

RePORT International Newsletter

May 2024

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FEATURING RePORT-SOUTH AFRICA



Message from Jerry Ellner

The May newsletter is devoted to RePORT South Africa. Mark Hatherill and associates provide a concise overview of activities at the sites including the plans for Phase 3. South Africa is an integral part of RePORT International and importantly the Subclinical TB protocol led by Tim Sterling. We appreciate the leadership roles of Mark, Tim, Tom Scriba and Gerhard Walzl in RePORT

International and look forward to their future scientific contributions.

RePORT South Africa – Where Innovation Emanates!

RePORT South Africa (SA) III is a collaborative research network, comprised of 14 research groups from seven South African and four US institutions, spearheading innovative research in the field of tuberculosis (TB) biomarkers. Led by eight clinical research sites and five analytical laboratories, the participating institutions in South Africa and the USA include the University of Cape Town, Stellenbosch University, Africa Health Research Institute, University of Pretoria, University of the Witwatersrand, Vanderbilt University Medical Center, University of California San Francisco, Colorado State University, and University of Washington.

A Strong Network

The network's structure is robust, with each institution playing a significant role in contributing to a wealth of TB biomarker knowledge and expertise. The University of Cape Town houses the South African Tuberculosis Vaccine Initiative (SATVI),

the UCT Lung Institute, and Red Cross Children's Hospital. Stellenbosch University's Immunology Research Group and SAMRC Centre for Tuberculosis Research, and the Africa Health Research Institute and University of Pretoria also play essential roles. The University of Witwatersrand hosts the Perinatal HIV Research Unit and the Kana Laboratory. The US institutions, including Vanderbilt University Medical Center, University of California San Francisco, Colorado State University, and University of Washington, provide data management and laboratory expertise to enrich the network's scope and impact.

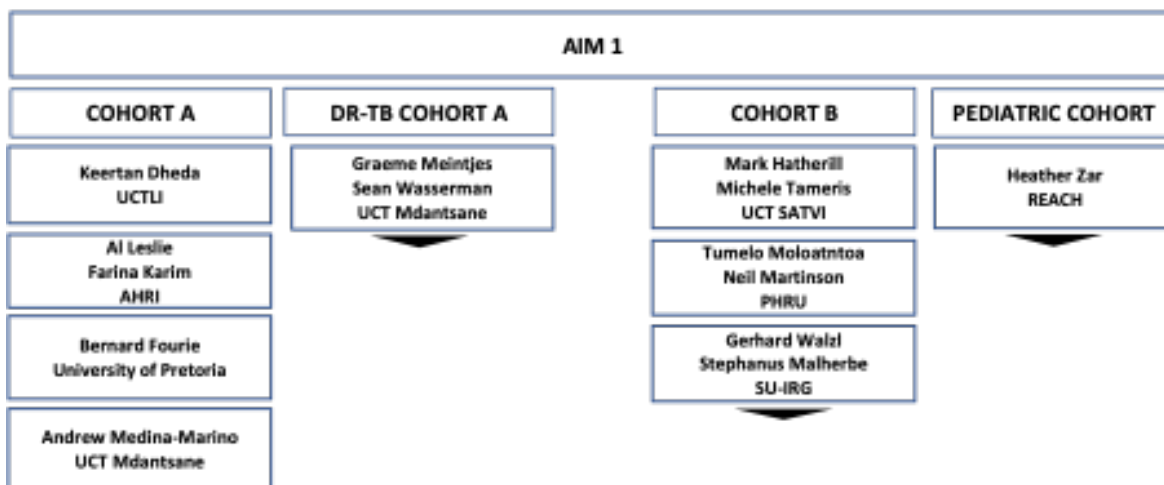
Insights gained from RePORT II have fueled the network's ongoing focus on research aims focusing on expanding and strengthening the network, discovering and validating biomarkers for TB triage and screening, delineating specific T-cell response attributes to vaccine antigens, evaluating treatment response biomarkers, and investigating microbial genotypic diversity related to TB disease outcomes. The network collaboration in the operational space ensures robust tracking of sample collection, biorepository storage, and logistics for analytical labs.

