] OR tenofovir alafenamide [TAF] PLUS any other ART drugs) prescribed for daily use by participants’ primary care providers	20 individuals
Cohort 2: NRTI-sparing ART (specifically: rilpivirine PLUS dolutegravir OR rilpivirine PLUS cabotegravir) prescribed for daily use by participants’ primary care providers	20 individuals

2.9 COVID-19 Screening. If there will be any in-person interactions with the subjects, describe how you will screen them for COVID-19 symptoms within the 24 hours before the interaction. Also, describe the COVID-19 screening procedures for the study staff who will interact with the subjects.

Acceptable procedures include some type of symptom check or attestation, or a SARS-CoV-2 test with quick access to results. Symptom attestation involves an individual reviewing a list of symptoms and declaring the presence or absence of those symptoms. HSD strongly encourages adapting this Washington State Department of Health Screening Tool <https://www.doh.wa.gov/Portals/1/Documents/1600/coronavirus/Employervisitorscreeningguidance.pdf> or the UW EH&S Example Symptom Self-Attestation in this document: <https://www.ehs.washington.edu/system/files/resources/guidance-symptom-monitoring-COVID-19.pdf>. If you will test for the virus, you must also describe here whether the testing lab is CLIA-certified and how the results will be reported to the subjects.

Before the first screening visit, study participants will have submitted a symptom self-attestation form. Symptom self-attestation involves an individual reviewing a list of symptoms and declaring the presence or absence of those symptoms. On the day of the hospital visit (and part of the general hospital admission protocol during COVID-19 pandemic), clinical staff may take the person's temperature before entering the clinic and if the person has fever (100.4 or higher), they will be required to stay home. Likewise, clinical personnel may ask the study participants in-person questions regarding cough/shortness of breath/sore throat/muscle pain or other symptoms.

3 NON-UW RESEARCH SETTING

*Complete this section only if UW investigators and people named in the **SUPPLEMENT: Non-UW Individual Investigators** will conduct research procedures outside of UW and Harborview*

3.1 Reason for locations. Describe the reason(s) for choosing the locations.

This is especially important when the research will occur in locations or with populations that may be vulnerable to exploitation. One of the three ethical principles the IRB must consider is justice: ensuring that reasonable, non-exploitative, and well-considered procedures are administered fairly, with a fair distribution of costs and potential benefits.

NA

3.2 Local context. Culturally appropriate procedures and an understanding of local context are an important part of protecting subjects. Describe any site-specific cultural issues, customs, beliefs, or values that may affect the research, how it is conducted, or how consent is obtained or documented.

Examples: It would be culturally inappropriate in some international settings for a woman to be directly contacted by a male researcher; instead, the researcher may need to ask a male family member for permission before the woman can be approached. It may be appropriate to obtain permission from community leaders prior to obtaining consent from individual members of a group. In some distinct cultural groups, signing forms may not be the norm.

This federal site maintains an international list of human research standards and requirements: <http://www.hhs.gov/ohrp/international/index.html>

NA

- 3.3 Location-specific laws.** Describe any local laws that may affect the research (especially the research design and consent procedures). The most common examples are laws about:
- **Specimens** – for example, some countries will not allow biospecimens to be taken out of the country.
 - **Age of consent** – laws about when an individual is considered old enough to be able to provide consent vary across states, and across countries.
 - **Legally authorized representative** – laws about who can serve as a legally authorized representative (and who has priority when more than one person is available) vary across states and countries.
 - **Use of healthcare records** – many states (including Washington State) have laws that are similar to the federal HIPAA law but that have additional requirements.

NA

- 3.4 Location-specific administrative or ethical requirements.** Describe local administrative or ethical requirements that affect the research.

Example: A school district may require researchers to obtain permission from the head district office as well as school principals before approaching teachers or students; a factory in China may allow researchers to interview factory workers but not allow the workers to be paid for their participation.

NA

- 3.5 If the PI is a student: Does the research involve traveling outside of the US?**

No

Yes

→ If yes, confirm by checking the box that (1) you will register with the [UW Office of Global Affairs](#) before traveling; (2) you will notify your advisor when the registration is complete; and (3) you will request a UW Travel Waiver if the research involves travel to the [list of countries](#) requiring a UW Travel Waiver.

Confirmed

4 RECRUITING and SCREENING PARTICIPANTS

- 4.1 Recruiting and Screening.** Describe how subjects will be identified, recruited, and screened. Include information about: how, when, where, and in what setting. Identify who (by position or role, not name) will approach and recruit subjects, and who will screen them for eligibility.

Note: Per UW Medicine policy, the UW Medicine eCare/MyChart system may not be used for research recruitment purposes.

Participants will be People living with HIV (PWH) on stable antiretroviral therapy (ART). Potentially eligible study participants will be identified by online database (Leaf, <https://www.iths.org/investigators/services/bmi/leaf/>) and contacted by the study coordinator, UW ACTU screening nurse or other UW ACTU clinical staff via phone call. Pre-screening may be conducted over the phone, including signing of consent using UW ITHS REDCap or in person in the clinic. Visits will occur at the UW AIDS Clinical Trials Unit and the GI Endoscopy Suite at Harborview Medical Center. The procedure visit can occur on the same day as the screening visit if all laboratory

results are obtained before any study procedures are initiated. Otherwise, it can occur later, but no more than one month after the screening visit.

4.2 Recruitment materials.

a. What materials (if any) will be used to recruit and screen subjects?

Examples: talking points for phone or in-person conversations; video or audio presentations; websites; social media messages; written materials such as letters, flyers for posting, brochures, or printed advertisements; questionnaires filled out by potential subjects.

The questions the participants will be asked are included in the uploaded document “Talking points for phone screening”.

b. Upload descriptions of each type of material (or the materials themselves) to **Zipline**. If letters or emails will be sent to any subjects, these should include a statement about how the subject’s name and contact information were obtained. No sensitive information about the person (such as a diagnosis of a medical condition) should be included in the letter.

HSD encourages researchers to consider uploading descriptions of most recruitment and screening materials instead of the materials themselves. The goal is to provide the researchers with the flexibility to change some information on the materials without submitting a Modification for IRB approval of the changes. Examples:

- *Provide a list of talking points that will be used for phone or in-person conversations instead of a script.*
- *For the description of a flyer, include the information that it will provide the study phone number and the name of a study contact person (without providing the actual phone number or name). This means that a Modification would not be necessary if/when the study phone number or contact person changes. Also, instead of listing the inclusion/exclusion criteria, the description below might state that the flyer will list one or a few of the major inclusion/exclusion criteria.*
- *For the description of a video or a website, include a description of the possible visual elements and a list of the content (e.g., study phone number; study contact person; top three inclusion/exclusion criteria; payment of \$50; study name; UW researcher).*

4.3 Relationship with participant population. Do any members of the study team have an existing relationship with the study population(s)?

Examples: a study team member may have a dual role with the study population (for example, being their clinical care provider, teacher, laboratory director or tribal leader in addition to recruiting them for his/her research).

<input checked="" type="checkbox"/>
<input type="checkbox"/>

No

Yes

→ If yes, describe the nature of the relationship.

4.4 Payment to participants. The IRB must evaluate subject payment for the possibility that it will unduly influence subjects to participate. Refer to [GUIDANCE Subject Payment](#) when designing subject payment plans. Provide the following information about your plans for paying research subjects in the text box below or note that the information can be found in the consent form.

- The total amount/value of the payment
- Schedule/timing of the payment [i.e., when will subjects receive the payment(s)]
- Purpose of the payment [e.g., reimbursement, compensation, incentive]
- Whether payment will be “pro-rated” so that participants who are unable to complete the research may still receive some part of the payment

The IRB expects the consent process or study information provided to the subjects to include all of the above-listed information about payment, including the number and amount of payments, and especially when subjects can expect to receive payment. One of the most frequent complaints received by HSD is from subjects who expected to receive cash or a check on the day that they completed a study and who were angry or disappointed when payment took 6-8 weeks to reach them.

The compensation for the study visit can be found in the consent form. They will receive \$100 for anoscopy and \$300 for EGD. These sums may be given as gift cards for grocery or variety stores, such as Safeway or Target. Participants will also receive reimbursement for parking or transportation.

Participants who are not eligible after the screening visit will receive compensation for parking or transportation only. This compensation will be given in a form of pre-paid parking vouchers or tickets or adult ORCA card (up to \$30/visit). Participants who are eligible and attempt blood donation and/or anoscopy/esophagogastroduodenoscopy for the research study will be compensated the full amount.

4.5 Non-monetary compensation. Describe any non-monetary compensation that will be provided. Example: extra credit for students; a toy for a child. If class credit will be offered to students, there must be an alternate way for the students to earn the extra credit without participating in the research.

We will provide limited travel support for those who would otherwise be unable to participate in the study.

4.6 Will data or specimens be accessed or obtained for recruiting and screening procedures prior to enrollment?

Examples: names and contact information; the information gathered from records that were screened; results of screening questionnaires or screening blood tests; Protected Health Information (PHI) from screening medical records to identify possible subjects.

No

→ If no, skip the rest of this section; go to [question 5.1](#).

Yes

→ If yes, describe the data and/or specimens (including PHI) and whether it will be retained as part of the study data.

Potential study participants will be identified by online database Leaf. It is a self-service tool which provides UW investigators with a user-friendly interface for querying the electronic health system records within UW Medicine. The study coordinator or nurse will be able to access identified patient information such as name, demographics, clinical records, etc. Study staff will review patient’s medical charts to confirm HIV status, use of ART for the two prior years, viral suppression on ART during the two prior years (by reading the results of all HIV plasma viral load tests done during the two prior years), and eligibility age (≥ 18 to ≤ 65 years old). We may also read other clinical laboratory results and information about medications taken. If the patient signs consent, this information will be retained as part of the study data. If the patient does not sign consent, these data will not be retained. The additional information will be collected from the phone

interview done. We will ask the participant how long has the participant been taking the HIV medication and if she/he has recently changed to other medications.

4.7 Consent for recruiting and screening. Will consent be obtained for any of the recruiting and screening procedures? ([Section 8: Consent of Adults](#) asks about consent for the main study procedures).

“Consent” includes: consent from individuals for their own participation; parental permission; assent from children; consent from a legally authorized representative for adult individuals who are unable to provide consent.

Examples:

- For a study in which names and contact information will be obtained from a registry: the registry should have consent from the registry participants to release their names and contact information to researchers.
- For a study in which possible subjects are identified by screening records: there will be no consent process.
- For a study in which individuals respond to an announcement and call into a study phone line: the study team person talking to the individual may obtain non-written consent to ask eligibility questions over the phone.

- No** → If no, skip the rest of this section; go to [question 5.1](#).
- Yes** → If yes, describe the consent process.

We will obtain consent from subjects for the preliminary phone screening through a brief verbal consent. Consent will be obtained from all study participants either by signing electronically the UW ITHS REDCap during the pre-screening, or signing a written form on the day of the screening visit.

a. Documentation of consent. Will a written or verifiable electronic signature from the subject on a consent form be used to document consent for the **recruiting and screening procedures**?

- No** → If no, describe the information that will be provided during the consent process and for which procedures.

- Yes** → If yes, upload the consent form to **Zipline**.

5 PROCEDURES

5.1 Study procedures. Using lay language, provide a complete description of the study procedures, including the sequence, intervention or manipulation (if any), drug dosing information (if any), blood volumes and frequency of draws (if any), use of records, time required, and setting/location. If it is available: Upload a study flow sheet or table to **Zipline**.

