Johns Hopkins University

# A Feasibility Study: Building and Operating a Biospecimen Repository in South Africa for Storage and Redistribution of Specimens from Large Scale, Multicenter Clinical Trials

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by
**Emily Higbee**

Baltimore, Maryland
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**Abstract**

Current annual cost estimates for storage and redistribution of biological specimens collected for large scale, multicenter clinical trials in sub-Saharan Africa conducted by the HIV Vaccine Trials Network (HVTN) are expected to reach $13 million in the next 10 years, likely totaling in excess of $29 million over the life of active study protocols. While similar biorepository expenses are covered by the U.S. Federal government for domestic studies, international samples collected and stored abroad remain the responsibility of each grant. As U.S. Federal funding remains flat, HVTN awards are presented with a substantial burden. The objective of this Capstone project was to provide research results and analysis of constructing and operating an independent biorepository in the country of South Africa, compared to existing contracted repository services. To meet the objective and provide recommendations to the HVTN for future steps, a multi-step approach was taken including: 1) a literature review; 2) oral interviews with personnel involved in repository functions; 3) data collection to assist in estimating anticipated numbers of biological specimens for storage and project expenses; 4) the creation of a biorepository space concept; and 5) a cost analysis for one-time building and ongoing operating expenses of an independent repository. Calculated estimates of $6,349,746 for construction and $2,456,172 for annual operating expenses in the first year, increasing at a rate of 7% per year with fewer freezer purchases in out years, indicate a cost savings to the HVTN, with initial one-time building expenses being recouped by Year 4 of operations. Literature and expert interviews confirm that the construction and operations of an independent biorepository in South Africa is a complex multi-variable endeavor that ultimately has no perfect approach. The data collected and analyzed here seem to indicate that there would be significant financial savings, and may be a favorable option for further pursuit. However, embarking on this operation

would be a large initial funding issue and complicated administrative and logistical undertaking, presenting risks to established partnerships and a liability for maintaining compliance with local, country-specific, U.S., and international regulations.

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## Abbreviations

| | |
|---|---|
| BMGF | *Bill & Melinda Gates Foundation*[1] |
| CHIL | *Cape Town HVTN Immunology Laboratory*[2] |
| DAIDS | *Division of AIDS*[3] |
| FDA | *United States Food and Drug Administration*[4] |
| FHCRC | *Fred Hutchinson Cancer Research Center*[5] |
| GLP | *Good Laboratory Practices* |
| HPCSA | *Health Professionals Council of South Africa* |
| HPTN | *HIV Prevention Trials Network*[6] |
| HVTN | *HIV Vaccine Trials Network*[7] |
| IATA | *International Air Transport Association* |
| ISBER | *International Society for Biological and Environmental Repositories*[8] |
| LIMS | *Laboratory Information Management System* |
| MTA | *Material Transfer Agreement* |
| NHA | *National Health Act* |
| NIAID | *National Institute of Allergy and Infectious Diseases*[9] |
| NIH | *National Institutes of Health*[10] |
| OSHA | *Occupational Safety and Health Administration* |

[1] https://www.gatesfoundation.org/
[2] www.chil.org.za
[3] https://www.niaid.nih.gov/about/daids
[4] https://www.fda.gov/
[5] www.fredhutch.org
[6] www.hptn.org
[7] www.hvtn.org
[8] www.isber.org
[9] https://www.niaid.nih.gov/
[10] https://www.nih.gov/

| | |
|---|---|
| PBMC | *Peripheral Blood Mononuclear Cell* |
| PHI | *Protected Health Information* |
| PII | *Personally Identifiable Information* |
| QA | *Quality Assurance* |
| QC | *Quality Control* |
| QMS | *Quality Management System* |
| SAMRC | *South African Medical Research Council*[11] |
| SARS | *South African Revenue Service* |
| SOP | *Standard Operating Procedures* |
| USD | *United States Dollars* |

[11] http://www.mrc.ac.za/

## Glossary

**(Bio)repository.** "A facility that collects, catalogs, and stores biospecimens."[12]

**Biospecimens.** "Samples of human, animal, or plant material, such as urine, blood, tissue, cells, DNA, RNA and protein stored in a biorepository and used for laboratory research."[13] For the context of this paper, biospecimens will refer to human tissue only.

**Peripheral blood mononuclear cell.** "Any peripheral blood cell with a round nucleus, isolated from whole blood, including lymphocytes, monocytes, and a small percentage of other immune cells." [14]

[12] National Cancer Institute [NCI]. *NCI best practices for biospecimen resources.* March 2016. Accessed February 17, 2018. https://biospecimens.cancer.gov/bestpractices/2016-NCIBestPractices.pdf

[13] NCI. *NCI best practices for biospecimen resources.* March 2016. Accessed February 17, 2018. https://biospecimens.cancer.gov/bestpractices/2016-NCIBestPractices.pdf

[14] Marine Barnabe. *Peripheral blood mononuclear cells: PBMC isolation, preservation, and culture.* May 30, 2017. Accessed February 17, 2018. https://blog.quartzy.com/2017/05/30/peripheral-blood-mononuclear-cells-pbmc-isolation-preservation-culture

# Chapter 1. Introduction

## 1.1 Background

Research institutions across the world acquire numerous amounts of biospecimens from research participants every day. For research purposes it is crucial that specimen integrity is maintained as specimens are processed and stored; specimen quality is preserved over periods of time; and legal and ethical regulations are followed. In order to do this, specimens are stored in a facility known as a biorepository or biobank specifically designed to meet these needs. This Capstone project will provide research results and analysis of the feasibility of building and operating such a biorepository in the country of South Africa for storage and redistribution of specimens collected from large scale, multicenter clinical trials conducted by the HIV Vaccine Trials Network.

### 1.1.1 What is the HIV Vaccine Trials Network?

The HIV Vaccine Trials Network (HVTN), based at Fred Hutchinson Cancer Research Center (FHCRC) in Seattle, Washington, "is the world's largest publicly funded multi-disciplinary international collaboration facilitating the development of vaccines to prevent HIV/AIDS. The HVTN conducts all phases of clinical trials, from evaluating experimental vaccines for safety and immunogenicity to testing vaccine efficacy."[15] The majority of funding for the HVTN comes from the National Institute of Allergy and Infectious Diseases (NIAID) of the National Institutes of Health (NIH) and the Bill & Melinda Gates Foundation (BMGF), and also includes support from the South African Medical Research Council (SAMRC). [16]

[15] HIV Vaccine Trials Network [HVTN]. *About.* n.d. Accessed February 17, 2018. https://www.hvtn.org/en/about.html

[16] HVTN. *About.* n.d. Accessed February 17, 2018. https://www.hvtn.org/en/about.html

### 1.1.2 Structure of the HIV Vaccine Trials Network

The HVTN is made up of three Centers: the Leadership Operations Center, Laboratory Center, and Statistical Data Management Center. While all three Centers are based in Seattle, Washington, the HVTN is dependent upon the engagement of the global community and study participants. HVTN collaborates with approximately 40 clinical trial sites across five continents (illustrated in **Figure 1**). These clinical trial sites are "selected through a competitive process administered by the National Institute of Allergy and Infectious Diseases"[17] and are responsible for engaging and enrolling participants in studies. Site staff at each HTVN clinical trial site include principal investigators, research scientists, clinicians, and laboratory, pharmacy, and outreach personnel.[18] More than 150 personnel are employed through FHCRC by the three HVTN Centers headquartered in Seattle, Washington and more than 275 personnel are funded through sub-awards across all clinical trial sites and labs globally.