Research - Not Without its Challenges

A large, state-of-the-art biorepository also brings challenges, such as continuous funding for sample storage, highlighting the need for sustained financial support to maintain the network's research momentum. However, RePORT South Africa III is well-positioned in the fight against TB, leveraging its multidisciplinary expertise and collaborative spirit to drive impactful research outcomes and evidence-based solutions for global TB prevention and care. The recent annual meeting in Pretoria provided a platform for sharing unpublished data and fostering collaboration across international networks, setting the stage for groundbreaking discoveries in the field. With a commitment to innovation and collaboration, RePORT South Africa III continues to lead the way in transforming TB research and shaping the future of global health.

Organogram - Progress in RePORT South Africa

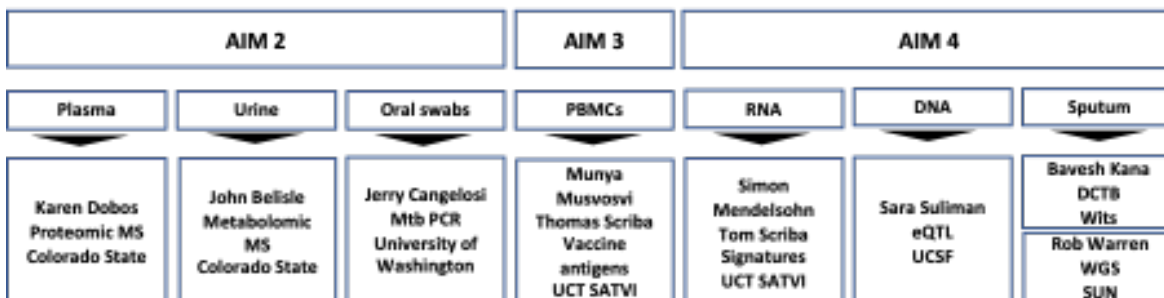
WP1: Project Core
Mark Hatherill PI SA
SATVI, Cape Town



WP2: Data Management & Harmonization
Timothy Sterling Co-PI US
Vanderbilt



WP3: Biomarkers
Thomas Scriba
SATVI, Cape Town



RePORT - 3rd Cycle

The RePORT III team includes current RePORT investigators with extensive experience in clinical and translational TB science, supplemented by new clinical and laboratory investigators with internationally recognized expertise in drug-sensitive (DS) and drug-resistant (DR) TB therapeutics and microbiology. With the addition of the Mdantsane site in the Eastern Cape Province, the network will include eight clinical sites with access to adult and pediatric populations with high TB/HIV incidence; large DS- and DR-TB cohorts aligned to the Common Protocol; and state-of-the-art laboratory capacity to conduct biomarker, immunological, genetic, and microbial assays, at seven SA and four US institutions with a strong track record of successful partnership.

The scientific focus of RePORT III is informed by progress made in RePORT II. It is essential that new triage and screening biomarkers can detect both clinical TB

in symptomatic patients presenting for healthcare, and undiagnosed subclinical TB in asymptomatic people, including *Mycobacterium tuberculosis* (Mtb-) exposed household contacts. Ongoing laboratory analyses of samples collected in RePORT II are testing a suite of novel biomarkers for this purpose in 845 symptomatic Cohort A patients (236; 28% clinical TB cases) and 982 Cohort B household contacts (53; 5.4% subclinical TB cases), using 72,607 well-characterized, stored samples. Advances on the work of RePORT II will include validation of serum exosomal, urine metabolomic, and oral swab molecular biomarkers that were discovered and tested in RePORT II; and prospective testing of promising new triage and screening biomarkers in the same populations.