For studies comparing standards of care: It is important to accurately identify the research procedures. See UW IRB [POLICY Risks of Harm from Standard Care](#) and the draft guidance from the federal Office of Human Research Protections, [“Guidance on Disclosing Reasonably Foreseeable Risks in Research Evaluating Standards of Care”](#); October 20, 2014. Information about pediatric blood volume and frequency of draws that would qualify for expedited review can be found in this [reference table](#) on the Seattle Children’s IRB website.

Visits will occur at the UW AIDS Clinical Trials Unit (ACTU) and the GI Endoscopy Suite at Harborview Medical Center.

Screening visit:

The following will occur at **Screening (UW ACTU, up to 90 minutes)**

- Informed consent for study participation (if not already signed via UW ITHS REDCap)
- Targeted medical history. Study participants will be asked to fill out a survey with questions related to his/her medical history, current use of medications, sexual history and substance abuse.
- Targeted physical exam, if not documented within the prior month
- Laboratory testing, if not documented within the prior month:

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Venipuncture (about 19 ml, 4 teaspoons of blood) for:

- HIV plasma viral load test
- Peripheral blood CD4+ T cell count
- Complete blood count
- PT/PTT (for blood clotting function)
- Renal (kidney) function panel
- Scheduling for entry procedures

Procedure visit (UW ACTU and HMC Gastroenterology Clinic, up to 4 hours).

The procedure visit can occur on the same day as the screening visit if all laboratory results are obtained before any study procedures are initiated. Otherwise, it can occur later, but no more than one month after the screening visit.

- Targeted medical history and physical exam
- Women of childbearing age: urine pregnancy test
- Venipuncture (about 40 ml of blood) for:
 - 4 PAXgene tubes with 2.5 mL each (RNA expression studies)
 - 3 ACD tubes with 10 mL each (PBMC isolation and storage; plasma storage)
- Anoscopy with 5 rectal biopsies and one cytobrush
- Esophagogastroduodenoscopy (EGD) with 5 duodenal biopsies and one cytobrush.

The anoscopy is an examination using a small, rigid, tubular instrument called anoscope (also called an anal speculum). This is inserted a few inches into the rectum in order to collect some small samples of mucosal tissue. You may feel pressure during the examination, and the anoscope will make one feel as if he or she were about to have a bowel movement. This is normal, however, and many patients do not feel pain from anoscopy.

The EGD procedure will be done at the HMC Gastroenterology Clinic and involves looking at the esophagus, stomach, and first and second portion of the duodenum (). This will also involve the use of an endoscope to remove small tissue samples. This procedure uses conscious sedation drugs given by a vein in your arm. The procedure will take about 1½-2 hours, including time for recovery. You will need to have someone drive you home.

In both cases (anoscopy and EGD), we will preserve some samples in RNA later (for RNA and DNA analysis and potentially immunohistology) and some biopsies may be dry frozen (for potential proteomics study and determination of drug levels).

All blood (except for routine blood work) and tissue specimens will be transported to the Hladik/Gornalusse Laboratory. Venipuncture specimens can be transported at room temperature. Biopsy specimens should be collected in RNAlater (n=3) and in empty tubes (n=2) and transported on ice. Cytobrushes will be placed into dry tubes and transported on ice. All studies will be performed in the Hladik/Gornalusse Lab.

5.2 Recordings. Does the research involve creating audio or video recordings?

No
 Yes

→ If no, go to [question 5.3](#).

→ If yes, verify that you have described what will be recorded in 5.1 and answer question a.

a. Before recording, will consent for being recorded be obtained from subjects and any other individuals who may be recorded?

No

→ If no, email hsdinfo@uw.edu before submitting this application in Zipline. In the email, include a brief description of the research and a note that individuals will be recorded without their advance consent.

Yes

5.3 MRI scans. Will any subjects have a Magnetic Resonance Imaging (MRI) scan as part of the study procedures?

This means scans that are performed solely for research purposes or clinical scans that are modified for research purposes (for example, using a gadolinium-based contrast agent when it is not required for clinical reasons).

No

→ If no, go to [question 5.4](#).

Yes → If yes, answer questions a through c.

a. Describe the MRI scan(s). Specifically:

- What is the purpose of the scan(s)? *Examples: obtain research data; safety assessment associated with a research procedure.*
- Which subjects will receive an MRI scan?
- Describe the minimum and maximum number of scans per subject, and over what time period the scans will occur. *For example: all subjects will undergo two MRI scans, six months apart.*

b. MRI facility. At which facility(ies) will the MRI scans occur? Check all that apply.

- | | |
|--------------------------|----------------------------------------------------------------------------------|
| <input type="checkbox"/> | UWMC Radiology/Imaging Services (the UWMC clinical facility) |
| <input type="checkbox"/> | DISC Diagnostic Imaging Sciences Center (UWMC research facility) |
| <input type="checkbox"/> | CHN Center for Human Neuroscience MRI Center (Arts & Sciences research facility) |
| <input type="checkbox"/> | BMIC Biomolecular Imaging Center (South Lake Union research facility) |
| <input type="checkbox"/> | Harborview Radiology/Imaging Services (the Harborview clinical facility) |
| <input type="checkbox"/> | SCCA Imaging Services |
| <input type="checkbox"/> | Northwest Diagnostic Imaging |
| <input type="checkbox"/> | Other: identify in the text box below: |

c. Personnel. For MRI scans that will be conducted at the DISC, CHN or BMIC research facilities: Indicate who will be responsible for operating the MRI scanner by checking all that apply.

- | | |
|--------------------------|---------------------------------------------------------------------------------------------|
| <input type="checkbox"/> | MRI technician who is formally qualified |
| <input type="checkbox"/> | Researcher who has completed scanner operator training provided by a qualified MRI operator |

5.4 Data variables. Describe the specific data that will be obtained (including a description of the most sensitive items). Alternatively, a list of the data variables may be uploaded to **Zipline**.

During the Screening visit at UW ACTU, we will obtain medical and sexual histories, and we will also collect information about drug use (type of drug and frequency), which will be the most sensitive data. We uploaded a document named “Questionnaires” indicating the types of question and information that will be gathered during this Screening visit.

From blood, duodenal and rectal biopsies, we will **obtain immune response data**. We will measure the level of expression of 3 genes that play a role in the response against HIV. These genes are named: ISG15, MX1 and IFI6. We will use digital droplet PCR (ddPCR) to determine mRNA copies from RNA.

From blood, we will measure **HIV copy numbers** and also, we will describe how intact or defective the latent HIV “hides” in white blood cells. .

Lastly, we may perform **global transcriptome analysis** using sequencing of biopsy mRNA, test for active **drug levels** in blood and tissues, and conduct **DNA sequencing of the bacterial 16S RNA gene** from cytobrush material to determine microbial composition in duodenum or rectum.

5.5 Data sources. For all types of data that will be accessed or collected for this research: Identify whether the data are being obtained from the subjects (or subjects' specimens) or whether they are being obtained from some other source (and identify the source).

If you have already provided this information in Question 5.1, you do not need to repeat the information here.

All medical and sexual history and drug use data will be obtained from the participants themselves or from medical records via LEAF.

All biological data will be derived from laboratory experiments.

5.6 Identifiability of data and specimens. Answer these questions carefully and completely. This will allow HSD to accurately determine the type of review that is required and the relevant compliance requirements. Review the following definitions before answering the questions:

Access means to view or perceive data, but not to possess or record it. See, in contrast, the definition of "obtain".

Identifiable means that the identity of an individual is or may be readily (1) ascertained by the researcher or any other member of the study team from specific data variables or from a combination of data variables, or (2) associated with the information.

Direct identifiers are direct links between a subject and data/specimens. Examples include (but are not limited to): name, date of birth, medical record number, email or IP address, pathology or surgery accession number, student number, or a collection of data that is (when taken together) identifiable.

Indirect identifiers are information that links between direct identifiers and data/specimens. Examples: a subject code or pseudonym.

Key refers to a single place where direct identifiers and indirect identifiers are linked together so that, for example, coded data can be identified as relating to a specific person. Example: a master list that contains the data code and the identifiers linked to the codes.

*Obtain means to possess or record in any fashion (writing, electronic document, video, email, voice recording, etc.) for research purposes and to retain for any length of time. This is different from **accessing**, which means to view or perceive data.*

a. Will you or any members of your team have access to any direct or indirect identifiers?

Yes

→ If yes, describe which identifiers and for which data/specimens.

The study coordinator and nurse will have access to the online database LEAF, so they will be able to access medical records, which include identifiable information such as patients name, DOB, SSN, address, current medications and others. All specimens sent from the clinic to the Hladik/Gornalusse Lab will be de-identified, i.e., specimen labels and accompanying information sheets will not allow the PIs or any laboratory members to identify the study subjects. So, only coded data is available to researchers and no one else. Communication with study subjects will only be done by clinic personnel.

No

→ If no, select the reason(s) why you (and all members of your team) will not have access to direct or indirect identifiers.

There will be no identifiers.

Identifiers or the key have been (or will have been) destroyed before access.

There is an agreement with the holder of the identifiers (or key) that prohibits the release of the identifiers (or key) to study team members under any circumstances.

This agreement should be available upon request from the IRB. Examples: a Data Use Agreement, Repository Gatekeeping form, or documented email.

There are written policies and procedures for the repository/database/data management center that prohibit the release of the identifiers (or identifying link). This includes situations involving an Honest Broker.

There are other legal requirements prohibiting the release of the identifiers or key. Describe them below.

b. Will you or any study team members obtain any direct or indirect identifiers?

Yes

→ If yes, describe which identifiers and for which data/specimens.

All study-related information will be stored securely at the study site (UW ACTU). All participant information (direct identifiers such as name, birthdates, phone numbers, emails, and addresses) will be stored in locked file cabinets in areas with access limited to study staff (i.e. study coordinator or nurses).

As part of the study, subjects will be given a study-specific code (e.g. Initials-####, indirect identifiers). All study-specific laboratory specimens, reports, study data collection, and administrative forms will be identified by this study code.

All records that contain names or other personal identifiers (e.g. consent forms, contact information) will be stored separately from study records identified by code number. All local databases will be secured with password-protected access systems.

All specimens sent from the clinic to the Hladik/Gornalusse Lab will be de-identified, i.e., specimen labels and accompanying information sheets will not allow the PIs or any laboratory members to identify the study subjects. Communication with study subjects will only be done by clinic personnel.

No

→ If no, select the reason(s) why you (and all members of your team) will not obtain direct or indirect identifiers.

There will be no identifiers.

Identifiers or the key have been (or will have been) destroyed before access.

There will be an agreement with the holder of the identifiers (or key) that prohibits the release of the identifiers (or key) under any circumstances.

This agreement should be available upon request from the IRB. Examples: a Data Use Agreement, Repository Gatekeeping form, or documented email.

There are written policies and procedures for the repository/database/data management center that prohibit the release of the identifiers (or identifying link). This includes situations involving an Honest Broker.

There are other legal requirements prohibiting the release of the identifiers or key. Describe them below.

c. If any identifiers will be obtained, indicate how the identifiers will be stored (and for which data). NOTE: Do not describe the data security plan here – that information is requested in section 9.6.