**Figure 1. Map of HVTN Clinical Trial Sites** (Map Data: Google)[19]

[17] HVTN. *About*. n.d. Accessed February 17, 2018. https://www.hvtn.org/en/about.html
[18] Ibid.
[19] HVTN. *International Sites*. n.d. Accessed March 17, 2018. http://www.hvtn.org/en/hvtn-international-sites.html

To account for the growing number of study protocols based in sub-Saharan Africa and the associated number of study participants, the HVTN in partnership with the HIV Prevention Trials Network (HPTN), has rapidly expanded in the region by developing clinical trial sites in Malawi, Mozambique, South Africa, Kenya, Tanzania, Zambia, and Zimbabwe (illustrated in **Figure 2**).[20] The majority of sites are located in South Africa.

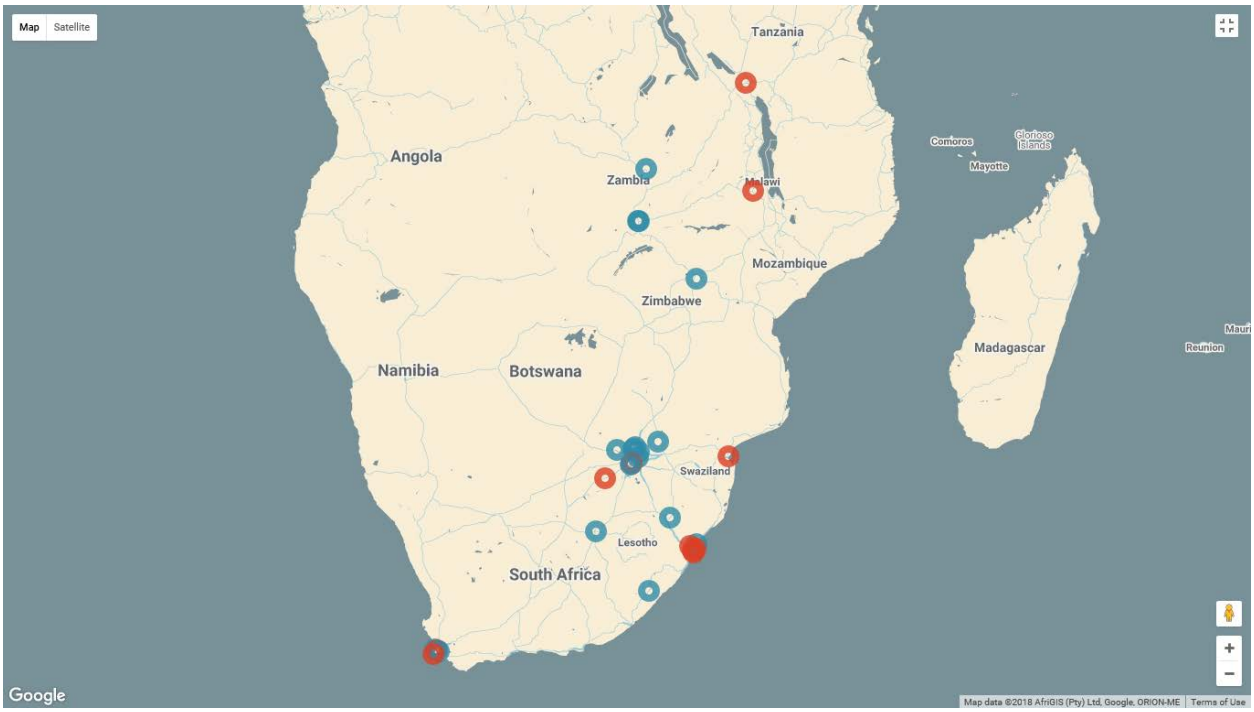


**Figure 2. Map of HVTN African Clinical Trial Sites** (Map Data: Google)[21]

### 1.1.3 Context of HIV Vaccine Studies

The direction of HVTN research is based on results identified through laboratory testing of various types of biological samples taken from all participants enrolled across all study protocols. Current studies focusing on specific HIV strains in sub-Saharan Africa are expected to

[20] HVTN. *About.* n.d. Accessed February 17, 2018. https://www.hvtn.org/en/about.html
[21] HVTN. *International Sites*. n.d. Accessed March 17, 2018. http://www.hvtn.org/en/hvtn-international-sites.html

enroll approximately 10,000 participants by mid-2019. The collection and preservation of the associated biological samples is critical to assessing vaccine-induced cellular immune functions in these studies.

### 1.1.4 Process of Collecting, Processing, Storing Biospecimen Samples

Typically, biological samples are collected from study participants at each clinical trial site, where they are processed in a laboratory and prepared for shipment to a facility for short and long term storage. Due to processing restrictions, samples collected from participants must be processed at laboratories near the clinical trial sites where they are collected, and then shipped to a central specimen repository within a given timeframe. Alternatively, each clinical trial site can store all the samples they collect, though consistency of specimen quality may vary and tracking of samples becomes cumbersome with large scale, multi-site clinical trials. For these reasons it is not recommended that each clinical trial site have its own repository.

When collecting biological specimens, Government and community concerns that samples not leave the home country or African continent, must be addressed. These concerns as well as the importance of maintaining the integrity of specimens during shipping, have led to restrictions around where specimens can be processed and stored. Thus, the HVTN engaged a third party commercial specimen repository located in Johannesburg, South Africa to house samples.

The commercial repository receives and accessions specimens utilizing a Laboratory Information Management System (LIMS), specifically LDMS,[22] for uploading specimen data, tracking, and storage. Samples are received and stored in random order, so a LIMS program is necessary for accurately tracking and pulling specimens. When the HVTN would like samples

[22] https://www.ldms.org/

pulled for further analysis, they are required to notify the vendor 2-3 weeks in advance, or pay extra for expedited shipments.

### 1.1.5 Existing Biospecimen Storage and Anticipated Costs

As of January 2018, approximately 718,000 specimens from both closed and active studies were being stored by the commercial repository. Projections indicate that another 2,756,000 peripheral blood mononuclear cells (PBMC) and other biospecimens including plasma, serum, mucosal swabs, and dried blood spots will be collected over the next 5 years, ultimately costing around $8 million USD in storage annually. This expense will continue to grow over time with estimations reaching annual costs of $13 million USD based on existing commercial repository fees and anticipated numbers of samples to be stored.

## 1.2 Statement of the Problem

When the HVTN first began conducting clinical trials in South Africa, specimens were stored locally at clinical trial sites. As the network of sites expanded and quality control became difficult to manage, it quickly became clear that the on-site storage model would not be ideal. However, a central biorepository to the meet the needs of the HVTN did not exist in South Africa. In 2012, after reviewing available options, the HVTN selected a for-profit third party company to partner with and invested a substantial amount in building out the necessary repository infrastructure.

Now, as the number of HVTN samples is projected to increase exponentially, so will the costs of storing, tracking, and shipping the samples utilizing the existing repository model. With annual storage costs expected to reach $13 million USD in the next 10 years, and as U.S. Federal funding remains flat, the HVTN grants are presented with a substantial burden. Funds awarded

for direct research will be compromised by the necessity to pay for and maintain valuable specimen collections.

To-date maintaining specimen collections has not been of great concern for U.S. Federally-funded research projects conducted in the United States. The U.S. Government fully funds a large national central biorepository which covers long term storage expenses. However, they have yet to establish or separately fund international biorepositories and continue to require each grant to fund their own repository costs. Furthermore, as specific studies and grants end, the need to identify funding for long term storage costs remain.