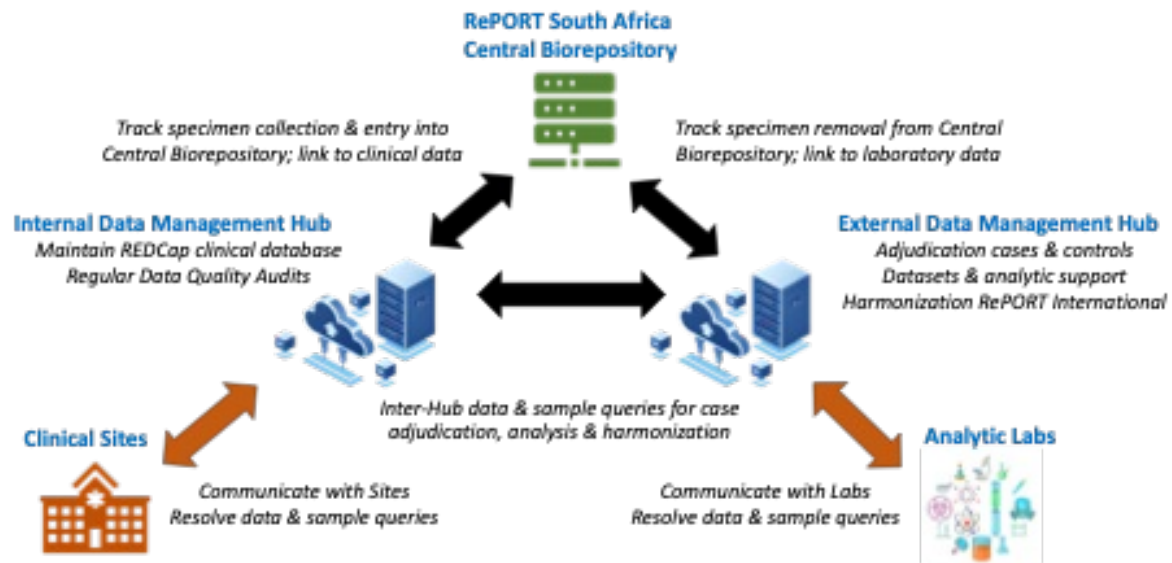
- AIM 1: Expand and strengthen the RePORT South Africa network.
- AIM 2: Discover, test and validate biomarkers for triage and screening of symptomatic and subclinical TB disease.
- AIM 3: Delineate specific T cell response attributes to high-priority vaccine antigens in clinical TB, subclinical TB, incident TB cases and controls.
- AIM 4: Evaluate biomarkers of treatment response.
 - Sub-aim 4a: Discover, test, and validate new host biomarkers of TB treatment response.
 - Sub-aim 4b: Evaluate the prevalence, phenotype and risk factors of post-TB lung disease.
 - Sub-aim 4c: Investigate microbial genotypic and phenotypic diversity related to subclinical/clinical TB disease phenotypes and poor treatment outcome.

Priority research areas that were not directly addressed in RePORT II include the immune response to high-priority TB vaccine antigens, prevalence and predictors of post-TB lung disease, and host transcriptomic, genetic and microbial markers of treatment outcome, including treatment of DR-TB. These knowledge gaps will be addressed in RePORT III by evaluation of specific T-cell responses to high-priority vaccine antigens in clinical TB, subclinical TB, incident TB cases and controls, to inform development of new preventive and therapeutic vaccines; addition of a standalone DR-TB cohort receiving the South African 6-month oral BPaLL regimen (bedaquiline, pretomanid, linezolid and levofloxacin); and addition of serial respiratory evaluations for DS- and DR-TB patients in Cohort A. Stored and prospectively collected blood RNA samples will be studied in tandem with genetic regulation of transcriptional responses associated with poor treatment outcomes, including death, treatment failure, recurrence, and post-TB lung disease. Stored and prospective sputum samples will be used to investigate microbial genotypic and phenotypic diversity related to these treatment outcomes. Thus, a standardized analytic approach will allow evaluation of the inter-relationships between host transcriptomic, genetic and microbial diversity and poor treatment outcomes, including post-TB lung disease, in both DS- and DR-TB cohorts.

These analyses of new and existing TB cohorts in diverse populations will inform evidence-based approaches for development of the most promising TB triage and screening biomarkers to impact global TB control. Notably, evaluation of biomarker performance for asymptomatic, subclinical TB will be interpreted and benchmarked against performance for symptomatic, clinical TB in the same populations. Our analyses of host transcriptomic and immunogenetic biomarkers will deliver novel insights into the DR-TB treatment response, benchmarked against parallel observations in DS-TB, and correlated with microbial

determinants of poor treatment outcome, including the severity, phenotype and risk factors of post-TB lung disease. Harmonization of data and specimen collection through the Common Protocol will enable validation of these findings in other RePORT countries.

Fig. 1. Scheme of data management hugs for tracking sample collection, biorepository storage, and shipping to analytic labs.