Identifiers will be stored with the data. Describe the data to which this applies:

Identifiers and study data will be stored separately but a link will be maintained between the identifiers and the study data (for example, through the use of a code). Describe the data to which this applies:

All records that contain names or other personal identifiers (e.g. consent forms, contact information) will be stored separately from study records identified by code number. They will be kept in locked cabinets at the UW ACTU unless they are actively being used. Access to the cabinets and the charts is limited to ACTU staff with a need to access the research chart or the coding list. The computer with the coding electronic list is double password protected and accessible only to the ACTU data staff. This computer is a UW main computer maintained by UW technology staff.

Data resulting from the study will be linked to indirect identifiers only. It will be possible for a study administrator to use data management software (redcap) to link indirect identifiers with direct identifiers, but laboratory research staff will not be able to do this.

Identifiers and study data will be stored separately, with no link between the identifiers and the study data. Describe the data to which this applies:

d. **Research collaboration.** Will individuals who provide coded information or specimens for the research also collaborate on other activities for this research? If yes, identify the activities and provide the name of the collaborator’s institution/organization.

Examples include but are not limited to: (1) study, interpretation, or analysis of the data that results from the coded information or specimens; and (2) authorship on presentations or manuscripts related to this work.

Yes. Clinicians that perform the EGD produce or anoscopy may be recognized as coauthor(s) for the potential manuscript(s) related to this study. Gastroenterologists are part of the HMC Gastroenterologist Clinic.

5.7 Protected Health Information (PHI). Will participants’ identifiable PHI be accessed, obtained, used, or disclosed for any reason (for example, to identify or screen potential subjects, to obtain study data or specimens, for study follow-up) that does not involve the creation or obtaining of a Limited Data Set?

PHI is individually identifiable healthcare record information or clinical specimens from an organization considered a “covered entity” by federal HIPAA regulations, in any form or media, whether electronic, paper, or oral. You must answer yes to this question if the research involves identifiable health care records (e.g., medical, dental, pharmacy, nursing, billing, etc.), identifiable healthcare information from a clinical department repository, or observations or recordings of clinical interactions.

- No** → If no, skip the rest of this question; [go to question 5.8](#)
- Yes** → If yes, answer all of the questions below.

a. Describe the PHI and the reason for using it. *Be specific. For example, will any “free text” fields (such as physician notes) be accessed, obtained, or used?*

PHI will be access through online database search (Leaf) to screen potential study subjects. We may need to review their medical or pharmacy records in order to determine past or current medications, past medical or surgical history, information about events or diagnoses that occur between visits. Pre-existing medical conditions, concomitant uptake of HIV medications and others as well as sexual behavior may influence the immune system and impact on the size of the HIV reservoir.

b. Is any of the PHI located in Washington State?

- No
 Yes

c. Describe the pathway of how the PHI will be accessed or obtained, starting with the source/location and then describing the system/path/mechanism by which it will be identified, accessed, and copied for the research. *Be specific. For example: directly view records; search through a department’s clinical database; submit a request to Leaf.*

We will submit a request to access Leaf (we will email biaccess@uw.edu). Also, PHI will be obtained through patient questionnaires.

d. For which PHI will subjects provide HIPAA authorization before the PHI is accessed, obtained and/or used?

A HIPAA authorization form will be signed after consent (during the screening and baseline visit period), before documenting any PHI in UW ITHS REDCap (data management software)

Confirm by checking the box that the UW Medicine [HIPAA Authorization](#) form maintained on the HSD website will be used to access, obtain, use, or disclose any UW Medicine PHI.

- Confirmed

e. For which PHI will HIPAA authorization NOT be obtained from the subjects?

Contact information for potential participants will be collected for the purposes of pre-screening and scheduling visits. This information will not be retained by study if someone does not enroll.

Provide the following assurances by checking the boxes.

- The minimum necessary amount of PHI to accomplish the purposes described in this application will be accessed, obtained and/or used.
- The PHI will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of PHI would be permitted.
- The HIPAA “accounting for disclosures” requirement will be fulfilled, if applicable. See [UW Medicine Compliance Policy #104](#).
- There will be reasonable safeguards to protect against identifying, directly or indirectly, any patient in any report of the research.

5.8 Genomic data sharing. Will the research obtain or generate genomic data?

No
 Yes → If yes, answer the question below.

a. Will genomic data from this research be sent to a national database (for example, NIH's dbGaP database)?

No
 Yes → If yes, complete the [SUPPLEMENT Genomic Data Sharing](#) and upload it to **Zipline**.

5.9 Whole genome sequencing. For research involving biospecimens: Will the research include whole genome sequencing?

Whole genome sequencing is sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen.

No
 Yes

5.10 Possible secondary use or sharing of information, specimens, or subject contact information. Is it likely that the obtained or collected information, specimens, or subject contact information will be used for any of the following:

- Future research not described in this application (in other words, secondary research)
- Submission to a repository, registry, or database managed by the study team, colleagues, or others for research purposes
- Sharing with others for their own research

Please consider the broadest possible future plans and whether consent will be obtained now from the subjects for future sharing or research uses (which it may not be possible to describe in detail at this time). Answer **YES** even if future sharing or uses will use de-identified information or specimens. Answer **NO** if sharing is unlikely or if the only sharing will be through the NIH Genomic Data Sharing described in question 5.8.

Many federal grants and contracts now require data or specimen sharing as a condition of funding, and many journals require data sharing as a condition of publication. "Sharing" may include (for example): informal arrangements to share banked data/specimens with other investigators; establishing a repository that will formally share with other researchers through written agreements; or sending data/specimens to a third party repository/archive/entity such as the Social Science Open Access Repository (SSOAR), or the UCLA Ethnomusicology Archive.

No
 Yes → If yes, answer all of the questions below.

a. Describe what will be stored for future use, including whether any direct or indirect (e.g., subject codes) identifiers will be stored.

Blood and biopsy samples will be stored for potential future profiling of genetic data. This study includes profiling of genetic information in the form of RNA sequences from duodenum and rectum. Future plans may include profiling DNA or RNA from any specimen obtained from participants. All genetic data will be linked to indirect identifiers only (subject ID). Results from genetic profiling may also be linked to results from immune assays and HIV data for each subject and analyzed using medical and sexual histories for de-identified subjects. Subject IDs will at no point be linked back to direct identifying information and laboratory researchers will not have access to direct identifying information.

- b. Describe what will be shared with other researchers or with a repository/database/registry, including whether direct identifiers will be shared and (for specimens) what data will be released with the specimens.

We may share information encompassing global transcriptome analysis (e.g. RNA-Seq data) derived from biopsy or PBMC mRNA, DNA sequencing of the bacterial 16S RNA gene from cytobrush material (to determine microbial composition in duodenum or rectum) and HIV proviral sequencing (to characterize the HIV reservoir, the pool of latent HIV proviruses integrated in cells). HIV status and the size/structure of the HIV reservoir will be data that will be shared. Direct identifiers will not be shared

- c. Who will oversee and/or manage the sharing?

The sharing will be managed by the 3 Co-PIs: Drs. Hladik, Gornalusse and Mackelprang.

- d. Describe the possible future uses, including limitations or restrictions (if any) on future uses or users. As stated above, consider the broadest possible uses.

Examples: data will be used only for cardiovascular research; data will not be used for research on population origins.

Data may be consulted by researchers from government (e.g. FDA), academic or commercial (e.g. pharmaceuticals) institutions. Data may be used, for example, to design new therapeutics to mitigate chronic immune activation in HIV positive patients (therefore, it can be used for pharmaceutical research). Additionally, it can be used for epidemiological purposes, correlating genomic variants with different transcriptomics signatures and HIV copies.

- e. Consent. Will consent be obtained now from subjects for the secondary use, banking and/or future sharing?

No
 Yes

→ If yes, be sure to include the information about this consent process in the consent form (if there is one) and in the answers to the consent questions in [Section 8](#).

- f. Withdrawal. Will subjects be able to withdraw their data/specimens from secondary use, banking or sharing?

No
 Yes

→ If yes, describe how, and whether there are any limitations on withdrawal.

Example: data can be withdrawn from the repository but cannot be retrieved after they are released.

- g. Agreements for sharing or release. Confirm by checking the box that the sharing or release will comply with UW (and, if applicable, UW Medicine) policies that require a formal agreement with the recipient for release of data or specimens to individuals or entities other than federal databases.

Data Use Agreements or Gatekeeping forms are used for data; Material Transfer Agreements are used for specimens (or specimens plus data). Do not attach any template agreement forms; the IRB neither reviews nor approves them

Confirmed

5.11 Communication with subjects during the study. Describe the types of communication (if any) the research team will have with already-enrolled subjects during the study. Provide a description instead of the actual materials themselves.

Examples: email, texts, phone, or letter reminders about appointments or about returning study materials such as a questionnaire; requests to confirm contact information.

After the screening visit, participants who will be asked to return for the second visit will be called to confirm continued eligibility and the date and time. Participants will be asked how their treatment is going. If the participant is not adhering to therapy (ART) they will not be eligible to come in for the final study visit at that time. There could also be other reasons to revoke eligibility.

If the participant still qualifies for the procedure visit, a date and time will be confirmed during this phone call. The Study Coordinator will send a brief reminder text message to these phone numbers, since they will have been confirmed to be associated with the participant, 1-2 days before the final visit appointment.

If we are repeatedly unable to reach participants via phone, or if they do not have a phone, they will be sent a generalized letter or e-mail (see attached draft letter) asking them to contact the study so that the Study Coordinator can assess their eligibility for the final (procedure) study visit. These emails and addresses are already obtained in the baseline visit questionnaire and we have prior approval to obtain this information. The letter will be vague and will not mention the nature of the study. We will also obtain contact information for another person from the participant that will be used only if the participant is not able to be contacted directly.

5.12 Future contact with subjects. Is there a plan to retain any contact information for subjects so that they can be contacted in the future?

No

Yes

→ If yes, describe the purpose of the future contact, and whether use of the contact information will be limited to the study team; if not, describe who else could be provided with the contact information. Describe the criteria for approving requests for the information.

Examples: inform subjects about other studies; ask subjects for additional information or medical record access that is not currently part of the study proposed in this application; obtain another sample.

Based on the data gathered from this study, new therapeutic approaches may arise to treat PWH so we may inform subjects about future interventional or observational research studies.

5.13 Alternatives to participation. Are there any alternative procedures or treatments that might be advantageous to the subjects?

If there are no alternative procedures or treatments, select "No". Examples of advantageous alternatives: earning extra class credit in some time-equivalent way other than research participation; obtaining supportive care or a standard clinical treatment from a health care provider instead of participating in research with an experimental drug.

No

Yes

→ If yes, describe the alternatives.

5.14 Upload to Zipline all data collection forms (if any) that will be directly used by or with the subjects, and any scripts/talking points that will be used to collect the data. Do not include data collection forms that will be used to abstract data from other sources (such as medical or academic records), or video recordings.

- *Examples: survey, questionnaires, subject logs or diaries, focus group questions.*
- *NOTE: Sometimes the IRB can approve the general content of surveys and other data collection instruments rather than the specific form itself. This prevents the need to submit a modification request for future minor changes that do not add*

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new topics or increase the sensitivity of the questions. To request this general approval, use the text box below to identify the questionnaires/surveys/ etc. for which you are seeking this more general approval. Then briefly describe the scope of the topics that will be covered and the most personal and sensitive questions. The HSD staff person who screens this application will let you know whether this is sufficient or whether you will need to provide more information.