Competition for central biorepositories in South Africa also remains low, leaving the HVTN few alternatives other than continuing with the existing partnership. Thus, HVTN has little leverage for cost negotiations. While current costs are high, alternative vendor prices are higher and would likely require additional significant capital investment to meet the HVTN's growing needs.

### 1.3 Research Question

In 2012, the HVTN identified several scenarios and cost projections for anticipated long term biorepository storage needs for the increasing numbers of clinical trials to be conducted in Africa. While few options were available, several considerations were investigated, to include: 1) the existing support model with the third party commercial repository; 2) storing samples at the commercial repository short-term and then shipping to a different repository in the U.S. for long-term storage; 3) keeping or shipping samples back to sites for longer-term storage; or 4) shipping to the U.S. for short and long-term storage at the national central repository. At the time, there was discussion about building and operating an HVTN biorepository in South Africa; however a feasibility study was never conducted.

Since 2012, larger phase clinical trials have been added to the list of pending and active HVTN protocols. Based on the high burden of anticipated costs, the HVTN has identified a need for research administration to examine and analyze whether it is economically feasible to build and operate a specimen repository in South Africa either independently, or possibly shared with the HPTN (HVTN's partner network for one of the larger phase trials). Thus, this Capstone project will analyze the pros and cons of the HVTN constructing and operating its own biorepository, and will provide recommendations to HVTN administration and research investigators that may be used in planning and costing out their studies.

### 1.4 Research Objectives

This Capstone project will identify the components required to construct and operate a specimen repository for the purposes of the HVTN, to include one-time and ongoing cost estimates, as well as administrative and regulatory considerations for operating such a facility in South Africa. This project will also compare calculated costs to the anticipated expense of continuing with the commercial repository.

More specifically, the following research objectives will be addressed:

1) Describe the function, operational and infrastructure components required to construct and operate a specimen repository through a literature review and interviews with personnel overseeing repository functions at FHCRC and in South Africa.
2) Identify and describe special considerations for operating a specimen repository internationally (i.e. permits, local regulations, cultural considerations, currency fluctuations, training and certifications, maintenance, safety planning, identifying appropriate space for the facility, etc.).

3) Estimate the total number of HVTN specimens to be accessioned and stored over the next 5 years across all active, pending, and closed protocols in sub-Saharan Africa.
4) Conduct a cost analysis for building and operating a specimen repository utilizing required components, estimated number of specimens, and other considerations.
5) Analyze the pros and cons for operating an independent specimen repository as opposed to existing practices utilizing a third party commercial company; including a formal cost comparison that requires an estimate of the internal "payback" time for building expenses.
6) Make recommendations for future steps that HVTN may take.

**1.5 Significance**

The establishment of central biorepositories in South Africa is still an emerging concept, though it is gaining greater visibility and support. However, there are still very few companies available to meet the needs of the HVTN and other research organizations. Due to limited competition in the market, existing biorepositories are allowed much greater control over their costs and profit margins. This Capstone project will help determine the feasibility and estimated cost savings to the HVTN should they pursue building and operating their own not-for-profit central biorepository in South Africa. The cost analysis may open doors for further cost negotiations with the existing commercial repository or provide background for new conversations with the U.S. or South African governments to provide long-term specimen storage support. Depending on the model and cost structure, the independent biorepository could expand its scope to partner with and support the repository needs of other non-profit research organizations that are facing similar challenges in Africa.

### 1.6 Exclusions and Limitations

This Capstone project is limited by the utilization of estimated projections and not knowing the exact numbers of biospecimens to be collected over the next 5 years, as well as estimated facility expenses and not exact quotes. It can be anticipated that building and operating expenses may exceed projected costs due to unexpected or unplanned events, changing infrastructure requirements, or evolving scientific protocols. Funding sources for this project are also not considered.

Transfer of existing specimens to the new biorepository facility will not be factored into the one-time costs, though if pursued must be considered. This should include deaccessioning, shipping and reaccessioning of samples. A decision would need to be made regarding the possible purchase and transport of freezers that currently house the samples at the commercial repository. For the purpose of this study, it will be assumed that the samples are all onsite at the newly constructed biorepository and only new equipment will be purchased and installed.

## Chapter 2. Literature Review

This chapter covers current literature relevant to (a) biospecimen repository best practices, (b) international considerations for operating a biospecimen repository, and (c) a review of the components of a cost analysis.

### 2.1 Biospecimen Repository Best Practices

Biospecimen repositories are complex entities that require many different elements to run a successful operation. According to the United States National Research Council Panel on Collecting, Storing, Accessing, and Protecting Biological Specimens and Biodata in Social Surveys,[23] there are three important reference materials regarding the best practices of biospecimen repositories: 1) *Best Practices for Repositories: Collection, Storage, Retrieval, and Distribution of Biological Materials for Research,*[24] prepared by the International Society for Biological and Environmental Repositories (ISBER); 2) the *National Cancer Institute Best Practices for Biospecimen Resources;*[25] and 3) *OECD Best Practice Guidelines for Biological Resource Centres.*[26] These three resources combined provide global recommendations for the consideration of building and operating a biospecimen repository and include planning, cost management, facilities, storage and processing, quality management, safety, and training considerations.

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[23] National Research Council (US) Panel on Collecting, Storing, Accessing, and Protecting Biological Specimens and Biodata in Social Surveys. *Conducting Biosocial Surveys: Collecting, Storing, Accessing, and Protecting Biospecimens and Biodata.* Washington, DC: National Academies Press (US), 2010. Accessed January 23, 2018. doi:10.17226/12942

[24] Lori D. Campbell, Jonas J. Astrin, Rachel Brody, Yvonne DeSouza, Judith Giri, Ashokkumar Patel, Melissa Rawley-Payne, Amanda Rush, and Nicole Sieffert, eds. *ISBER Best Practices: Recommendations for Repositories, Fourth Edition.* N.p.: International Society for Biological and Environmental Repositories (ISBER), 2018.

[25] National Cancer Institute National Institutes of Health, U.S. Department of Health and Human Services. *NCI Best Practices for Biospecimen Resources.* By National Cancer Institute. 2016. Accessed February 5, 2018. https://biospecimens.cancer.gov/bestpractices/2016-NCIBestPractices.pdf.

[26] Organization for Economic Co-Operation and Development (OECD). *OECD Best Practice Guidelines for Biological Resource Centres*. Paris, France: OECD Publishing, 2007. Accessed February 18, 2018. http://www.oecd.org/sti/biotech/38777417.pdf.

### 2.1.1 Repository Planning Considerations

ISBER's *Best Practices for Repositories* is referenced as a gold standard across biorepository literature. According to ISBER's latest 2018 edition, when planning the creation of a biorepository, there are several key components to consider including: governance, repository development, funding and other financial considerations, personnel, contracted laboratory services and consultants.[27]

With regard to governance, a governing body must "comply with applicable regulations, provide good stewardship of repository specimen and data collections to include quality control through Quality Management System adherence, and be a part of a business plan that addresses long term sustainability."[28] It is important that the vision and mission of the repository be clearly defined and operational policies be established regarding acquisition, accessioning, deaccessioning, and participant-requested withdrawal of biological specimens.[29] Operational policies and governance structures should be made visible to stakeholders.[30]

When thinking through the development of a biorepository, ISBER describes different models that organizations may wish to follow for the management of biological sample collections: a) investigator-driven and institutional collections; b) federated collections; c) virtual collections; and d) biodiversity and environmental banks.[31] For the purposes of this project, the repository model most applicable to the HVTN is the investigator-driven and institutional