RePORT SA Annual Meeting 2023, Pretoria, South Africa



RePORT-BRAZIL'S PRODUCTIVE APRIL EVENTS

By Marina Cruvinel Figueiredo and Mariana Pereira

Semi-Annual Meeting Showcases the Innovation of the Network

The Semi-Annual Meeting of RePORT-Brazil was held in Manaus from April 8-12,

2024. Since its inception in 2014, RePORT-Brazil has been a pioneer in tuberculosis (TB) research and is part of the global RePORT International consortium. Now in its second phase, the leadership team includes Dr. Bruno Andrade (Brazil Chair), Dr. Valeria Rolla (Co-Chair), Dr. Marcelo Cordeiro (Brazil Co-Chair), Dr. Afrânio Kritski (Brazil Co-Chair), and Dr. Timothy Sterling (US Chair). This event highlighted the network's investment in nurturing new TB scientific leadership. Postdoctoral fellows from RePORT-Brazil, Rodrigo Menezes and Isabella Brige, presented their current projects. Additionally, Carina Carvalho was introduced as the recipient of the Early Career Development Award for 2024-2025.

Discussions at the meeting covered a broad range of topics including TB biomarkers, precision medicine, lung health, genomics, drug resistance, and epidemiological data. The team also strategized on developing new technologies and identifying biomarkers for predicting unfavorable treatment outcomes. The next Semi-Annual Meeting is scheduled to be held in Brasilia, where RePORT-Brazil principal investigators will engage with representatives from the Brazilian Ministry of Health and the National Institute of Health (NIH). The focus will be on fostering collaborations and advancing projects that align with public health needs and the global goal of TB eradication.



This year, RePORT-Brazil is proud to host the 10th RePORT-International Meeting, which will take place from August 20 to 23 at the Gran Palladium Imbassai Resort & Spa. This significant event will bring together researchers, clinicians, and experts from various countries, facilitating a valuable exchange of knowledge and advancements in TB research. The choice of the venue reflects the organization's commitment to fostering collaboration and learning in an inspiring

setting.



RePORT International Lab Trainees

April also saw the conduct of the second Luminex training session for fellows of the RePORT International Lab Training Program. Participants included John Carlo Malabad from the Philippines, Amsaveni Sivaprakasam from India, and Prakash Babu Narasimhan from India. They joined Dr. Bruno Andrade's team at Fiocruz in Salvador for this hands-on training, enhancing their skills in advanced lab technologies. This session underscores RePORT-Brazil's commitment to fostering international collaboration and skill development in the fight against TB.



ANNOUNCEMENTS



Meet our New Program Officer from the National Institute of Allergy and Infectious Diseases

Nicole Espy, Ph.D., is a Program Officer in the Laboratory and Clinical Sciences Branch of the Therapeutics Research Program at the Division of AIDS, National Institute of Allergy and Infectious Diseases. Her portfolio focuses on HIV and TB diagnostics and biomarker development. Dr. Espy's research background includes a wide-range of

disease areas, including HIV, COVID-19, Ebola, and Malaria, and expertise in global health, epidemiology, viral immunology, clinical trials, diagnostics, genomics and laboratory quality assurance and quality control.

She received her B.S. in Molecular Biophysics and Biochemistry from Yale University, and her doctorate degree in Biological Sciences in Public Health at Harvard. She completed her post-doctoral training at the U.S. Army Medical Research Institute for Infectious Diseases. She also worked as a Diagnostic Project Manager, supporting specimen processing and other diagnostic and laboratory quality assurance oversight activities for DAIDS HIV and COVID-19 vaccine networks. Most recently, Nicole served as a Program Manager and Research & Technical Advisor at the U.S. Department of State, where she provided technical support for PEPFARs Asia Regional Program, working with local partners to help curb the HIV epidemic and achieve progress towards UNAIDS 95-95-95 goals in this region.

Requests for Feedback

Educational Offerings

Deadline: May 24, 2024

The RePORT International Coordinating Center is looking to expand its educational offerings based on the needs and interests of RePORT International's personnel and partners. In our inaugural year, we created two courses, Epidemiology for Tuberculosis and TB: Topics in Professional Development.

We welcome your feedback to create new mini-courses in our second year.

SURVEY

Refine our Newsletter

Help us make the newsletter reflect the content you want to see! We need to learn more about your work, your interests, and how you consume and share our content.

