IRO REC'D 07/20/2022

**Version 3.0**
**July 19, 2022**

**HIV/AIDS Clinical Trials Networks**

# Title: Red Ribbon Registry

**A database of people interested in HIV clinical trials.**

**Principal Investigator:**
James G. Kublin, MD, MPH

**Sponsor:**
Fred Hutchinson Cancer Research Center
Vaccine and Infectious Disease
1100 Fairview Ave N, # E3-300
Seattle, WA 98109-1024

FHCRC IRB Approval
07 27 2022
Document Released Date

## KEY ROLES AND CONTACTS

**Principal Investigator:** James G. Kublin, MD, MPH
Fred Hutchinson Cancer Research Center
1100 Fairview Ave N, # E3-300
Seattle, WA 98109-1024
Phone: (206) 667-1970
Fax: (206) 667-6366
jkublin@fredhutch.org

## Principal Investigator Protocol Signature Page

By my signature below, I agree to conduct the study according to this protocol version as approved by the IRB of record, in accordance with applicable IRB requirements, Good Clinical Practice and federal and local regulations. I will not modify the protocol without first obtaining an IRB approved amendment and new protocol version unless it is necessary to protect the health and welfare of study participants.

James G. Kublin, MD, MPH

_____

Print Investigator Name

_____ _____

Investigator Signature Date

## Table of Contents

**Principal Investigator Protocol Signature Page** ..... **3**

**Table of Contents** ..... **4**

**1.0 Background and Rationale** ..... **6**
**1.1 HIV Pandemic** ..... **6**
**1.2 DAIDS/NIAID/NIH HIV Clinical Trials Networks** ..... **7**
**1.3 Rationale for Establishment of the Red Ribbon Registry** ..... **7**

**2.0 Study Design** ..... **8**
**2.1 Overview** ..... **8**
**2.2 Study Objectives** ..... **8**
**2.2.1 Primary Objective** ..... **8**
**2.2.2 Secondary Objective** ..... **9**
**2.2.3 Exploratory Objective** ..... **9**

**3.0 Eligibility/Participants** ..... **9**

**4.0 Red Ribbon Registry Details** ..... **9**
**4.1 Registry Platform** ..... **9**
**4.2 Volunteer Recruitment** ..... **9**
**4.3 Informed Consent** ..... **9**
**4.4 Clinical Research Site Approvals** ..... **10**
**4.5 Contacting Potential Volunteers** ..... **10**
**4.6 Updating Existing Volunteer Registry Entries** ..... **10**

**5.0 Potential Risks and Benefits** ..... **10**
**5.1 Potential Risks of Participating in the Registry** ..... **10**
**5.2 Benefits of Participation** ..... **11**

**6.0 Ethics and Responsibility** ..... **11**
**6.1 Investigator Responsibilities** ..... **11**
**6.2 IRB Review** ..... **11**
**6.3 Clinical Research Site (CRS) Review** ..... **11**
**6.4 Research Related Injury** ..... **11**

**References** ..... **12**

## Abbreviations and Acronyms

| Abbreviation/Acronym | Term |
|---|---|
| HIV-1 | Human Immunodeficiency Virus 1 |
| ACTG | AIDS Clinical Trials Group |
| HPTN | HIV Prevention Trials Network |
| HVTN | HIV Vaccine Trials Network |
| IMPAACT | International Maternal Pediatric Adolescent AIDS Clinical Trials |
| CTMS | Clinical Trials Management System |
| IRB | Institutional Review Board |
| NIAID | National Institute of Allergy and Infectious Diseases |
| NIH | National Institutes of Health |
| CRS | Clinical Research Site |