[27] ISBER, *Best Practices*, 2018
[28] Ibid., 8
[29] Ibid., 9
[30] Ibid., 8
[31] Ibid., 10-11

collections model in which the repository is driven by an investigator or group within an institution to manage specimen collections obtained for defined studies.[32]

Funding required to build and operate a biorepository can be substantial, and a sustainable financial plan should be created for the lifetime of the required activities before engaging in such an endeavor.[33]

When developing the organizational structure and design of the biorepository, the following personnel should be considered at a minimum:

- Director – oversees repository management, general operations, personnel supervision, and Quality Management System
- Quality Manager – manages the Quality Management System
- Technical staff – responsible for receipt, accessioning, storage, retrieval, packing and shipping, quality control, data management, and/or facility and equipment management[34]
- Consultants as needed – critical in the development phase to advise on "strategic planning, equipment selection, and decisions surrounding automation, SOP development, vendor selection, grants and cost recovery, contract management, quality assurance, and regulatory affairs"[35,36]

In consideration of ongoing biorepository operations, critical elements that will be discussed in more detail in the following sections include: facilities, storage and processing

[32] Ibid., 10
[33] ISBER, *Best Practices*, 2018, 12
[34] Ibid., 13
[35] Ibid., 13
[36] Ibid., 13

equipment, quality management, safety, training, cost management, legal and ethical issues, and management of biological specimens.

### 2.1.2 Facilities

Biorepository facilities must be designed to "ensure the safe-keeping of the material stored, support the equipment employed, and provide a safe and effective working environment for the repository staff."[37] To meet these requirements, ISBER believes the following design components should be included:

- Heating and air conditioning – temperatures must be monitored and controlled
- Ventilation – monitoring devices for oxygen and/or $CO_2$ with sufficient alarms should be installed in combination with a dedicated exhaust system; a dehumidification system may also be required
- Lighting (general, task, and emergency) – consider the handling of materials that may be sensitive to certain lighting conditions when installing lights
- Flooring - easy to clean, can withstand liquid nitrogen spills and heavy equipment, and provide anti-fatigue mats for staff who must stand for long periods of time
- Back-up power – incorporate an uninterruptable power supply for specific equipment and install generators that have extra fuel supply for 48-72 hours
- Security systems – must monitor equipment and building 24 hours a day, seven days per week
- Intrusion detection systems
- Visitor access policy – maintain records of visitors and their access to the facility
- Fire prevention plan

[37] ISBER, *Best Practices*, 2018, 14

- Fire detection systems
- Fire extinguishing/suppression systems – sprinkler systems and non-water-based fire retardants
- Emergency response planning
- Pest and contamination control [38]

Further recommendations from the NCI and OECD regarding infrastructure requirements, include designing the facility with ample space for the following functions, as appropriate:

- Collection, receiving, accessioning, tracking, and shipping of biological samples and supplies
- Immediate and interim processing of biological samples
- Areas to prepare and process blood products
- Equipment such as safety hoods, centrifuges, freezers
- Short and long-term storage for biological specimens, consumables, and related records
- Decontamination and cleaning of equipment, and processing of wastes
- "Office work areas to support data, operational, and end user management"[39,40]

The actual location of the facility is also important, and should take into account environmental conditions, accessibility, and availability of resources. [41]

[38] ISBER, *Best Practices*, 2018
[39] NCI, 2016, 9-10
[40] OECD, 2007, 36
[41] ISBER, *Best Practices*, 2018

### 2.1.3 Storage and Processing Equipment

When planning for storage and processing equipment it is necessary to know the anticipated number of specimens to be stored, "the type of specimens and/or samples to be stored, the anticipated length of time the specimens will be stored, the intended use for the specimens, and the resources available for purchasing the equipment."[42] According to the NCI, storage equipment should be housed in a location only accessible by authorized personnel, and continuously monitored and alarmed to notify individuals if equipment failure occurs.[43] In the event of a power disruption, the equipment should be connected to an alternative power source that automatically activates when necessary.[44]

ISBER considers the following elements necessary specifically for the storage and processing of biological specimens:

- Redundant compressors
- Signage
- Decontamination equipment
- Oxygen monitors/alarms for liquid nitrogen use or other oxygen-depriving compressed gases
- Personal protective equipment
- Identification of specimen storage containers
- Liquid nitrogen storage systems
- Specimen storage containers
- Liquid nitrogen supply

[42] ISBER, *Best Practices*, 2018, 20
[43] NCI, 2016, 16
[44] Ibid., 16

- Liquid nitrogen safety (oxygen sensors, personal protective equipment)
- Mechanical freezers
- Automated storage systems
- Refrigerators
- Walk-in environmental storage systems
- Ambient temperature storage
- Contamination issues
- Back-up storage capacity
- Environmental monitoring systems
- Automated liquid-handling robotics
- Equipment maintenance, repair, and replacement
- Electronic data storage, security and back-ups[45]

### 2.1.4 Quality Management

The NCI states that "the aim of every biospecimen resource should be to collect, maintain, and disseminate the highest quality biospecimens, based on the intended research use."[46] Thus, it is critical that each repository has its own Quality Management System (QMS) to include programs on Quality Assurance (QA)/Quality Control (QC) necessary for delivering and maintaining high quality samples and sustaining operations.[47] When possible, the QMS should be managed by individuals outside of repository operations.[48]

[45] ISBER, *Best Practices*, 2018
[46] NCI, 2016, 11
[47] ISBER, *Best Practices*, 2018, 30
[48] NCI, 2016, 18

When developing QA/QC policies, ISBER, Good Laboratory Practices (GLP), International Organization for Standardization, and the U.S. Food and Drug Administration (FDA) Quality System Regulation 21 CFR 820 should be referenced.[49] Such resources should also be used in the development and oversight of a Standard Operating Procedures (SOPs) Manual that covers the following areas and processes: informed consent; equipment monitoring, calibration, maintenance, and repair; control of biospecimen collection supplies (disposables and reagents); biospecimen identification and labeling conventions; biospecimen collection and processing methods; storage and retrieval; shipping and receiving; laboratory tests performed in-house including biospecimen quality control testing; biospecimen data collection and management (informatics); biosafety; training; and security.[50]

It is highly recommended that any organization attempt to attain standards for Good Laboratory/Clinical Practices and the International Organization for Standardization. While costly, accreditations and certifications in these areas prove that the repository meets certain quality standards and operating procedures.[51] This ultimately could prove essential for sponsor audits and U.S. FDA acceptance of research results.

### 2.1.5 Safety

For the safety of all involved, "repositories should ensure they have reviewed and comply with national/federal, regional, and local regulations regarding the health and safety of employees."[52] This includes acquiring and maintaining the appropriate equipment and systems described in previous sections, as well as investing in the following:

[49] NCI, 2016,18
[50] NCI, 2016
[51] ISBER, *Best Practices*, 2018
[52] Ibid., 43

- Personnel training on biological hygiene plans, chemical safety and hygiene plans, compressed gases, and electrical, fire, physical, radiological, dry ice, liquid nitrogen, and carbon dioxide safety
- Personal protective equipment such as face and eye protection, gloves, and lab coats[53]

### 2.1.6 Training

While all individuals hired to work in the biorepository should already be trained in the fundamentals of their work, some institutions may offer additional training for certain functions necessary for the job.[54] Upon hire and on a periodic basis thereafter, in accordance with applicable regulations, ISBER recommends staff be trained on "facility security and procedures, including emergency response; workplace health and safety; technical procedures, including handling of all materials in the repository; management of records and databases; ethical issues surrounding biospecimen research, as applicable; participant privacy and confidentiality; material release, including samples and information; and Good Practices (GLP, GCP, GMP), as applicable."[55]