- **For materials that cannot be uploaded:** upload screenshots or written descriptions that are sufficient to enable the IRB to understand the types of data that will be collected and the nature of the experience for the participant. You may also provide URLs (website addresses) or written descriptions below. Examples of materials that usually cannot be uploaded: mobile apps; computer-administered test; licensed and restricted standardized tests.
- **For data that will be gathered in an evolving way:** This refers to data collection/questions that are not pre-determined but rather are shaped during interactions with participants in response to observations and responses made during those interactions. If this applies to the proposed research, provide a description of the process by which the data collection/questions will be established during the interactions with subjects, how the data collection/questions will be documented, the topics likely to be addressed, the most sensitive type of information likely to be gathered, and the limitations (if any) on topics that will be raised or pursued.

Use this text box (if desired) to provide:

- Short written descriptions of materials that cannot be uploaded, such as URLs
- A description of the process that will be used for data that will be gathered in an evolving way.
- The general content of questionnaires, surveys and similar instruments for which general approval is being sought. (See the **NOTE** bullet point in the instructions above.)

5.15 SARS-CoV-2 testing. Will the subjects be tested for the SARS-CoV-2 coronavirus?

If the only testing is to screen the subjects (question 2.8), you do not need to answer this question

<input checked="" type="checkbox"/>	No
<input type="checkbox"/>	Yes

→ If yes:

- Name the testing lab
- Confirm that the lab and its use of this test is CLIA-certified or certified by the Washington State Department of Health
- Describe whether you will return the results to the participants and, if yes, who will do it and how (including any information you would provide to subjects with positive test results).

5.16 Research equipment and COVID-19. Does your research involve any equipment that will be used on more than one subject that is not part of a clinical facility?

Examples: a computer tablet, a portable research ultra-sound device).

<input type="checkbox"/>	No
<input checked="" type="checkbox"/>	Yes

→ If yes: confirm by checking the box below that the disinfection and cleaning of the equipment will meet the enhanced UW Environmental Health & Safety requirements described here:

<https://www.ehs.washington.edu/system/files/resources/cleaning-disinfection-protocols-covid-19.pdf>

<input checked="" type="checkbox"/>	Confirmed
-------------------------------------	-----------

6 CHILDREN (MINORS) and PARENTAL PERMISSION

6.1 Involvement of minors. Does the research include minors (children)?

Minor or child means someone who has not yet attained the legal age for consent for the research procedures, as described in the applicable laws of the jurisdiction in which the research will be conducted. This may or may not be the same as the definition used by funding agencies such as the National Institutes of Health.

- In Washington State the generic age of consent is 18, meaning that anyone under the age of 18 is considered a child.
- There are some procedures for which the age of consent is much lower in Washington State.
- The generic age of consent may be different in other states, and in other countries.

No → If no, go to [Section 8](#).

Yes → If yes, provide the age range of the minor subjects for this study and the legal age for consent in the study population(s). If there is more than one answer, explain.

Don't know → This means is it not possible to know the age of the subjects. For example, this may be true for some research involving social media, the Internet, or a dataset that is obtained from another researcher or from a government agency. Go to [Section 8](#).

6.2 Parental permission. Parental permission means actively obtaining the permission of the parents. This is not the same as “passive” or “opt out” permission where it is assumed that parents are allowing their children to participate because they have been provided with information about the research and have not objected or returned a form indicating they don't want their children to participate.

a. Will parental permission be obtained for:

All of the research procedures → Go to [question 6.2b](#).

None of the research procedures → Use the table below to provide justification, and skip question 6.2b.

Some of the research procedures → Use the table below to identify the procedures for which parental permission will not be obtained.

Be sure to consider all research procedures and plans, including screening, future contact, and sharing/banking of data and specimens for future work.

Children Group ¹	Describe the procedures or data/specimen collection (if any) for which there will be NO parental permission ²	Reason why parental permission will not be obtained	Will parents be informed about the research? ³	
			YES	NO
			<input type="checkbox"/>	<input type="checkbox"/>
			<input type="checkbox"/>	<input type="checkbox"/>
			<input type="checkbox"/>	<input type="checkbox"/>
			<input type="checkbox"/>	<input type="checkbox"/>

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<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>

Table footnotes

1. If the answer is the same for all children groups or all procedures: collapse the answer across the groups and/or procedures.
2. If identifiable information or biospecimens will be obtained without parent permission, any waiver granted by the IRB does not override parents' refusal to provide broad consent (for example, through the Northwest Biotrust).
3. Will parents be informed about the research beforehand even though active permission is not being obtained?

b. Indicate the plan for obtaining parental permission. One or both boxes must be checked.

- Both parents, unless one parent is deceased, unknown, incompetent, or not reasonably available; or when only one parent has legal responsibility for the care and custody of the child
- One parent, even if the other parent is alive, known, competent, reasonably available, and shares legal responsibility for the care and custody of the child.

This is all that is required for minimal risk research.

If both boxes are checked, explain:

6.3 Children who are wards. Will any of the children be wards of the State or any other agency, institution, or entity?

No
 Yes

→ If yes, an advocate may need to be appointed for each child who is a ward. The advocate must be in addition to any other individual acting on behalf of the child as guardian or in loco parentis. The same individual can serve as advocate for all children who are wards.

Describe who will be the advocate(s). The description must address the following points:

- Background and experience
- Willingness to act in the best interests of the child for the duration of the research
- Independence of the research, research team, and any guardian organization

6.4 UW Office for Youth Programs Development and Support. If the project involves interaction (in-person or remotely) with individuals under the age of 18, researchers must comply with **UW Administrative Policy Statement 10.13** and the requirements listed at [this website](#). This includes activities that are deemed to be Not Research or Exempt. It does not apply to third-party led research (i.e., research conducted by a non-UW PI). [Information and FAQs](#) for researchers are available.

This point is advisory only; there is no need to provide a response.

7 ASSENT OF CHILDREN (MINORS)

Go to [Section 8](#) if your research does not involve children (minors).

7.1 Assent of children (minors). Though children do not have the legal capacity to “consent” to participate in research, they should be involved in the process if they are able to “assent” by having a study explained to them and/or by reading a simple form about the study, and then giving their verbal choice about whether they want to participate. They may also provide a written assent if they are older. See [WORKSHEET Children](#) for circumstances in which a child’s assent may be unnecessary or inappropriate.

a. Will assent be obtained for:

- | | |
|----------------------------------------------------------------------------|-------------------------------------------------------------------------------------------|
| <input type="checkbox"/> All research procedures and child groups | → Go to question 7.2 . |
| <input type="checkbox"/> None of the research procedures and child groups | → Use the table below to provide justification, then skip to question 7.6 |
| <input type="checkbox"/> Some of your research procedures and child groups | → Use the table below to identify the procedures for which assent will not be obtained. |

Be sure to consider all research procedures and plans, including screening, future contact, and sharing/banking of data and specimens for future work.

Children Group ¹	Describe the procedures or data/specimen collection (if any) for which assent will NOT be obtained	Reason why assent will not be obtained

Table footnotes

1. If the answer is the same for all children groups or all procedures, collapse your answer across the groups and/or procedures.

7.2 Assent process. Describe how assent will be obtained, for each child group. If the research involves children of different ages, answer separately for each group. If the children are non-English speakers, include a description of how their comprehension of the information will be evaluated.

7.3 Dissent or resistance. Describe how a child’s objection or resistance to participation (including non-verbal indications) will be identified during the research, and what the response will be.

7.4 E-consent. Will any electronic processes (email, websites, electronic signatures, etc.) be used to present assent information to subjects/and or to obtain documentation (signatures) of assent? If yes, describe how this will be done.

7.5 Documentation of assent. Which of the following statements describes whether documentation of assent will be obtained?

- None of the research procedures and child groups → Use the table below to provide justification, then go to [question 7.5.b](#)

- All of the research procedures and child groups → Go to [question 7.5.a](#), do not complete the table

- Some of the research procedures and/or child groups → Complete the table below and then to go [question 7.5.a](#)

Children Group ¹	Describe the procedures or data/specimen collection (if any) for which assent will NOT be documented

Table footnotes

1. If the answer is the same for all children groups or all procedures, collapse the answer across the groups and/or procedures.

a. Describe how assent will be documented. If the children are functionally illiterate or are not fluent in English, include a description of the documentation process for them.

b. Upload all assent materials (talking points, videos, forms, etc.) to **Zipline**. Assent materials are not required to provide all of the standard elements of adult consent; the information should be appropriate to the age, population, and research procedures. The documents should be in Word, if possible.

7.6 Children who reach the legal age of consent during participation in longitudinal research.

Children who were enrolled at a young age and continue for many years: It is best practice to re-obtain assent (or to obtain it for the first time, if it was not obtained at the beginning of their participation).

Children who reach the legal age of consent: Informed consent must be obtained from the now-adult subject for (1) any ongoing interactions or interventions with the subjects, or (2) the continued analysis of specimens or data for which the subject's identify is readily identifiable to the researcher, unless the IRB waives this requirement.

a. Describe the plans (if any) to re-obtain assent from children.

- b. Describe the plans (if any) to obtain consent for children who reach the legal age of consent.
- If adult consent will be obtained from them, describe what will happen regarding now-adult subjects who cannot be contacted.
 - If consent will not be obtained or will not be possible: explain why.

7.7 Other regulatory requirements. (This is for information only; no answer or response is required.) Researchers are responsible for determining whether their research conducted in schools, with student records, or over the Internet comply with permission, consent, and inspection requirements of the following federal regulations:

- PPRA – Protection of Pupil Rights Amendment
- FERPA – Family Education Rights and Privacy Act
- COPPA – Children’s Online Privacy Protection Act

8 CONSENT OF ADULTS

Review the following definitions before answering the questions in this section.

CONSENT	is the <u>process</u> of informing potential subjects about the research and asking them whether they want to participate. It does not necessarily include the signing of a consent form.
CONSENT DOCUMENTATION	refers to how a subject’s decision to participate in the research is documented. This is typically obtained by having the subject sign a consent form.
CONSENT FORM	is a document signed by subjects, by which they agree to participate in the research as described in the consent form and in the consent process.
ELEMENTS OF CONSENT	are specific information that is required to be provided to subjects.
CHARACTERISTICS OF CONSENT	<p>are the qualities of the consent process as a whole. These are:</p> <ul style="list-style-type: none"> • Consent must be legally effective. • The process minimizes the possibility of coercion or undue influence. • Subjects or their representatives must be given sufficient opportunity to discuss and consider participation. • The information provided must: <ul style="list-style-type: none"> ○ Begin with presentation of key information (for consent materials over 2,000 words) ○ Be what a reasonable person would want to have ○ Be organized and presented so as to facilitate understanding ○ Be provided in sufficient detail ○ Not ask or appear to ask subjects to waive their rights
PARENTAL PERMISSION	is the parent’s active permission for the child to participate in the research. Parental permission is subject to the same requirements as consent, including written documentation of permission and required elements.
SHORT FORM CONSENT	is an alternative way of obtaining written documentation of consent that is most commonly used with individuals who are illiterate or whose language is one for which translated consent forms are not available.

means there is IRB approval for not obtaining consent or for not including some of the elements of consent in the consent process.

WAIVER OF CONSENT

NOTE: If you plan to obtain identifiable information or identifiable biospecimens without consent, any waiver granted by the IRB does not override a subject’s refusal to provide broad consent (for example, the Northwest Biotrust).