# 1.0 Background and Rationale

## 1.1 HIV Pandemic

The global HIV-1 epidemic continues and while many countries have made progress toward leveling HIV prevalence over the last few years, micro-epidemics of infection continue to occur in nearly all regions, even in countries possessing the full toolkit of proven prevention approaches [1-3]. The World Health Organization (WHO) estimates that there were 1.5 million new HIV infections worldwide in 2020 the last year for which data are available [4-5]. Antiretroviral drugs (ARVs) have been shown to be effective for HIV prevention in serodiscordant couples when administered to HIV-infected individuals as treatment as prevention (TasP) and clinical trials are now underway to evaluate the efficacy of TasP at a population level [6]. ARVs have also been shown to be effective as pre- or post-exposure prophylaxis (PrEP or PEP) [7]. At present daily oral emtricitabine (FTC)/tenofovir disoproxil fumarate (TDF) (Truvada) is the only drug approved for PrEP use, but this drug combination has significant known side effects [8]. The requirement for daily use and the side effect profile have made adherence to this drug regimen challenging, especially over long periods of time [9]. As a consequence, the capacity of currently available ARV regimens to reduce HIV incidence or prevalence is less than optimal. Furthermore, sustained use of ARVs for HIV prevention will increase the already significant burden of ARV manufacturing and delivery for HIV treatment, especially in countries bearing the highest burden of HIV disease. For these reasons, a biomedical HIV prevention approach that exhibits sustained activity over an extended time period, that has a safety profile acceptable for healthy persons, and whose effectiveness is less dependent upon individual adherence, is still needed.

In addition to more advanced prevention interventions against HIV, improved therapeutics for HIV are also needed. Tremendous progress has been made over the past thirty years in the development of antiretroviral therapy (ART), but important challenges remain in achieving viral supperssion among greater numbers of people, reducing the burden of tuberculosis (TB) globally and reducing morbidity from chronic disease and hepatitis B among people living with HIV. ART has improved the quality and the quantity of life of people living with HIV infection and has reduced new infections by decreasing transmission rates, but ART is not a cure. People living with HIV still have to take medicines for life and still have the burden of complications, malignancies, cost and the stigma of HIV infection. The recent report of a second individual “cured” of HIV infection [10] confirmed that although exceedingly rare [11] it is possible to attain ART-free remission. In addition to striving for ART-free remission as a potential cure strategy, novel therapeutics are also needed. Safe and effective treatment to control HIV infection is one of the greatest scientific and public health achievements of the past century. Despite these successes, many challenges remain in delivering effective lifelong therapy to those most in need, especially vulnerable and at risk populations both in the US and the areas most affected worldwide. This gap imperils the goal of achieving virologic suppression targets worldwide.

## 1.2 DAIDS/NIAID/NIH HIV Clinical Trials Networks

The NIAID HIV/AIDS Clinical Trials Networks have been designed to address NIAID's HIV/AIDS scientific priorities, and each has a specific scope of work assigned. The Networks include:

- AIDS Clinical Trials Group (ACTG): The mission of the AIDS Clinical Trials Group (ACTG) is to cure HIV and reduce the burden of disease due to HIV and its complications including TB and viral hepatitis. The scientific priorities of the ACTG network include research to: 1) Identify strategies to cure and/or achieve a functional cure for HIV; 2) Improve the diagnosis and treatment of tuberculosis, especially in those co-infected with HIV; 3) Identify strategies to cure infectious hepatitis; 4) Prevent or improve the treatment of non-infectious co-morbidities and evaluate novel interventions targeting HIV infection; and 5) Improve the treatment for viral-related malignancies in HIV-infected adults.

- HIV Prevention Trials Network (HPTN): The HIV Prevention Trials Network develops and tests the safety and efficacy of primarily non-vaccine interventions designed to prevent the transmission of HIV. Its main area of focus is to discover and develop new and innovative strategies to reduce the acquisition and transmission of HIV.

- HIV Vaccine Trials Network (HVTN): The HVTN's main area of focus is to fully characterize the safety, immunogenicity, and efficacy of HIV vaccine candidates with the goal of developing a safe, effective vaccine as rapidly as possible for prevention of HIV infections globally. The HVTN also pursues passive immunoprophylaxis for HIV, and preventive TB vaccines.

- International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT): IMPAACT evaluates interventions to treat and prevent HIV infection and its consequences in infants, children, adolescents, and pregnant/postpartum women through the conduct of high quality clinical trials. Its main areas of focus are to significantly decrease incident HIV and HIV-associated infections, and to decrease mortality and morbidity due to HIV and HIV-associated infections and co-morbidities among infants, children, adolescents, and pregnant/postpartum women.

## 1.3 Rationale for Establishment of the Red Ribbon Registry

This protocol is designed to create a database of people interested in participating in NIAID-funded HIV clinical trials: the HIV Clinical Trials Volunteer Screening Registry, named the Red Ribbon Registry (R3). The R3 will collect preliminary data from these volunteers to categorize their potential for participation in a diverse set of HIV clinical trials conducted by the networks as described above. Data will be made available to the clinical trials site(s) in the vicinity of the participant's residence for outreach and recruitment into appropriate HIV clinical trials.