### 2.1.7 Cost Management

In the consideration of creating a sustainable financial plan for building and operating a biorepository, costs should be assessed for the following elements:

- Initial start-up and construction costs
- Physical facilities (e.g., lease, electricity, water, overhead)
- Staffing and administrative costs (e.g., payroll including overtime, benefits, contract support, consultant fees, IT services)

[53] ISBER, *Best Practices*, 2018, 44-47
[54] ISBER, *Best Practices*, 2018, 48
[55] ISBER, *Best Practices*, 2018, 48; NCI, 2016, 7

- Specimen processing and storage equipment (e.g. freezers, cabinets, liquid handling machinery, cryostats, nucleic acid extractors), and periodic calibration by vendors
- Office and capital equipment inventory management software, licenses, training and maintenance
- Consumables, operating supplies and gases (e.g., buffers, reagents, chemicals, disposables, disinfectants, laboratory safety supplies, personal protective wear, liquid nitrogen, diesel)
- Minor equipment (e.g., monitoring equipment, barcode scanners, computers, office equipment, telecommunications, audio-visual equipment)
- Service contracts for equipment maintenance, disaster recovery, and other necessary insurance
- Possible certification and/or accreditation fees or other Quality Management fees
- Culling and/or transferring collections
- Laboratory Information Management system
- Packaging and shipping materials[56]
- Shipping costs (i.e. World Courier)
- Travel for training and conferences
- Legal services
- Management of anticipated cost fluctuations due to specimen level and activity for immunologic testing

[56] ISBER, *Best Practices*, 2018, 51

### 2.1.8 Legal and Ethical Issues for Biospecimens

Legal and ethical considerations may be among the most complex issue surrounding the operations of a biorepository. ISBER summarizes this issue nicely, stating

> The collection, storage, distribution, and use of biological materials in research raises many legal and ethical issues with repositories often serving as the intermediary between study participants and the scientific research community. On an international level, the collection and use of these materials is currently regulated by an amalgam of differing, and occasionally conflicting, laws and policies. Thus, repositories should proceed carefully, not only in their daily work, but also with respect to international exchange of specimens and associated data.[57]

To familiarize oneself with ethical issues, resources such as the Declaration of Helsinki and the Belmont Report should be referenced and followed in the management of biological samples.[58] These documents refer to key ethical issues involving human subjects in research: respect of autonomy; protection from breaches of privacy and confidentiality; and minimizing individual and group harms.[59]

Additional legal and policy issues must also be adhered to including "relevant federal, state, and local laws and regulations surrounding the collection, storage, dissemination, and use of biospecimens; developing appropriate guidelines for biospecimen and associated data access; ensuring that biospecimens are used in scientifically meritorious research; and establishing biospecimen resource governance."[60] As laws and regulations change, biorepositories must keep up-to-date on all relevant regulations and international, national/federal, regional, and local laws.[61]

[57] ISBER, *Best Practices*, 2018, 77
[58] Ibid., 77
[59] NCI, 2016: 30
[60] NCI, 2016, 30
[61] ISBER, *Best Practices*, 2018, 77

Careful attention must also be provided to the import and/or export of biological specimens, and regulations such as the Convention on Biological Diversity should be observed.[62] The NCI recommends consulting ISBER Best Practices, International Air Transport Association (IATA), and the Occupational Safety and Health Administration (OSHA) regulations on toxic and hazardous substances (29 CFR 1910 Subpart Z) for "information concerning international transport regulations and classifying samples for shipment."[63]

Further care should be given to the destruction of biological specimens, as there could be ethical and cultural considerations for certain populations.[64]

### 2.1.9 Specimen Management

The system around acquisition, accessioning, deaccessioning, and participant-requested withdrawal of biological specimens is the heart of every biorepository. Without a good management system, the repository would cease to function. When identifying or building a specimen tracking system, the NCI encourages the engagement of all stakeholders (IT, clinicians, researchers, etc.) to ensure the needs of all users are reflected and the system complies with data protection policy.[65] The system should meet state and federal, privacy protection, and security regulations, and be 508 compliant.[66] Any protected health information (PHI) or personally identifiable information (PII) should be masked and protected from incidental viewing, only accessible to users with specific authorization, whose use is "logged in a secure, non-editable, permanent audit trail."[67]

[62] ISBER, *Best Practices*, 2018, 77
[63] NCI, 2016, 18
[64] ISBER, *Best Practices*, 2018, 82
[65] NCI, 2016, 27
[66] Ibid., 29
[67] Ibid., 29

Once the tracking system has been established, ISBER recommends creating "written policies and procedures addressing how specimens and associated data will be accessed, what will constitute appropriate uses of the specimens preserved in the repository, and how decisions will be made to approve requests for specimens."[68] Material Transfer Agreements (MTA), contracts that govern the transfer of tangible biological research materials between two organizations, may be required between the biorepository and the institutions providing the samples.[69]

As part of the tracking system, every biological specimen should have a unique identifier that is "firmly affixed to the container…clearly and legibly marked, and able to endure storage conditions."[70] All other information should be tied to the unique identifier "bearing in mind research participant confidentiality, security, and informed consent provisions."[71] The tracking system should have the capability to identify the exact location each specimen is stored (i.e., in a specific freezer, shelf, box, row and column) and thought should be given when storing specimens to allow for the most efficient subsequent retrieval, as appropriate.[72]

**2.2 International Considerations**

There are many issues relating to the establishment of biorepositories in international locations. For the purpose of this Capstone project, only issues identified specific to South Africa will be addressed.

In the article "Challenges of biobanking in South Africa to facilitate indigenous research in an environment burdened with Human Immunodeficiency Virus, Tuberculosis, and emerging

[68] ISBER, *Best Practices*, 2018, 87
[69] ISBER, *Best Practices*, 2018, 89
[70] NCI, 2016, 16
[71] Ibid., 16
[72] Ibid., 16

noncommunicable diseases," Abayomi et al. identify biorepository issues pertaining to governance, legal and ethical considerations, infrastructure, the biorepository laboratory information management system (LIMS), and sustainability.[73]

Abayomi et al. explain that centralized biorepositories in South Africa are still an emerging and evolving concept, recently driven by the "launch of the H3Africa consortium, which includes the development of harmonized and standardized biobanking operating procedures."[74] Despite this new effort, South Africa still has many complex societal considerations, ethical-legal challenges, and lack of support and understanding by national stakeholders that must be overcome. To further hinder the development of biorepositories, there are "inadequate or nonexistent legislative structures that specifically regulate the storage, use, dispersal, and disposal of human biological samples."[75] Additionally, consent for unspecified future uses and access and protection to information and data are new standards that require more socialization and public engagement.[76]

In South Africa, as described by Abayomi et al., "all matters relating to the use of blood and blood products, cell-based therapy, tissue transplants, information derived from genetic research, biological tissue banking, use, and dispersal and disposal of human biological samples" are governed by the following regulations and bodies: the National Health Act (NHA), Act No 61 of 2003 (specifically Chapters 8 and 9); the Health Professionals Council of South Africa (HPCSA); the South African Medical Research Council (SAMRC); and the South Africa

[73] Akin Abayomi, Alan Christoffels, Ravnit Grewal, Locunda A. Karam, Catherine Rossouw, Ciara Staunton, Carmen Swanepoel, and Beverly van Rooyen. "Challenges of Biobanking in South Africa to Facilitate Indigenous Research in an Environment Burdened with Human Immunodeficiency Virus, Tuberculosis, and Emerging Noncommunicable Diseases." *Biopreservation and Biobanking.* 11, no. 6 (2013). DOI:10.1089/bio.2013.0049.