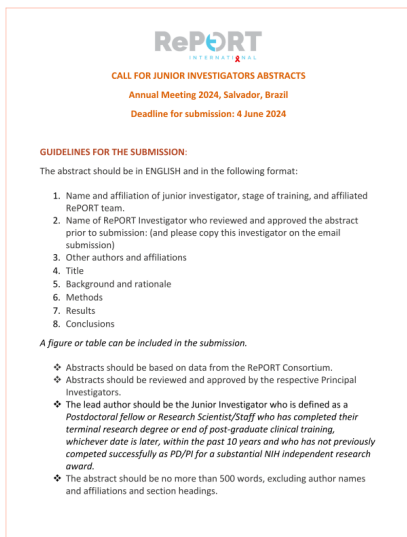
Please take our communications survey and let us know what works best for you.

SURVEY

Call for Junior Investigators Abstracts Deadline: June 4, 2024

The 2024 RePORT International Annual Meeting in Salvador, Brazil, has released a call for Junior Investigator abstracts. Abstracts should be submitted to tbricc@njms.rutgers.edu, where they can be contact for more information.

Notifications will be made in the week of **11th June**. The final review will be conducted by Leadership Group and External Reviewers. **Travel arrangements and funding will be provided to those selected.**



RePORT INTERNATIONAL
CALL FOR JUNIOR INVESTIGATORS ABSTRACTS
Annual Meeting 2024, Salvador, Brazil
Deadline for submission: 4 June 2024

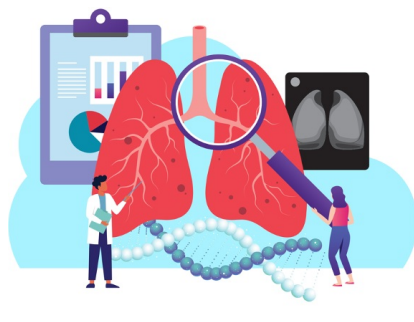
GUIDELINES FOR THE SUBMISSION:
The abstract should be in ENGLISH and in the following format:

1. Name and affiliation of junior investigator, stage of training, and affiliated RePORT team.
2. Name of RePORT Investigator who reviewed and approved the abstract prior to submission: (and please copy this investigator on the email submission)
3. Other authors and affiliations
4. Title
5. Background and rationale
6. Methods
7. Results
8. Conclusions

A figure or table can be included in the submission.

- ◆ Abstracts should be based on data from the RePORT Consortium.
- ◆ Abstracts should be reviewed and approved by the respective Principal Investigators.
- ◆ The lead author should be the Junior Investigator who is defined as a *Postdoctoral Fellow or Research Scientist/Staff* who has completed their terminal research degree or end of post-graduate clinical training, whichever date is later, within the past 10 years and who has not previously competed successfully as PD/PI for a substantial NIH independent research award.
- ◆ The abstract should be no more than 500 words, excluding author names and affiliations and section headings.

PDF & INFORMATION



Webinar: TB Portals

Deadline: June 24, 2024

TB-RICC will be hosting a webinar on the use of **TB Portals**, NIAIDs open, web-based platform to facilitate meta-domain and domain specific TB data exploration and analysis. The TB Portals database contains linked clinical, bacterial genomic, and medical imaging data from TB

patient cases. These data directly feed into our four data tools, and each tool

provides a unique way of exploring and analyzing TB Portals data. This webinar will provide an overview of how TB Portals can be used for learning and for research.

[REGISTER](#)



2024 CFAR HIV/AIDS Training Fellowship Awards

Intent to Apply Deadline: May 17, 2024
Submission Deadline: July 31, 2024

CRDF Global is accepting proposals from Centers for AIDS Research (CFARs) to support early-stage investigators from India working in the field of HIV/AIDS research for the 2024 CFAR HIV/AIDS Training Fellowship Awards. A list of CFAR sites can be found [here](#). This initiative is supported by the National Institutes of Health (NIH) and the National Institute of Allergy and Infectious Diseases (NIAID). This fellowship program aims to promote the training and inclusion of Indian early-stage scientists in HIV-related collaborative research within the CFAR program.

[LEARN MORE](#)

Cross Consortium Funding for the RePORT International Consortium

Deadline: June 21, 2024

RePORT International is accepting proposals for the Competition titled “Cross Consortium Funding for the RePORT International Consortium.” This Competition is organized by the RePORT International Coordinating Center and administered by CRDF Global, on behalf of the National Institute of Allergies and Infectious Diseases (NIAID). This cross consortium supplemental funding will support cross-cutting research activities and develop or strengthen collaborations across RePORT scientists. Investigators and study populations must derive from at least two RePORT country networks.