In anticipation of trials that will enroll special populations, the registry may also include pregnant women. This will allow us to build capacity for enrolling people from this population going forward.

# 2.0 Study Design

## 2.1 Overview

See Figure 1 for an overview of the registry process. Data collected as part of the R3 outlined in this study protocol may be used to support eligibility determination for current or future HIV trials as allowed by the protocol-specific eligibility criteria within a protocol-defined screening period or window.

In order to maximize efficiency of the screening process, select data will be collected from potential participants. They will complete the informed consent process and the registry Intake Survey on their mobile phone, computer, tablet, or other electronic device. Participants in the R3 will be included in the database and accessible to clinical trial sites in their proximity as future contacts for upcoming or current HIV clinical trials.

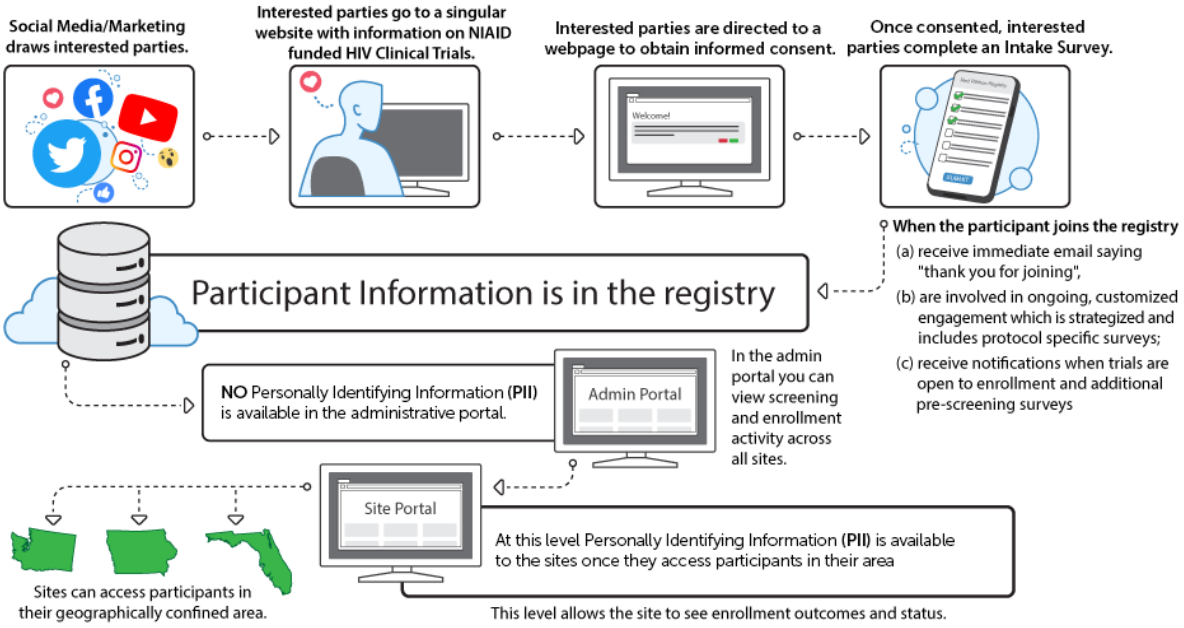


**Figure 1 Overview of Red Ribbon Registry**

## 2.2 Study Objectives

### 2.2.1 Primary Objective

*Establish a screening registry to identify potential volunteers to participate in HIV clinical trials conducted by the NIAID HIV Clinical Trials Networks*.

This registry will be comprised of user-reported personal information, demographics, contact information, and a limited list of pre-existing conditions and symptoms associated with HIV clinical trial eligibility.

### 2.2.2 Secondary Objective

*Identifying demographics of those interested in HIV research to support production of better targeted outreach materials for sites recruiting for phase 1-3 HIV clinical trials.*

A secondary objective of the registry will be to identify characteristics, trends and demographics of participants over time and in response to recruitment campaigns. Anonymized data may be used for the purpose of defining marketing strategies to enhance interest in participating in HIV clinical trials.