[74] Abayomi et al., 2013

[75] Ibid.

[76] Ibid.

Intellectual Property Rights from Publicly Financed Research and Development Act (IPR Act).[77] However, it is noted that these regulations are out dated and do not address the future use of biological samples, broad informed consent, or anonymization of data. An article written by Staunton and Moodley echoes issues pertaining to consent procedures, confidentiality, and also delves into importing and exporting biological samples. Of note, is that "a biological sample may not be imported or exported without a permit issued by the Director-General;" however, documentation of donor consent is not required prior to issuing an export permit.[78]

Infrastructure required for the successful operation of a biorepository is another special consideration when operating internationally. Biorepositories require "constant power, efficient transport logistics, the availability of liquid nitrogen and dry ice, as well as location…in terms of climate conditions."[79] While South Africa is classified as a middle-income country, it is able to provide sufficient supplies of the required resources. However, since 2007, the supply of power to generate electricity has proven to be a challenge due to increased demands, aging infrastructure and limited supplies, suggesting that generators or other alternative power sources are critical to the uninterrupted function of a biorepository.[80]

To-date, establishing central biobanks in South Africa has been "hampered by myriad complex considerations associated with the concept of long-term storage of biological samples, namely ethical, legal, political, societal, religious, cultural, financial, and educational challenges not previously examined or debated to any great depth in Africa before."[81]

[77] Abayomi et al., 2013
[78] Ciara Staunton and Keymanthri Moodley. "Challenges in biobank governance in Sub-Saharan Africa." *BMC Medical Ethics* 14, no. 35 (September 11, 2013). Accessed February 17, 2018. doi:10.1186/1472-6939-14-35.
[79] Abayomi et al., 2013
[80] Abayomi, et al., 2013
[81] Abayomi, et al., 2013, 348

## 2.3 Components of a Cost Analysis

To determine the feasibility of building and operating a biorepository, a cost analysis must be conducted for both the initial one-time costs associated with the build-out of the facility and programming of the LIMS, as well as ongoing annual operating costs. A cost analysis can be defined as involving "the systematic collection, categorization, and analysis of the costs [resources/inputs] associated with"[82] building and operating a biorepository. The key components of a cost analysis include: defining purpose/scope; development of cost categories; data collection; and finally, cost calculation.[83]

The purpose of the cost analysis should articulate the full range of costs from initiation to implementation and onward, while the scope defines the focus of the project, including specific components, duration, and perspectives. Literature reviews help inform the landscape of related costs, but are not essential. Cost categories should be developed that are reflective of the program utilizing the literature review, review of existing tools, program documents and interviews, followed by data collection. Once all pieces have been collected, a cost calculation is performed to include personnel salaries and benefits, as well as ongoing operational direct and in-direct expenses. [84]

[82] Alberta M. Mirambeau, "CDC Coffee Break: Conducting a Cost Analysis." Lecture, January 8, 2013. Accessed February 17, 2018. https://www.cdc.gov/dhdsp/pubs/docs/cb_january_2013.pdf.

[83] Mirambeau, 2013

[84] Mirambeau, 2013

## Chapter 3. Project Description

To meet the aim and objectives of this Capstone project and to provide research results and analysis of building and operating an independent biorepository in the country of South Africa, a multi-step approach was taken. A thorough literature review was conducted to capture the components and considerations required to build, operate, and estimate the costs for the creation of a biospecimen repository, taking into account administrative, regulatory, and international biorepository issues. Expert opinions were sought through oral interviews to corroborate the literature review findings; ensure specific components were considered in the cost analysis; and to identify relevant barriers, challenges, and benefits to embarking on building and operating an independent biorepository, while moving away from the utilization of a third party vendor. An internal custom-built Microsoft SharePoint workflow was utilized to calculate the projected number of HVTN's biological specimens likely to require storage in South Africa. Also, an extensive cost analysis was conducted, including prior work conducted by HVTN Laboratory personnel and utilizing other available data, to estimate costs and determine the feasibility of the operation.

As described, the goal of this Capstone project was to produce a feasibility study document that examined and analyzed the economic feasibility of constructing and operating a biospecimen repository in the country of South Africa as an alternative to the currently contracted services. Through this project, the HVTN will also assess feasibility given the complexity and organizational impact of operating said biorepository.

## Chapter 4. Need Assessment

Both principal investigators of the HVTN Laboratory Center and Leadership Operations Center, and the HVTN Laboratory Operations Associate Director, identified the need for this Capstone project after seeing future cost projections utilizing the commercial repository in South Africa. Annual long-term storage costs approaching $13 million USD to maintain the biological specimens of HIV vaccine studies in sub-Saharan Africa is so substantial that a review of alternative storage options, such as operating an independent biorepository, was deemed essential.

# Chapter 5. Methodology

This chapter discusses a) the oral interview questionnaire design, b) participants, and c) internal tools and resources used to project the number of biological samples requiring storage, the design of a biorepository floor plan, and cost analysis process.

## 5.1 Oral Interview Questionnaire Design

To corroborate findings in the literature review, capture additional cost components, and identify barriers, challenges, and benefits to establishing an independent biorepository in the country of South Africa, an oral interview questionnaire was designed (**Appendix 1**). The questionnaire was used to guide each interview, and captured the name, title and institution of the individual responding, as well as their responses to ten (10) yes/no, multiple choice, and open-ended questions. The questionnaire was used to assess the individual's experience and expertise in building and/or operating a biorepository and in what capacity; identify critical cost components of building and operating a biorepository; define special issues in the operations of an international facility; determine required documentation to build and operate a biorepository in South Africa; and describe barriers, risks, and benefits to operating an independent biorepository. Recommendations for additional resources were also sought.

## 5.2 Interview Participants

The interview questionnaire targeted specific experts and consultants associated with the HVTN and FHCRC. Six (6) experts crossing multiple fields were identified in order to capture input from varying areas of expertise in facilities, grants, scientific research, laboratory operations, repository, and regulatory fields. All individuals identified agreed to participate in the interview.

### 5.3 Tools and Resources Utilized

Four individuals, the Managing Director of International and Special Projects, the Associate Director of HVTN Laboratory Operations, the HVTN Laboratory Fiscal Manager and a South African Quality Assurance Consultant were closely consulted. They provided their own experience and knowledge of biorepositories, understanding of HVTN protocols, sample projections, and tools and data specific to this project. Monthly statements from the commercial repository, an internal custom-built SharePoint workflow and Microsoft Excel templates were utilized to estimate the number and types of biological specimens currently stored and projected to be stored in South Africa over the next five years, taking into account all currently known closed, active and pending HIV vaccine studies and associated specimen collections. It should be noted that all protocols with future start dates are highly changeable and any static estimate is quickly out of date.

The current number of specimens stored at the commercial repository was calculated by adding the number of PBMCs and other specimens reflected on monthly billing statements through January 2018. Projected numbers and types of samples to be collected for each active protocol were estimated utilizing the SharePoint workflow tool. These monthly figures were added to an Excel spreadsheet template and totals were calculated by year through 2022.

The total number of PBMC specimens was used to estimate the number of liquid nitrogen freezers that would need to be purchased and maintained, while the total number of all other specimen types informed the number of -80$^{o}$C freezers that would need to be purchased and maintained. These figures also informed the number of personnel required to operate the facility and the desired space concept and footprint.