[LEARN MORE](#)

Online Research in Progress

Wednesday 28 August 9am-1pm BST
and Thursday 29 August 1pm-5pm BST

#RSTMH2024 | RSTMH.org/events

RSTMH Research in Progress

The **Online Royal Society of Tropical Medicine and Hygiene Research in Progress** meeting is taking place virtually on 28 August 9am-1pm BST and 29 August 1pm-5pm BST.

The **RSTMH Research in Progress** events are designed specifically for early career investigators to present their unpublished research in progress to peers and senior experts in all fields of tropical medicine and global health. Certificates of attendance will be provided.

There will be guidance sessions during the event on how to: get funding, get published, and communicate your research.

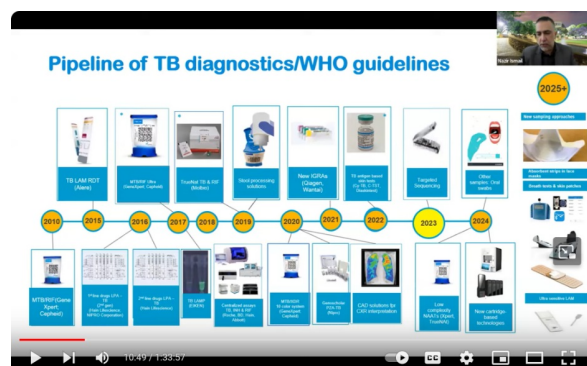
The event is free to attend for members and fellows or £5 per person for non-members.

LEARN MORE

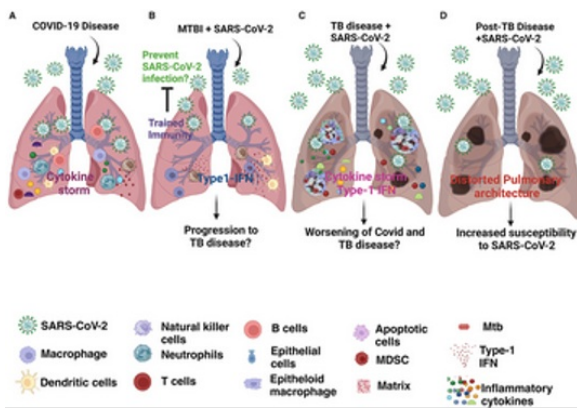
RESOURCES

TB Webinar Available

[FIND](#), [USAID](#), [Unitaid](#), and [Global Laboratory Initiative](#) have sponsored a webinar on the use of targeted Next-Generation Sequencing for detection of drug-resistant TB.



WATCH



Double Trouble: TB and COVID-19

The article, *Diverse Interactions of Mycobacterium tuberculosis infection and of BCG vaccination with SARS-CoV-2* has been published by RePORT International authors, Padmini Salgame, Sri Ram Pentakota, John Carlo M. Malabad, Prakash Babu Narasimhan, Sheetal Verma, Senbagavalli Prakash Babu, Vartika

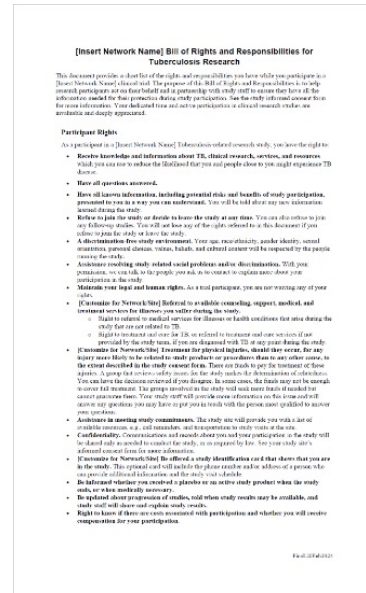
Sharma, Sonali Sarkar, Marissa Alejandria, and Jerrold Ellner.

[READ MORE](#)

TB Research Template Available

Bill of Rights and Responsibilities for Tuberculosis Research is a template that outlines the rights and responsibilities an individual has while they participate in a clinical trial or other type of research.

The document can be modified to meet the needs of a specific study. It was developed by the [TB Vaccine Community Engagement Strategy Working Group](#) and the [Tuberculosis Trials Consortium](#) Community Research Advisors Group.



[DOWNLOAD](#)

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