WAIVER OF DOCUMENTATION OF CONSENT

means that there is IRB approval for not obtaining written documentation of consent.

8.1 Groups Identify the groups to which the answers in this section apply.

- Adult subjects
- Parents who are providing permission for their children to participate in research

→ If you selected **PARENTS**, the word “consent” below should also be interpreted as applying to parental permission and “subjects” should also be interpreted as applying to the parents.

8.2 The consent process and characteristics. This series of questions is about whether consent will be obtained for all procedures except recruiting and screening and, if yes, how.

The issue of consent for recruiting and screening activities is addressed in [question 4.7](#). You do not need to repeat your answer to question 4.6.

a. Are there any procedures for which consent will not be obtained?

- No**
- Yes** → If yes, use the table below to identify the procedures for which consent will not be obtained. “All” is an acceptable answer for some studies.

Be sure to consider all research procedures and plans, including future contact, and sharing/banking of data and specimens for future work.

Group ¹	Describe the procedures or data/specimen collection (if any) for which there will be NO consent process	Reason why consent will not be obtained	Will subjects be provided with info about the research after they finish?	
			YES	NO
			<input type="checkbox"/>	<input type="checkbox"/>
			<input type="checkbox"/>	<input type="checkbox"/>
			<input type="checkbox"/>	<input type="checkbox"/>
			<input type="checkbox"/>	<input type="checkbox"/>
			<input type="checkbox"/>	<input type="checkbox"/>

Table footnotes

1. If the answer is the same for all groups, collapse your answer across the groups and/or procedures.

b. Describe the consent process, if consent will be obtained for any or all procedures, for any or all groups. Address groups and procedures separately if the consent processes are different.

Be sure to include:

- The location/setting where consent will be obtained
- Who will obtain consent (refer to positions, roles, or titles, not names)
- How subjects will be provided sufficient opportunity to discuss the study with the research team and consider participation

Subjects will be contacted by the study coordinator or by the ACTU Screening Nurse via phone call. During this pre-screening call, participants may be invited to signed the informed consent from using UW ITHS REDCap or in-person in the clinic. At the first screening visit (at UW ACTU), one of the ACTU clinicians, physician investigators or clinical staff will ask the participant to sign a form for screening and study participation. The informed consent process includes discussion of the study, ensuring that the subject has read the document, review of the sections of the informed consent document by the staff member with the potential subject, and time for the potential subject to have any questions about the study they have answered. This process of consent discussion will occur before the subject signs the consent form either before the screening visit or at the screening visit.” All potential participants will be encouraged to discuss their study participation with their primary care provider and or family/close friends before signing the informed consent document. As part of the informed consent, each potential participant’s understanding is assessed by the UW ACTU staff member using language appropriate to the educational level and background of the potential participant. At the screening and procedure visits, subjects are again provided with an overview of the study procedures and an opportunity to have any questions that they have about the study answered. (At each subsequent visit, any new information relevant to the study is provided to subjects and they have an opportunity to have any questions about the study answered.). Subjects will have the EGD at the Gastroenterology Clinic at HMC, and they will give separate consent for that procedure.

c. Comprehension. Describe the methods that will be used to ensure or test the subjects’ understanding of the information during the consent process.

The Screening Nurse will ask appropriate questions to determine the subjects’ comprehension of the study purpose and procedures. Subjects will be asked to sign a form stating they understand the study and have had an opportunity to ask questions.

d. Influence. Does the research involve any subject groups that might find it difficult to say “no” to participation because of the setting or their relationship with someone on the study team, even if they aren’t pressured to participate?

Examples: Student participants being recruited into their teacher’s research; patients being recruited into their healthcare provider’s research, study team members who are participants; outpatients recruited from an outpatient surgery waiting room just prior to their surgery.

<input type="checkbox"/>
<input checked="" type="checkbox"/>

No

Yes

→ If yes, describe what will be done to reduce any effect of the setting or relationship on the participation decision.

Examples: a study coordinator will obtain consent instead of the subjects’ physician; the researcher will not know which subjects agreed to participate; subjects will have two days to decide after hearing about the study.

We will emphasize to potential subjects that participation is voluntary and that they need not join the research if they do not wish to. If any potential subject has one of the study staff members as their primary care physician, informed consent will not be provided by that staff member and that responsibility will be given to a different staff member.

- e. Information provided is tailored to needs of subject population. Describe the basis for concluding that the information that will be provided to subjects (via written or oral methods) is what a *reasonable member of the subject population(s)* would want to know. If the research consent materials contain a key information section, also describe the basis for concluding that the information presented in that section is that which is *most likely* to assist the selected subject population with making a decision. See [GUIDANCE Key Information for Consent Materials](#).

For example: Consultation with publications about research subjects' preferences, disease-focused nonprofit groups, patient interest groups, or other researchers/study staff with experience with the specific population. It may also involve directly consulting selected members of the study population.

As part of the ongoing collaboration with Dr. Stekler, we consulted the already approved study ACTU 3500 to make sure the information provided is suitable for the subject population.

- f. Ongoing process. For research that involves multiple or continued interaction with subjects over time, describe the opportunities (if any) that will be given to subjects to ask questions or to change their minds about participating.

Participants will be informed in the consent document that they may withdraw participation at any time. Participants will have the contact information for the Harborview Medical Center/ UW ACTU and will have the opportunity to ask questions at any time.

8.3 Electronic presentation of consent information. Will any part of the consent-related information be provided electronically for some or all of the subjects?

This refers to the use of electronic systems and processes instead of (or in addition to) a paper consent form. For example, an emailed consent form, a passive or an interactive website, graphics, audio, video podcasts. See [GUIDANCE Electronic Informed Consent](#) for information about electronic consent requirements at UW.

- No** → If no, skip to [question 8.4](#)
 Yes → If yes, answer questions a through e

- a. Describe the electronic consent methodology and the information that will be provided.

All informational materials must be made available to the IRB. Website content should be provided as a Word document. It is considered best practice to give subjects information about multi-page/multi-screen information that will help them assess how long it will take them to complete the process. For example, telling them that it will take about 15 minutes, or that it involves reading six screens or pages.

UW ITHS RedCap will be used for electronic consent. The UW ITHS-supported version of REDCap can be configured to capture legally valid electronic signatures.

- b. Describe how the information can be navigated (if relevant). *For example, will the subject be able to proceed forward or backward within the system, or to stop and continue at a later time?*

Yes, the subject will be able to go forward and backward within the system.

- c. In a standard paper-based consent process, the subjects generally have the opportunity to go through the consent form with study staff and/or to ask study staff about any question they may have after reading the consent form. Describe what will be done, if anything, to facilitate the subject's comprehension and opportunity to ask questions when consent information is presented electronically. Include a description of any provisions to help ensure privacy and confidentiality during this process.

Examples: hyperlinks, help text, telephone calls, text messages or other type of electronic messaging, video conference, live chat with remotely located study team members.

The subject has the option to fill out the electronic form while being on a phone or a video call with the study nurse or coordinator. Alternatively, the call can be done after the subject has read the form but before signing, to clarify any points that remain unclear.

- d. What will happen if there are individuals who wish to participate but who do not have access to the consent methodology being used, or who do not wish to use it? Are there alternative ways in which they can obtain the information, or will there be some assistance available? If this is a clinical trial, these individuals cannot be excluded from the research unless there is a compelling rationale.

For example, consider individuals who lack familiarity with electronic systems, have poor eyesight or impaired motor skills, or who do not have easy email or internet access.

A subject will have the option to obtain a printed consent form in the clinic and receive assistance from the study coordinator or nurse to explain the content and with signing it.

- e. How will the research team ensure continued accessibility of consent materials and information during the study?

Each participant will receive a printed copy of the signed consent form during the screening visit.

- f. How will additional information be provided to subjects during the research, including any significant new findings (such as new risk information) If this is not an issue, explain why.

Subjects are receiving medication as part of their primary care. Thus, any potential medication risks are not related to this study. The risks of specimen collection are clear at the outset and will not change during the study. Thus, new information with the need to be provided to the participant while in the study is not anticipated.

8.4 Written documentation of consent. Which of the statements below describe whether documentation of consent will be obtained? NOTE: This question does not apply to screening and recruiting procedures which have already been addressed in [question 4.7](#).

Documentation of consent that is obtained electronically is not considered written consent unless it is obtained by a method that allows verification of the individual's signature. In other words, saying "yes" by email is rarely considered to be written documentation of consent

- a. Is written documentation of consent being obtained for:

- None of the research procedures → Use the table below to provide justification then go to [question 8.5](#).
-
- All of the research procedures → Do not complete the table; go to [question 8.4.b](#).
-

Some of the research procedures

→ Use the table below to identify the procedures for which written documentation of consent will not be obtained from adult subjects.

Adult subject group ¹	Describe the procedures or data/specimen collection (if any) for which there will be NO documentation of consent	Will they be provided with a written statement describing the research (optional)?	
		YES	NO
		<input type="checkbox"/>	<input type="checkbox"/>
		<input type="checkbox"/>	<input type="checkbox"/>
		<input type="checkbox"/>	<input type="checkbox"/>
		<input type="checkbox"/>	<input type="checkbox"/>
		<input type="checkbox"/>	<input type="checkbox"/>

Table footnotes

1. If the answer is the same for all adult groups or all procedures, collapse the answer across the groups and/or procedures.

b. Electronic consent signature. For studies in which documentation of consent will be obtained: will subjects use an electronic method to provide their consent signature?

- See the [GUIDANCE Electronic Informed Consent](#) for information about options (including REDCap e-signature and the DocuSign system) and any associated requirements.
- FDA-regulated studies must use a system that complies with the FDA’s “Part 11” requirements about electronic systems and records. Note that the UW-IT supported DocuSign e-signature system does not meet this requirement.
- Having subjects check a box at the beginning of an emailed or web-based questionnaire is not considered legally effective documentation of consent.

No

Yes → If yes, indicate which methodology will be used.

UW ITHS REDCap

→ Please name the institutional version you will be using (e.g. Vanderbilt, Univ. of Cincinnati) in the field below and provide a completed **SUPPLEMENT Other REDCap Installation** with your submission.

Other REDCap installation

UW DocuSign

Other

→ Please describe in the field below

b.1 Is this method legally valid in the jurisdiction where the research will occur?

NOTE: UW ITHS REDCap and UW DocuSign have been vetted for compliance with WA State and federal laws regarding electronic signatures.

No

Yes → If yes, what is the source of information about legal validity?

UW HSD

b.2 Will verification of the subject's identity be obtained if the signature is not personally witnessed by a member of the study team? Note that this is required for FDA-regulated studies.

See the [GUIDANCE Electronic Informed Consent](#) for information and examples

No → If no, provide the rationale for why this is not required or necessary to protect subjects or the integrity of the research. Also, what would be the risks to the actual subject if somebody other than the intended signer provides the consent signature?

Yes → If yes, describe how subject identity will be verified, providing a non- technical description that the reviewer will understand.

We will verify the subject's identity during the screening visit.

b.3 How will the requirement be met to provide a copy of the consent information (consent form) to individuals who provide an e-signature?

The copy can be paper or electronic and may be provided on an electronic storage device or via email. If the electronic consent information uses hyperlinks or other websites or podcasts to convey information specifically related to the research, the information in these hyperlinks should be included in the copy provided to the subjects and the website must be maintained for the duration of the entire study.