### 2.2.3 Exploratory Objective

*Utilize machine learning to improve predictive analytics.*

As enrollment and in-person screening proceeds, our large screening database and other publicly available and anonymized data sources will continue to shed light on specific risk groups and risk factors important to achieve our enrollment targets. To leverage these resources, we will explore statistical and machine learning methods including logistic regression with Lasso, ADA boost, random forest, Cox proportional hazards, and DeepSurv to develop more sensitive and specific predictors of HIV infection and AIDS disease severity risks.

## 3.0 Eligibility/Participants

Adults who are interested in HIV clinical trials, and who are able to provide informed consent, will be eligible to participate in this registry.

## 4.0 Red Ribbon Registry Details

### 4.1 Registry Platform

The registry will be maintained in a secure database, and registration will occur through an encrypted Hypertext Transfer Protocol Secure (HTTPS) web interface. Permissions for access to registry data will be limited to study staff, with access by site staff further restricted to geographically proximal records. The Principal Investigator (PI) of each Clinical Research Site (CRS) will sign a Data Use Agreement to ensure that the use of the data is clear and under the terms of this protocol.

### 4.2 Volunteer Recruitment

Volunteers will be directed to the Registry by a link on public websites, QR codes on social media, digital advertising, print materials, or any other means of community and stakeholder outreach. Any materials developed to advertise the registry will be submitted for Institutional Review Board (IRB) approval.

### 4.3 Informed Consent

Appropriate informed consent will be obtained for participation in the registry prior to entering personal information in the Intake Survey. Volunteers will be informed that the information obtained during the screening will be entered into a secure, password protected database.

### 4.4 Clinical Research Site Approvals

Each CRS that is intending to use the registry must obtain IRB approval before contacting potential clinical trial volunteers. This may occur via either a stand-alone recruitment method for general CRS outreach or a clinical trial protocol-specific approval under the sIRB that holds the protocol file. Once the site approval is granted and staff are trained and authorized by the CRS PI to access the registry, the CRS staff may contact potential volunteers.

### 4.5 Contacting Potential Volunteers

As new clinical trials become available, potential volunteers may be contacted by a local clinical research site to assess their interest in HIV clinical trials. Any trial-specific information will only be given to a volunteer once study-specific IRB approval has been obtained, although the potential timing of upcoming studies may be discussed to assess interest and availability.

Registry volunteers may also be contacted for their feedback on the registry and their motivation(s) for participating in it. Their feedback may be used to help develop national ad campaigns and/or educational or community engagement materials to promote the Registry and enhance participation in upcoming HIV clinical trials.

### 4.6 Updating Existing Volunteer Registry Entries

The registry is built to allow for both solicited and voluntary updates. Requests will be made by the study team on an approximately annual basis asking existing volunteers to update their information if anything has changed (i.e., health related information). Additionally, volunteers will be able to update their contact information, registry participation, and communications preferences at any time via an online secure portal.

## 5.0 Potential Risks and Benefits

### 5.1 Potential Risks of Participating in the Registry

Participants will be asked questions of a personal nature and may feel uncomfortable providing private health and other personal information. Participants will be informed that they do not have to answer any questions that they do not want to answer. All efforts to maintain confidentiality will be made, but absolute confidentiality cannot be guaranteed. Risks of sharing health information include unintentional disclosure of personal medical conditions, and other aspects of personal health history and personal characteristics to persons beyond the study-associated staff. There may be unknown risks that cannot be determined at this time.

Every precaution will be made to ensure the privacy of registry participants. To mitigate this risk, volunteers' data, including contact information and screening responses, will be

stored securely. Access to the data will be via a password protected database that requires two-factor authentication by an approved user for access. Access to and use of the database is restricted to study staff in support of HIV clinical trials and is controlled by the PI of the CRS and database administrator(s).

### 5.2 Benefits of Participation

Participation in the registry is voluntary. There may be no direct benefit to the volunteer for participating in the study. However, this registry will expedite enrollment into specific IRB-approved HIV-related clinical trials once they are open for enrollment by establishing a pool of potentially eligible and interested volunteers. This will streamline the conduct of current and future HIV clinical trials, and facilitate the process of bringing HIV vaccines, monoclonal antibodies and/or new therapies to the public for preventing and controlling the HIV pandemic and its associated comorbidities.