Further consultation with the FHCRC Vice President of Facilities & Operations and Facilities Project Manager provided details for the design and costing of building a biorepository, referencing their past experience building repositories in Seattle, Washington; a laboratory in Cape Town, South Africa; and a research, training and outpatient clinic in Kampala, Uganda. An Excel-based custom cost modeling tool and existing knowledge of equipment and vendor costs were leveraged in the cost analysis. The currency exchange rate between the United States and South Africa was also considered.[85]

Following the collection of the above information, Microsoft Visio software was used to draw the space concept and footprint of the biorepository and to estimate square footage needs. Such space requirements were utilized in estimating real estate options and leasing costs found through an online search.

[85] www.oanda.com

# Chapter 6. Project Results and Discussion

## 6.1 Specimen Collection Projections

To understand the number and types of freezers required to successfully operate a biorepository, and thus the square footage of space needed, it is critical to know the anticipated number and types of biological specimens to be accessioned and stored. For the purposes of the HVTN studies, PBMC specimens are stored in vials in liquid nitrogen freezers, and all other biological samples collected such as plasma, serum, semen, etc. are stored in -80$^{o}$C freezers.

It was determined that approximately 517,031 PBMC samples/vials and 2,957,457 vials of other specimen types will require storage over at least the next five years, as shown in **Table 1**. As of January 2018, of those total quantities, 116,197 PBMCs and 601,992 other specimen types have been accessioned and stored by the commercial repository. If the HVTN were to move forward with building a biorepository, projected to open in late 2019, it is estimated that 403,475 PBMC samples and 2,433,992 other specimen types would have been collected and require storage upon facility opening.

**Table 1: Current and Projected Numbers and Types of Biological Specimens for HVTN Studies Requiring Processing and Storage in a Biorepository in South Africa through November 2022.**

| | **Storage Requirements** | **Projected # Samples/Vials Requiring Storage 2020-2022** | | | | |
|---|---|---|---|---|---|---|
| | | **Upon New Repository Open – Includes Closed & Active Studies** (late 2019) | **2020** | **2021** | **2022** | **Total Specimens Requiring Storage** (through 2022) |
| **PBMC Vials** | $LN_2$ | 403,475 | 71,990 | 38,726 | 2,840 | **517,031** |
| **Other Samples** *(plasma, serum, mucosal swabs, dried blood spots, etc.)* | -80$^{o}$C freezers (use upright or chest freezers) | 2,433,992 | 343,063 | 169,752 | 10,650 | **2,957,457** |

These figures equate to the need for 12-15 liquid nitrogen freezers[86] with a 36,400 vial capacity, and 62-75 -80ºC chest freezers[87] with a 39,600 vial capacity or 35-43 -80ºC upright freezers[88] with a 70,000 vial capacity (**Table 2**). -80ºC freezers can either be purchased as chest or upright models and there is some debate as to which freezer is optimal.

Laboratory scientists argue that chest freezers are better, as they maintain the cold temperatures and better preserve specimen quality, but have a larger footprint, less storage capacity, and are more expensive. Others argue that with changing technology, the upright freezers are just as good, take up a smaller footprint, have a much larger storage capacity, and are less expensive as a result, but may have greater fluctuations in temperature as cold air pours out every time the door is opened possibly affecting specimen quality. With regard to space and financial considerations, a combination model may be best, but for purposes of this project the upright freezers will be used in space and cost estimations.

**Table 2: Projected Numbers and Types of Freezers Required for Storing HVTN Specimens in a Biorepository in South Africa through November 2022**.

| | **Vial Capacity** | **Total # Freezers Required at New Repository Open** (late 2019) | **Projected Annual Freezer Needs** | | | **Total # Freezers Required** (through 2022) |
|---|---|---|---|---|---|---|
| | | | **2020** | **2021** | **2022** | |
| **$LN_2$ Freezers** | 36400 | 11.1 (12) | 2.0 (2) | 1.1 (1) | 0.1 (0) | **14.2 (15)** |
| **-80ºC Upright Freezers** | 70000 | 34.8 (35) | 4.9 (5) | 2.4 (3) | 0.2 (0) | **42.2 (43)** |
| **-80ºC Chest Freezers** | 39600 | 61.5 (62) | 8.7 (9) | 4.3 (4) | 0.3 (0) | **74.7 (75)** |

Only one type of -80ºC freezers are needed, but numbers are shown for both upright and chest freezers for comparison.

[86] http://www.labcatalogue.com/index.php?route=product/product&product_id=8787
[87] https://www.mcqueenlabs.com/coldstorage/thermo-tsc2090a.php
[88] http://www.thermofisher.com/us/en/home/life-science/lab-equipment/cold-storage/lab-freezers/ultra-low-temperature-freezers-minus-80/premium-tsx-ult-freezers.html

## 6.2 Space Requirements and Design

After consulting with FHCRC Facilities personnel, HVTN Laboratory Operations personnel, a South African consultant with experience in designing and operating biospecimen repositories, and considering best practices as defined in the literature review, a general floorplan and space concept for an HVTN biorepository was created as detailed in **Figure 3**.