We will provide a copy of the signed consent form during the screening visit.

8.5 Non-English-speaking or -reading adult subjects. Will the research enroll adult subjects who do not speak English or who lack fluency or literacy in English?

No

Yes → If yes, describe the process that will be used to ensure that the oral and written information provided to them during the consent process and throughout the study will be in a language readily understandable to them and (for written materials such as consent forms or questionnaires) at an appropriate reading/comprehension level.

a. Interpretation. Describe how interpretation will be provided, and when. Also, describe the qualifications of the interpreter(s) – for example, background, experience, language proficiency in English and in the other language, certification, other credentials, familiarity with the research-related vocabulary in English and the target language.

b. Translations. Describe how translations will be obtained for all study materials (not just consent forms). Also, describe the method for ensuring that the translations meet the UW IRB's requirement that translated documents will be linguistically accurate, at an appropriate reading level for the participant population, and culturally sensitive for the locale in which they will be used.

8.6 Barriers to written documentation of consent. There are many possible barriers to obtaining written documentation of consent. Consider, for example, individuals who are functionally illiterate; do not read English well; or have sensory or motor impairments that may impede the ability to read and sign a consent form.

a. Describe the plans (if any) for obtaining written documentation of consent from potential subjects who may have difficulty with the standard documentation process (that is, reading and signing a consent form). Skip this question if written documentation of consent is not being obtained for any part of the research.

Examples of solutions: Translated consent forms; use of the Short Form consent process; reading the form to the person before they sign it; excluding individuals who cannot read and understand the consent form.

The study coordinators will read consent forms to any participants who need help.

8.7 Deception. Will information be deliberately withheld, or will false information be provided, to any of the subjects?

Note: "Blinding" subjects to their study group/condition/arm is not considered to be deception, but not telling them ahead of time that they will be subject to an intervention or about the purpose of the procedure(s) is deception.

No

Yes → If yes, describe what information and why.

Example: It may be necessary to deceive subjects about the purpose of the study (describe why).

a. Will subjects be informed beforehand that they will be unaware of or misled regarding the nature or purposes of the research? (Note: this is not necessarily required.)

<input type="checkbox"/>	No
<input type="checkbox"/>	Yes

b. Will subjects be debriefed later? (Note: this is not necessarily required.)

<input type="checkbox"/>	No
<input type="checkbox"/>	Yes

→ If yes, describe how and when this will occur. Upload any debriefing materials, including talking points or a script, to **Zipline**.

8.8 Cognitively impaired adults, and other adults unable to consent. Will such individuals be included in the research?

Examples: individuals with Traumatic Brain Injury (TBI) or dementia; individuals who are unconscious, or who are significantly intoxicated.

<input checked="" type="checkbox"/>	No
<input type="checkbox"/>	Yes

→ If no, go to [question 8.9](#).

→ If yes, answer the following questions.

a. Rationale. Provide the rationale for including this population.

b. Capacity for consent / decision making capacity. Describe the process that will be used to determine whether a cognitively impaired individual is capable of consent decision making with respect to the research protocol and setting.

b.1. If there will be repeated interactions with the impaired subjects over a time period when cognitive capacity could increase or diminish, also describe how (if at all) decision-making capacity will be re-assessed and (if appropriate) consent obtained during that time.

c. Permission (surrogate consent). If the research will include adults who cannot consent for themselves, describe the process for obtaining permission (“surrogate consent”) from a legally authorized representative (LAR).

For research conducted in Washington State, see the [GUIDANCE Legally Authorized Representative](#) to learn which individuals meet the state definition of “legally authorized representative”.

- d. Assent. Describe whether assent will be required of all, some, or none of the subjects. If some, indicate which subjects will be required to assent and which will not (and why not). Describe any process that will be used to obtain and document assent from the subjects.

- e. Dissent or resistance. Describe how a subject's objection or resistance to participation (including non-verbal) during the research will be identified, and what will occur in response.

8.9 Research use of human fetal tissue obtained from elective abortion. Federal and UW Policy specify some requirements for the consent process. If you are conducting this type of research, check the boxes to confirm these requirements will be followed.

- Informed consent for the donation of fetal tissue for research use will be obtained by someone other than the person who obtained the informed consent for abortion.
- Informed consent for the donation of fetal tissue for research use will be obtained after the informed consent for abortion.
- Participation in the research will not affect the method of abortion.
- No enticements, benefits, or financial incentives will be used at any level of the process to incentivize abortion or the donation of human fetal tissue.
- The informed consent form for the donation of fetal tissue for use in research will be signed by both the woman and the person who obtains the informed consent.

8.10 Consent-related materials. Upload to **Zipline** all consent scripts/talking points, consent forms, debriefing statements, Information Statements, Short Form consent forms, parental permission forms, and any other consent-related materials that will be used. Materials that will be used by a specific site should be uploaded to that site's **Local Site Documents** page.

- *Translations must be submitted and approved before they can be used. However, we strongly encourage you to wait to provide them until the IRB has approved the English versions.*
- *Combination forms: It may be appropriate to combine parental permission with consent, if parents are subjects as well as providing permission for the participation of their children. Similarly, a consent form may be appropriately considered an assent form for older children.*
- *For materials that cannot be uploaded: upload screenshots or written descriptions that are sufficient to enable the IRB to understand the types of data that will be collected and the nature of the experience for the participant. URLs (website addresses) may also be provided, or written descriptions of websites. Examples of materials that usually cannot be uploaded: mobile apps; computer-administered test; licensed and restricted standardized tests.*

9 PRIVACY AND CONFIDENTIALITY

9.1 Privacy protections. Describe the steps that will be taken, if any, to address possible privacy concerns of subjects and potential subjects.

Privacy refers to the sense of being in control of access that others have to ourselves. This can be an issue with respect to recruiting, consenting, sensitivity of the data being collected, and the method of data collection.

Examples:

- *Many subjects will feel a violation of privacy if they receive a letter asking them to participate in a study because they have ___ medical condition, when their name, contact information, and medical condition were drawn from medical records without their consent. Example: the IRB expects that "cold call" recruitment letters will inform the subject about how their information was obtained.*
- *Recruiting subjects immediately prior to a sensitive or invasive procedure (e.g., in an outpatient surgery waiting room) will feel like an invasion of privacy to some individuals.*
- *Asking subjects about sensitive topics (e.g. details about sexual behavior) may feel like an invasion of privacy to some individuals.*

All participants in this study have been diagnosed with HIV/AIDS and may have concerns for their private medical history. Thus, privacy and sensitivity are important concerns. For all participants, if they choose to participate, the first step will be reading and signing a consent form which states they will be asked about private and sensitive information including sexual and medical history and drug use habits, and subject will have the opportunity to decline participation at this time. The study questionnaire taken on a computer may increase the sense of privacy for participants.

9.2 Identification of individuals in publications and presentations. Will potentially identifiable information about subjects be used in publications and presentations, or is it possible that individual identities could be inferred from what is planned to be published or presented?

No
 Yes → If yes, will subject consent be obtained for this use?

Yes
 No → If no, describe the steps that will be taken to protect subjects (or small groups of subjects) from being identifiable.

9.3 State mandatory reporting. Each state has reporting laws that require some types of individuals to report some kinds of abuse, and medical conditions that are under public health surveillance. These include:

- Child abuse
- Abuse, abandonment, neglect, or financial exploitation of a vulnerable adult
- Sexual assault
- Serious physical assault
- Medical conditions subject to mandatory reporting (notification) for public health surveillance

Are you or a member of the research team likely to learn of any of the above events or circumstances while conducting the research **AND** feel obligated to report it to state authorities?

No
 Yes → If yes, the UW IRB expects subjects to be informed of this possibility in the consent form or during the consent process, unless you provide a rationale for not doing so:

The only reporting that will be conducted is mandatory notifications for new infectious disease (e.g. hepatitis B or C). We will not report the HIV status of study participants. The fact that this

information will be reported to the King County Department of Health is included in the consent form.

9.4 Retention of identifiers and data. Check the box below to indicate assurance that any identifiers (or links between identifiers and data/specimens) and data that are part of the research records will not be destroyed until after the end of the applicable records retention requirements (e.g. Washington State; funding agency or sponsor; Food and Drug Administration). If it is important to say something about destruction of identifiers (or links to identifiers) in the consent form, state something like “the link between your identifier and the research data will be destroyed after the records retention period required by state and/or federal law.”

This question can be left blank for conversion applications (existing paper applications that are being “converted” into a Zipline application.)

See the “Research Data” sections of the following website for UW Records management for the Washington State research records retention schedules that apply in general to the UW (not involving UW Medicine data):

<http://f2.washington.edu/fm/recmgt/gs/research?title=R>

See the “Research Records and Data” information in Section 8 of this document for the retention schedules for UW Medicine Records: <https://www.uwmedicine.org/recordsmanagementuwm-records-retention-schedule.pdf>

Confirm

9.5 Certificates of Confidentiality. Will a federal Certificate of Confidentiality be obtained for the research data?
NOTE: Answer “No” if the study is funded by NIH or the CDC, because all NIH-funded and CDC-funded studies automatically have a Certificate.

No
 Yes

9.6 Data and specimen security protections. Identify the data classifications and the security protections that will be provided for all sites where data will be collected, transmitted, or stored, referring to the [GUIDANCE Data and Security Protections](#) for the minimum requirements for each data classification level. ***It is not possible to answer this question without reading this document. Data security protections should not conflict with records retention requirements.***

a. Which level of protections will be applied to the data and specimens? If more than one level will be used, describe which level will apply to which data and which specimens and at which sites.

Research personnel in direct contact with study participants will use level 5 protections, due to the fact that diagnosis of HIV/AIDS can be considered very sensitive Personal Health Information (it can be stigmatizing in some cultures). We will implement all provisions for level 5 as outlined in HSD’s Guidance Data Security Protections Data will be appropriately protected at all times.

b. Use this space to provide additional information, details, or to describe protections that do not fit into one of the levels. If there are any protections within the level listed in 9.6.a which will *not* be followed, list those here, including identifying the sites where this exception will apply.

We plan to keep the subject’ identifiers and links between data and the subject’s identifiers indefinitely. The reason for this is that individuals often choose to participate in multiple studies at the UW and prospectively collected information is very valuable, in particular if it can be linked to the same subjects participating again in future studies.

Only coded data will be sent to Drs. Hladik/Gornalusse or their laboratory, or any of the laboratories that are conducting study-related tests. The Study Coordinator, UW ACTU Clinic staff, the UW IRB, NIH and their monitors, and representatives of UW oversight groups, would have access to the onsite data and records.

The consent form and other study information will be kept in each participant's research record. A copy of the study consent form may be sent to their Harborview Medical Center medical record if they receive primary care at Harborview. With the participant's permission, copies of the consent form and routine lab test results may be sent to his/her primary care provider, regardless of whether they receive care at Harborview Medical Center or elsewhere. We will use EPIC to send results to participants whose primary care providers are affiliated with EPIC and mail or fax routine lab results to medical care providers who are not part of EPIC. A copy of the HIPAA Authorization and our Medical Release of Information Form (which will be used during the study to obtain medical records from a different provider/facility) are included.