## 6.0 Ethics and Responsibility

### 6.1 Investigator Responsibilities

The Principal Investigator will obtain IRB approval, conduct the study according to the sponsor-approved and IRB-approved protocol/amendments and government regulations, and will only make changes after notifying the IRB or to eliminate an immediate hazard in order to protect the safety, rights, or welfare of participants. The Investigator will ensure continuing review of the study and follow IRB guidelines for investigators.

### 6.2 IRB Review

The Principal Investigator must obtain approval of the protocol, amendments, informed consent tools, and recruitment and advertising materials from a duly constituted IRB and comply with its policies, procedures and conditions.

### 6.3 Clinical Research Site (CRS) Review

The Clinical Research Site (CRS) staff must agree to proper containment and use of the data obtained from the Registry in order to maintain participant confidentiality (see section 4.1). CRS staff will use the Registry data in accordance with all applicable laws, organizational guidelines, and policies.

### 6.4 Research Related Injury

No funds have been set aside to cover costs associated with injuries related to the research conducted in this protocol.

## References


1. UNAIDS. Report on the Global AIDS Epidemic, 2012 country progress reports. https://www.unaids.org/en/dataanalysis/knowyourresponse/countryprogressreports/2020countries. 2020. Acessed September 10, 2021
2. UNAIDS. *Global AIDS Update. Seizing the moment: tackling entrenched inequalities to end epidemics*. Geneva: UNIADS, 2020. https://www.unaids.org/sites/default/files/media_asset/2020_global-aids-report_en.pdf. Accessed September 10, 2021
3. HIV/AIDS Fact Sheet.07-2021. https://www.who.int/en/news-room/fact-sheets/detail/hiv-aids. Accessed September 10, 2021.
4. WHO. Global HIV Programme. https://www.who.int/teams/global-hiv-hepatitis-and-stis-programmes/hiv/strategic-information/hiv-data-and-statistics (2021). Accessed September 10, 2021.
5. hhttps://www.unaids.org/sites/default/files/media_asset/UNAIDS_FactSheet_en.pdf. (UNAIDS Fact Sheet – 2021). Accessed September 10, 2021
6. Cohen MS, Chen YQ, McCauley M, Gamble T, Hosseinipour MC, Kumarasamy N, Hakim JG, Kumwenda J, Grinsztejn B, Pilotto JH, Godbole SV, Mehendale S, Chariyalertsak S, Santos BR, Mayer KH, Hoffman IF, Eshleman SH, Piwowar-Manning E, Wang L, Makhema J, Mills LA, de BG, Sanne I, Eron J, Gallant J, Havlir D, Swindells S, Ribaudo H, Elharrar V, Burns D, Taha TE, Nielsen-Saines K, Celentano D, Essex M, Fleming TR. Prevention of HIV-1 infection with early antiretroviral therapy. N Engl J Med 2011;365:493-505.
7. Grant RM, Lama JR, Anderson PL, McMahan V, Liu AY, Vargas L, Goicochea P, Casapia M, Guanira-Carranza JV, Ramirez-Cardich ME, Montoya-Herrera O, Fernandez T, Veloso VG, Buchbinder SP, Chariyalertsak S, Schechter M, Bekker LG, Mayer KH, Kallas EG, Amico KR, Mulligan K, Bushman LR, Hance RJ, Ganoza C, Defechereux P, Postle B, Wang F, McConnell JJ, Zheng JH, Lee J, Rooney JF, Jaffe HS, Martinez AI, Burns DN, Glidden DV. Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. N Engl J Med 2010;363:2587-99.
8. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. Department of Health and Human Services. Available at https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/AdultandAdolescentGL.pdf. Accessed September 10, 2021.
9. van der Straten A, Van Damme L, Haberer JE, Bangsberg DR. Unraveling the divergent results of pre-exposure prophylaxis trials for HIV prevention. *AIDS*. 2012;26(7):F13-F19.
10. Gupta RK, Abdul-Jawad S, McCoy LE, Mok HP, Peppa D, Salgado M, et al. HIV-1 remission following CCR5Δ32/Δ32 haematopoietic stem-cell transplantation. Nature. 2019:1.
11. Hütter G, Nowak D, Mossner M, Ganepola S, Müßig A, Allers K, et al. Long-term control of HIV by CCR5 Delta32/Delta32 stem-cell transplantation. New England Journal of Medicine. 2009;360(7):692-8.