10 RISK / BENEFIT ASSESSMENT

10.1 Anticipated risks. Describe the reasonably foreseeable risks of harm, discomforts, and hazards to the subjects and others of the research procedures. For each harm, discomfort, or hazard:

- Describe the magnitude, probability, duration, and/or reversibility of the harm, discomfort, or hazard, AND
- Describe how the risks will be reduced or managed. Do not describe data security protections here, these are already described in Question 9.6.
- *Consider possible physical, psychological, social, legal, and economic harms, including possible negative effects on financial standing, employability, insurability, educational advancement or reputation. For example, a breach of confidentiality might have these effects.*
- *Examples of "others": embryo, fetus, or nursing child; family members; a specific group.*
- *Ensure applicable risk information from any Investigator Brochures, Drug Package Inserts, and/or Device Manuals is included in your description.*
- *Do not include the risks of non-research procedures that are already being performed.*
- *If the study design specifies that subjects will be assigned to a specific condition or intervention, then the condition or intervention is a research procedure - even if it is a standard of care.*
- *Examples of mitigation strategies: inclusion/exclusion criteria; applying appropriate data security measures to prevent unauthorized access to individually identifiable data; coding data; taking blood samples to monitor something that indicates drug toxicity.*
- *As with all questions on this application, you may refer to uploaded documents.*

Esophagogastroduodenoscopy (EGD): The specific procedural risks of EGD with biopsies are bleeding, infection and mucosal perforation, which can happen in the stomach, duodenum or esophagus. We quote risk of any of these happening to be less than 0.01%. These complications, should they occur, may require hospitalization, surgery, repeat EGD and/or a blood transfusion.

An additional risk is:

-

A subject could have a reaction to the sedating medications used during the procedure, which could cause:

-

- Nervous System: Sedation, sleepiness, blurred vision, dizziness (lightheadedness), headache, disturbed coordination, rigidity, abnormal sweating, transient memory loss (amnesia), agitation, rapid involuntary muscle jerking or twitching (including tonic/clonic movements and muscle tremor), hyperactivity and combativeness
- Gastrointestinal System: nausea, vomiting, abdominal cramping
- Respiratory System: hiccoughs, thickening of bronchial secretions (sputum or expectorated mucus), respiratory depression, airway obstruction, laryngospasm (sudden spasm or closure of vocal cords), oxygen desaturation (lower percentage of oxygen in your blood), apnea (not breathing), coughing, If these effects remain untreated, respiratory arrest can occur.
- Cardiovascular: low blood pressure (hypotension), high blood pressure (hypertension), bradycardia (slow heart rate)

- Local effects at intravenous injection site: pain (burning and stinging), induration (hardening of the skin), redness, tenderness
- Anaphylaxis (severe allergic reaction) with red rash and itching (hives).

Heart attack or stroke. We quote this risk to be less than 0.01%.

Thus, less than 0.02% is the estimated incidence rate of having any adverse event considering the combined risk of the EGD procedure and sedating medications. *Anoscopy*: Risks of anoscopy with biopsies are highly uncommon but could include mild to moderate discomfort, bleeding, or infection.

The anoscopy will be performed by a physician assistant, and the esophagogastroduodenoscopy will be performed by a gastroenterologist. Both are employed by the UW and have been trained in and have performed the procedures to minimize risks.

Risks of Drawing Blood: Having blood drawn may cause some discomfort, lightheadedness, bleeding, swelling, or bruising where the needle enters the body, and in rare cases, fainting, or infection. Experienced licensed individuals (MD, PA-C, RN, all licensed in WA state) will do the blood draws to minimize risk.

Risks of Social Harm: Although the study site will make every effort to protect subjects' privacy and confidentiality, it is possible that their involvement in the study as a participant could become known to others (if it is not already) and that social harm may result (they could become labeled as being infected with HIV). For example, they could be treated unfairly or discriminated against by family members, friends, and/or the community. Likewise, the breach of confidentiality could make the participants' relatives or acquaintances stigmatize or discriminate them based on information related to illegal substance abuse (if any) and sexual history. In our laboratory, studies with blood and biopsy samples previously unknown medical conditions may be discovered. If this happens, we will provide the participant with the information about the finding, counsel them about its significance, and if indicated refer them to a primary care provider for further management. Overall, to minimize risks of harm and to protect subjects' rights and welfare, we will apply the mitigation approaches cited below.

Children less than 18 years of age are excluded. Women of childbearing potential should not be pregnant to participate. There is a clinician on call 24 hours per day to handle medical problems. We take multiple measures to protect the confidentiality of our subjects. All staff members involved with the study have the appropriate training to perform their duties. We will provide limited travel support for those who would otherwise be unable to participate in the study.

10.2 Reproductive risks. Are there any risks of the study procedures to men and women (who are subjects, or partner of subjects) related to pregnancy, fertility, lactation or effects on a fetus or neonate?

Examples: direct teratogenic effects; possible germline effects; effects on fertility; effects on a woman's ability to continue a pregnancy; effects on future pregnancies.

- No** → If no go to [question 10.3](#)
- Yes** → If yes, answer the following questions:

a. Risks. Describe the magnitude, probability, duration and/or reversibility of the risks.

b. Steps to minimize risk. Describe the specific steps that will be taken to minimize the magnitude, probability, or duration of these risks.

Examples: inform the subjects about the risks and how to minimize them; require a pregnancy test before and during the study; require subjects to use contraception; advise subjects about banking of sperm and ova.

If the use of contraception will be required: describe the allowable methods and the time period when contraception must be used.

c. Pregnancy. Describe what will be done if a subject (or a subject's partner) becomes pregnant

For example; will subjects be required to immediately notify study staff, so that the study procedures can be discontinued or modified, or for a discussion of risks, and/or referrals or counseling?

10.3 MRI risk management. A rare but serious adverse reaction called nephrogenic systemic fibrosis (NSF) has been observed in individuals with kidney disease who received gadolinium-based contrast agents (GBCAs) for the scans. Also, a few healthy individuals have a severe allergic reaction to GBCAs.

a. Use of gadolinium. Will any of the MRI scans involve the use of a gadolinium-based contrast agent (GBCA?)

X	No
	Yes

→ If yes, which agents will be used? *Check all that apply.*

	Brand Name	Generic Name	Chemical Structure
<input type="checkbox"/>	Dotarem	Gadoterate meglumine	Macrocylic
<input type="checkbox"/>	Eovist / Primovist	Gadoxetate disodium	Linear
<input type="checkbox"/>	Gadavist	Gadobutro	Macrocylic
<input type="checkbox"/>	Magnevist	Gadpentetate dimeglumine	Linear
<input type="checkbox"/>	MultiHance	Gadobenate dimeglumine	Linear
<input type="checkbox"/>	Omniscan	Gadodiamide	Linear
<input type="checkbox"/>	OptiMARK	Gadoversetamide	Linear
<input type="checkbox"/>	ProHance	Gadoteridol	Macrocylic
<input type="checkbox"/>	Other, provide name:	NA	

- 1.) The FDA has concluded that gadolinium is retained in the body and brain for a significantly longer time than previously recognized, especially for linear GBCAs. The health-related risks of this longer retention are not yet clearly established. However, the UW IRB expects researchers to provide a compelling justification for using a linear GBCA instead of a macrocyclic GBCA, to manage the risks associated with GBCAs.

Describe why it is important to use a GBCA with the MRI scan(s). Describe the dose that will be used and (if it is more than the standard clinical dose recommended by the manufacturer) why it is necessary to use a higher dose. If a linear GBCA will be used, explain why a macrocyclic GBCA cannot be used.

NA

- 2.) Information for subjects. Confirm by checking this box that subjects will be provided with the FDA-approved Patient Medication Guide for the GBCA being used in the research or that the same information will be inserted into the consent form.

Confirmed

- b. Who will (1) calculate the dose of GBCA; (2) prepare it for injection; (3) insert and remove the IV catheter; (4) administer the GBCA; and (5) monitor for any adverse effects of the GBCA? Also, what are the qualifications and training of these individual(s)?

NA

- c. Describe how the renal function of subjects will be assessed prior to MRI scans and how that information will be used to exclude subjects at risk for NSF.

NA

- d. Describe the protocol for handling a severe allergic reaction to the GBCA or any other medical event/emergency during the MRI scan, including who will be responsible for which actions.

NA

10.4 Unforeseeable risks. Are there any research procedures that may have risks that are currently unforeseeable?

Example: using a drug that hasn't been used before in this subject population.

No
 Yes → If yes, identify the procedures.

10.5 Subjects who will be under regional or general anesthesiology. Will any research procedures occur while patients are under general or regional anesthesia, or during the 3 hours preceding general or regional anesthesia (supplied for non-research reasons)?

No
 Yes → If yes, check all the boxes that apply.

Administration of any drug for research purposes

- Inserting an intra-venous (central or peripheral) or intra-arterial line for research purposes
- Obtaining samples of blood, urine, bone marrow or cerebrospinal fluid for research purposes
- Obtaining a research sample from tissue or organs that would not otherwise be removed during surgery
- Administration of a radio-isotope for research purposes**
- Implantation of an experimental device
- Other manipulations or procedures performed solely for research purposes (e.g., experimental liver dialysis, experimental brain stimulation)

If any of the boxes are checked:

Provide the name and institutional affiliation of a physician anesthesiologist who is a member of the research team or who will serve as a safety consultant about the interactions between the research procedures and the general or regional anesthesia of the subject-patients. If the procedures will be performed at a UW Medicine facility or affiliate, the anesthesiologist must be a UW faculty member, and the Vice Chair of Clinical Research in the UW Department of Anesthesiology and Pain Medicine must be consulted in advance for feasibility, safety and billing.

*** If the box about radio-isotopes is checked: the study team is responsible for informing in advance all appropriate clinical personnel (e.g., nurses, technicians, anesthesiologists, surgeons) about the administration and use of the radio-isotope, to ensure that any personal safety issues (e.g., pregnancy) can be appropriately addressed. This is a condition of IRB approval.*

10.6 Data and Safety Monitoring. A Data and Safety Monitoring Plan (DSMP) is required for clinical trials (as defined by NIH). If required for this research, or if there is a DSMP for the research regardless of whether it is required, upload the DSMP to **Zipline**. If it is embedded in another document being uploading (for example, a Study Protocol) use the text box below to name the document that has the DSMP. Alternatively, provide a description of the DSMP in the text box below.

NA

10.7 Un-blinding. If this is a double-blinded or single-blinded study in which the participant and/or relevant study team members do not know the group to which the participant is assigned: describe the circumstances under which un-blinding would be necessary, and to whom the un-blinded information would be provided.

NA

10.8 Withdrawal of participants. If applicable, describe the anticipated circumstances under which participants will be withdrawn from the research without their consent. Also, describe any procedures for orderly withdrawal of a participant, regardless of the reason, including whether it will involve partial withdrawal from procedures and any intervention but continued data collection or long-term follow-up.

If a participant withdraws from the study, is lost to follow-up, or is withdrawn by the study staff, they will be replaced in order to ensure we have a correct total number of participants who complete the entire study. We will still use the data collected from withdrawn participants in our data analysis.

Reasons for withdraw may include but are not limited to: non-compliance (non-adherence to ART), presence of a sexually transmitted or opportunistic infection like hepatitis C or herpes, abnormal unexpected medical condition that appeared between the first and second visit. Once a participant has withdrawn, there will be no additional procedures or data collection.

10.9 Anticipated direct benefits to participants. If there are any direct research-related benefits that some or all individual participants are likely to experience from taking part in the research, describe them below:

Do not include benefits to society or others, and do not include subject payment (if any). Examples: medical benefits such as laboratory tests (if subjects receive the results); psychological resources made available to participants; training or education that is provided.

No direct benefits anticipated.

10.10 Return of individual research results.

In this section, provide your plans for the return of individual results. An “individual research result” is any information collected, generated or discovered in the course of a research study that is linked to the identity of a research participant. These may be results from screening procedures, results that are actively sought for purposes of the study, results that are discovered unintentionally, or after analysis of the collected data and/or results has been completed.

See the [GUIDANCE Return of Individual Results](#) for information about results that should and should not be returned, validity of results, the Clinical Laboratory Improvement Amendment (CLIA), consent requirements and communicating results.

a. Is it anticipated that the research will produce any individual research results that are clinically actionable?

“Clinically actionable” means that there are established therapeutic or preventive interventions or other available actions that have the potential to change the clinical course of the disease/condition, or lead to an improved health outcome.

In general, every effort should be made to offer results that are clinically actionable, valid and pose life-threatening or severe health consequences if not treated or addressed quickly. Other clinically actionable results should be offered if this can be accomplished without compromising the research.

No
 Yes

→ If yes, answer the following questions (a.1-a.3).

a.1. Describe the clinically actionable results that are anticipated and explain which results, if any, could be urgent (i.e. because they pose life-threatening or severe health consequences if not treated or addressed quickly).

Examples of urgent results include very high calcium levels, highly elevated liver function test results, positive results for reportable STDs.

Some of the study evaluations may reveal previously unknown health conditions like new infections (hepatitis B, hepatitis C or other STIs)In the event this occurs, subjects will be referred to their primary health care provider for treatment or management. We do not anticipate finding clinically actionable, valid and urgent (life-threatening) results. However, if this happens, we will notify the study participant and his/her primary health provider. We may discover clinically actionable non-urgent results obtained from lab results (kidney test, liver function, differential white blood cell count, CD4 levels, HIV viral load, etc.) as well as findings from the physical exam. In these latter examples of non-urgent information, we will post the results on the patient’s portal (EPIC) and will communicate them with the primary health care provider.

a.2. Explain which of these results will be offered to subjects.

. We will perform urine pregnancy tests. The results will be provided in-person during the clinic visit when results are available. The participant will have a chance to discuss the results with the study clinician. Lab results (kidney test, liver function, differential white blood cell count, CD4 levels, HIV viral load, etc.) and findings from the physical exam will be posted on the patient's portal (EPIC). Abnormalities from lab results or from the medical exam will be communicated to the patient through the primary health care provider. The study participants will **not** have the option to **exclude** study results from their medical records.

a.3. Explain which results will not be offered to subjects and provide the rationale for not offering these results.

Reasons not to offer the results might include:

- *There are serious questions regarding validity or reliability*
- *Returning the results has the potential to cause bias*
- *There are insufficient resources to communicate the results effectively and appropriately*
- *Knowledge of the result could cause psychosocial harm to subjects*

We will not return results derived from genomic sequencing to the participants because of two following reasons. First, the techniques of genomic sequencing we will be using (RNA-Seq applied on mRNA and HIV site integration analysis on genomic DNA) very unlikely will uncover disease predisposing traits. In other words, we will not generate inherited information that can be useful for the study subject. Second, the results will be obtained in a research lab and will not be certified.

b. Is there a plan for offering subjects any results that are not clinically actionable?

Examples: non-actionable genetic results, clinical tests in the normal range, experimental and/or uncertain results.

<input checked="" type="checkbox"/>	No
<input type="checkbox"/>	Yes

→ If yes, explain which results will be offered to subjects and provide the rationale for offering these results.

c. Describe the validity and reliability of any results that will be offered to subjects.

The IRB will consider evidence of validity such as studies demonstrating diagnostic, prognostic, or predictive value, use of confirmatory testing, and quality management systems.

Lab results will be generated at University of Washington AIDS Clinical Trials Unit (UW ACTU). The laboratory or laboratories that ACTU will send the samples are part of UWMC and as such, they have their own certification program. The Washington State Department of Health has accredited Harborview Medical Center Dept of Lab Medicine by RCW 70.42 to have a medical test site license. Therefore, the validity and reliability of the results will follow the HSD's [GUIDANCE Return of Individual Results. On the other hand, the results derived from genomic sequencing will be obtained in a research lab that is non-CLIA compliant and therefore will not be returned to the study subject.](#)

d. Describe the process for communicating results to subjects and facilitating understanding of the results. In the description, include who will approach the participant with regard to the offer of results, who will communicate the result (if different), the circumstances, timing, and communication methods that will be used.

The urine-pregnancy results will be directly provided to the study participant in-person during the clinic visit when results are available. The participant will have a chance to discuss the results with the study clinician/physician assistant or nurse. Lab results (kidney test, liver function, differential white blood cell count, CD4 levels, HIV viral load, etc.) and findings from the physical exam will be posted on the patient's portal (EPIC). Abnormalities from lab results or from the medical exam will be communicated to the patient through the primary health care provider. The study participants will **not** have the option to

exclude study results from their medical records. The primary care provider will receive an alert when new test results are available for their patient. The study coordinator or staff will contact the patient by phone and he/she will be asked to make an in-person appointment with their primary health care provider. During that in-person appointment, the patient will have the opportunity to discuss the abnormal results with their primary physician and decide on a reasonable therapeutic/follow up approach. We will communicate clinically actionable and urgent results by phone calling both the patient and their primary physician.

- e. Describe any plans to share results with family members (e.g. in the event a subject becomes incapacitated or deceased).

NA

- f. Check the box to indicate that any plans for return of individual research results have been described in the consent document. If there are no plans to provide results to participants, this should be stated in the consent form.

See the [GUIDANCE Return of Individual Results](#) for information about consent requirements.

Confirmed

- 10.11 Commercial products or patents.** Is it possible that a commercial product or patent could result from this study?

No
 Yes

→ If yes, describe whether subjects might receive any remuneration/compensation and, if yes, how the amount will be determined.

11 ECONOMIC BURDEN TO PARTICIPANTS

- 11.1 Financial responsibility for research-related injuries.** Answer this question only if the lead researcher is not a UW student, staff member, or faculty member whose primary paid appointment is at the UW.

For each institution involved in conducting the research: Describe who will be financially responsible for research-related injuries experienced by subjects, and any limitations. Describe the process (if any) by which participants may obtain treatment/compensation.

NA

- 11.2 Costs to subjects.** Describe any research-related costs for which subjects and/or their health insurance may be responsible (examples might include: CT scan required for research eligibility screening; co-pays; surgical costs when a subject is randomized to a specific procedure; cost of a device; travel and parking expenses that will not be reimbursed).

Study participants and/or their health insurance will be responsible for the cost of potential appointment(s) with their primary physician in case abnormal results are found during this study and a follow up visit takes place.

12 RESOURCES

12.1 Faculty Advisor. (For researchers who are students, residents, fellows, or post-docs.) Provide the following information about the faculty advisor.

- Advisor's name
- Your relationship with your advisor (for example: graduate advisor; course instructor)
- Your plans for communication/consultation with your advisor about progress, problems, and changes.

NA

12.2 UW Principal Investigator Qualifications. Upload a current or recent Curriculum Vitae (CV), Biosketch (as provided to federal funding agencies), or similar document to the Local Site Documents page in Zipline. The purpose of this is to address the PI's qualifications to conduct the proposed research (education, experience, training, certifications, etc.).

For help with creating a CV, see http://adai.uw.edu/grants/nsf_biosketch_template.pdf and <https://education.uwmedicine.org/student-affairs/career-advising/year-4/residency-applications/curriculum-vitae/>

The CV will be uploaded.

12.3 UW Study team qualifications. Describe the qualifications and/or training for each UW study team member to fulfill their role on the study and perform study procedures. (You may be asked about non-UW study team members during the review; they should not be described here.) You may list these individuals by name, however if you list an individual by name, you will need to modify this application if that individual is replaced. Alternatively, you can describe study roles and the qualifications and training the PI or study leadership will require for any individual who might fill that role. The IRB will use this information to assess whether risks to subjects are minimized because study activities are being conducted by properly qualified and trained individuals.

Describe: The role (or name of person), the study activities they will perform, and the qualifications or training that are relevant to performing those study activities.

Examples:

Research Study Coordinator: Obtain consent, administer surveys, blood draw. Will have previous experience coordinating clinical research and be a certified phlebotomist in WA.

Undergraduate Research Assistant: Obtain consent, perform all study procedures. Will have had coursework in research methods, complete an orientation to human subjects protections given by the department, and will receive training from the PI or the graduate student project lead on obtaining consent and debriefing subjects.

Acupuncturist: Perform acupuncture procedures and administer surveys. Must be licensed with WA State DoH and complete training in administering research surveys given by the project director, an experienced survey researcher.

Co-Investigator: Supervise MRI and CT scan procedures and data interpretation, obtain consent. MD, specialty in interventional radiology and body imaging. 5-years clinical research experience.

Research Study Coordinator and Study Nurse: Pre-screen participants by online database (Leaf), contact patients, administer questionnaires, and draw blood. These persons will have had previous experience coordinating clinical research. The Study Nurse, and perhaps also the Study Coordinator, will also be a certified phlebotomist in WA state.

Study Physician and Physician Assistant: Will be an MD licensed in WA state and employed by WA. They may administer questionnaires, obtain consent, conduct targeted medical history and physical exam. They will carry out the anoscopy.

Gastroenterologist: A licensed gastroenterologist will carry out the esophagogastroduodenoscopy. He/She will be employed by UW and will have been trained in and have performed many of these procedures before.

Study scientists: May conduct de-identified on-line database screening using Leaf. Will conduct laboratory assays with de-identified specimens. May provide informational sessions in the clinic to support recruitment or to answer questions of potential or participating study subjects.

12.4 Study team training and communication. Describe how it will be ensured that each study team member is adequately trained and informed about the research procedures and requirements (including any changes) as well as their research-related duties and functions.

There is no study team.

Each study member must have training in human subjects research. Pre-study meeting have been held to ensure each member understands the research procedures and their own duties and responsibilities.

13 OTHER APPROVALS, PERMISSIONS, and REGULATORY ISSUES

13.1 Approvals and permissions. Identify any other approvals or permissions that will be obtained. For example: from a school, external site/organization, funding agency, employee union, UW Medicine clinical unit.

Do not attach the approvals and permissions unless requested by the IRB.

NA

13.2 Financial Conflict of Interest. Does any UW member of the team have ownership or other Significant Financial Interest (SFI) with this research as defined by [UW policy GIM 10](#)?

No

Yes → If yes, has the Office of Research made a determination regarding this SFI as it pertains to the proposed research?

No → If no, contact the Office of Research (206.616.0804, research@uw.edu) for guidance on how to obtain the determination

Yes → If yes, upload the Conflict Management Plan for every UW team member who has a FCOI with respect to the research, to **Zipline**. If it is not yet available, use the text box to describe whether the Significant Financial Interest has been disclosed already to the UW Office of Research and include the FIDS Disclosure ID if available.

13.3 UW ITHS COVID review. Confirm by checking the box that you will obtain this additional review if it is applicable to your research (see "Proposal Eligibility" at this link <https://www.iths.org/iths-covid-19-research-resources/covid-19-research-portal/>).

Confirmed