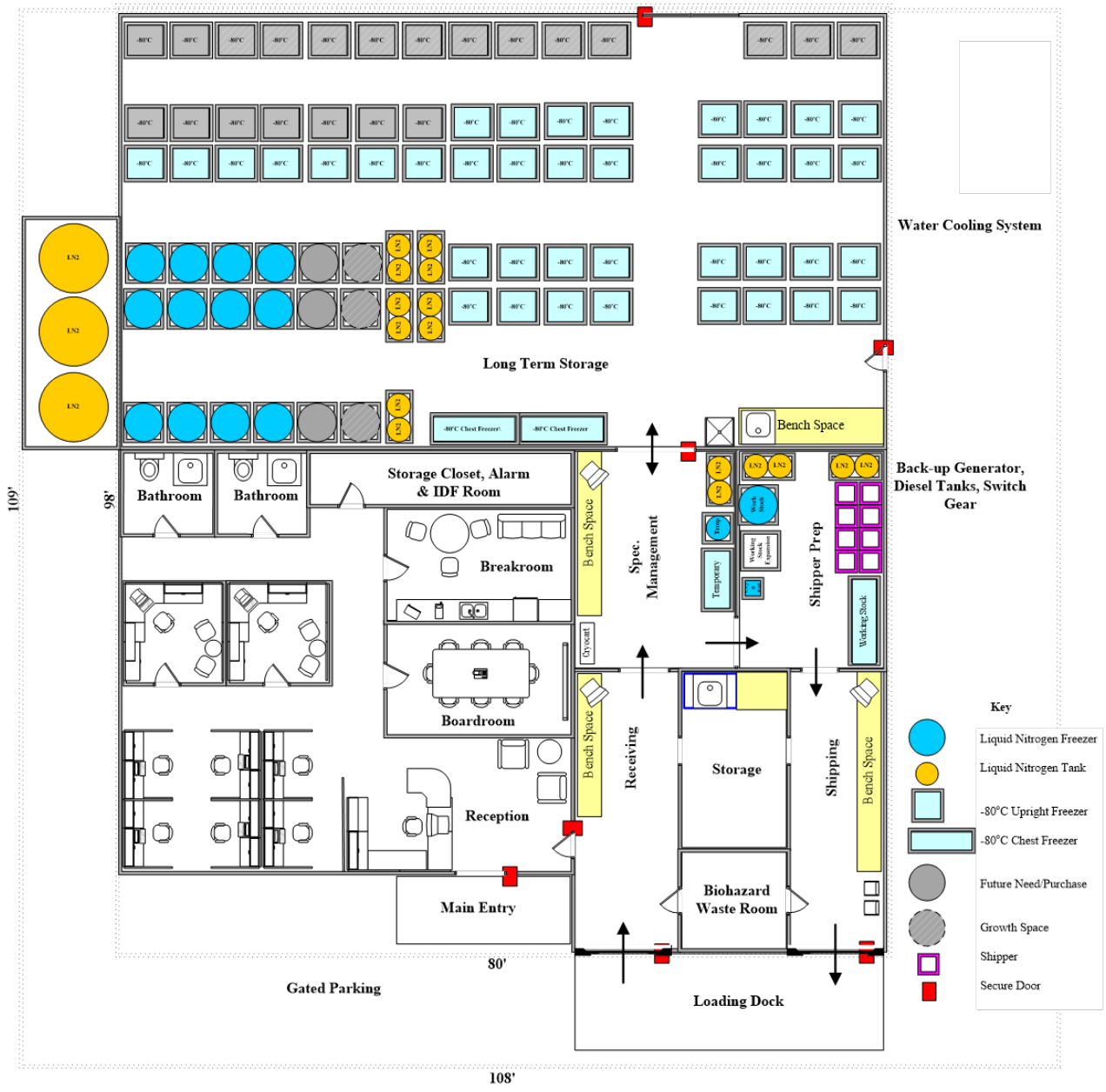


**Figure 3: Space Concept for a Biorepository Floorplan**

The space requirements suggest an interior footprint of approximately 7,840 square feet or 2,390 square meters, not including such things as external fixtures and parking. However, it is important to note that this schematic shows approximate dimensions and requires review by a laboratory architect. The layout is also hypothetical and dependent upon the final location of the facility.

The floor plan shows three designated areas: 1) office and administrative space; 2) shipping, receiving, and specimen management space; and 3) long term freezer storage. All entry doors into the facility are secure and proper emergency equipment and exits are included. A back-up generator and water cooling system would be located on the exterior of the facility.

In the long term storage area, colored freezers indicate required equipment needed to be operational upon building opening and gray freezers indicate future needs and projected growth space. Repository experts strongly recommend that exterior bulk storage for liquid nitrogen tanks be used for a long-term biorepository, although they are more expensive up front. If cost is an issue, smaller interior liquid nitrogen tanks may be used.

Private office and administrative space is sufficient for start-up operations, although it is modest and may not be sufficient long term. When looking at facility options, space for additional growth should be factored into the decision for the final location.

### 6.3 Cost Analysis

To project the costs of building and operating a biorepository in South Africa, a complete analysis was conducted to include one-time build-out expenses and ongoing operating costs.

#### 6.3.1 Building Costs

Assuming the facility is leased space, with rent, utilities and insurance captured under the annual operating budget in section 6.3.2, one-time building costs are calculated to be $6,349,746

USD (**Table 3**). Built-in customized formulas in the FHCRC Facilities cost model referenced the estimated 7,840 square footage to help calculate these amounts. Since many of the expenses to be incurred are in the local South African currency of Rand, both Rand (R) and US Dollars ($) are shown. As the exchange rate fluctuates this table can easily be updated to reflect more current estimates. More accurate and updated market quotes would be developed if this endeavor moves forward.

**Table 3: Budget Summary Estimate for Build-out of Biorepository in South Africa.**

| Item | Budget Estimate ($) | Budget Estimate (R) |
|---|---|---|
| **Hard Costs** | | |
| Construction | $ 2,352,000 | R 27,982,214 |
| Owners Construction Contingency | $ 164,640 | R 1,958,755 |
| VAT Tax (15%) | $ 377,496 | R 4,491,145 |
| Total, Hard Costs | $ 2,894,136 | R 34,432,115 |
| **Soft Costs** | | |
| Design Fees | | |
| Design Fees, Basic Services | $ 188,160 | R 2,238,577 |
| Design Fees, Additional Services | $ 1,500 | R 17,846 |
| Specialty Consultants | $ 20,000 | R 237,944 |
| Total, Design Fees | $ 209,660 | R 2,494,367 |
| **Other Soft Costs** | | |
| Project Management | $ 75,000 | R 892,290 |
| Signage | $ 5,000 | R 59,486 |
| FFE, Furniture | $ 14,000 | R 166,561 |
| FFE, Lab Equipment | $ 2,231,950 | R 26,553,956 |
| Chilling Plant | $ 780,000 | R 9,279,816 |
| IT Network Equipment, Computers and Phones | $ 42,000 | R 499,682 |
| LIMS system | $ 20,000 | R 237,944 |
| Permits | $ 18,000 | R 214,150 |
| Soft Cost Contingency | $ 60,000 | R 713,832 |
| **Total Project Costs** | **$ 6,349,746** | **R 75,544,198** |
| Exchange rate | 1 USD: 11.90 ZAR | |
| www.oanda.com (as of Mar 4, 2018) | | |

Budget justification for the building costs in **Table 3** is as follows:

**HARD COSTS**

**Construction ($2,352,000)**

Request costs to make renovations to an existing space yet to be identified, customizing to enhance repository functions. This calculation is based upon a trusted/tested formula of $300 per square foot.

**Hard Cost Contingency ($164,640)**

Request a 7% contingency fund for unanticipated changes in costs and issues specific to the final build-out.

**VAT Tax ($377,496)**

South African Value Added Tax (VAT) is currently set at 15%. Assumption is that this cost will be necessary, although it could be reimbursable if the FHCRC South African subsidiary organization remains tax exempt by the South Africa Revenue Service (SARS).

**SOFT COSTS**

**Design Fees ($209,660)**

Request an 8% pool of funds for basic design fees, supplemented by a small amount for additional services and consultants.

**OTHER SOFT COSTS**

**Project Management ($75,000)**

Request salary for a construction project manager for one year. This position will be responsible for coordinating all efforts related to the actual construction and remodeling of the facility.

**Signage ($5,000)**

Request a small amount for required building signage. This includes all hallway room signs as well as emergency and repository specific permanent signage.

**FFE, Furniture ($14,000)**

Request costs to build out offices (two private offices, six technician cubicles, and reception area), boardroom/conference room, and break room.

**FFE, Lab Equipment ($2,231,950)**

Request funds for 39 -80ºC upright freezers ($15,000 each), 12 $LN_2$ freezers ($36,000 each), and freezer racks ($5,200 for each $LN_2$ freezer) for specimen storage. Additional funds will be needed to cover additional equipment such as $LN_2$ tanks, cryo-cart, dry shippers, specialized shelving, barcode scanner, barcode labeler, and other items.

**Chilling Plant ($780,000)**

Request a water cooling system for -80ºC freezers. This system will provide a better work environment due to 50% less heat being emitted to room surroundings and enhances freezer compressor stability and reliability.

**IT Network Equipment, Computers and Phones ($42,000)**

Request funds for a robust server, back-up server, cloud services, staff computers and peripherals, copier/scanner, and phones. Include A/V equipment in board/conference room to enhance communication between FHCRC offices and international repository ($12,000).

**LIMS Software ($20,000)**

Request funds for Laboratory Information Management Systems software, such as LDMS. A LIMS system is critical to maintain chain of custody of specimens and to facilitate ease of

location for removal of specific vials for testing. Cost includes customization that will be necessary.

**Permits ($18,000)**

Request funds for required building permits. Estimate based on prior renovation and alteration experience in South Africa.

**Soft Cost Contingency ($60,000)**

Request a 2% contingency fund for unanticipated changes in costs and issues specific to the general non-design soft costs.

### 6.3.2 Independent Ongoing Operations

Annual operating costs for this operation were estimated to be $2,456,172 USD in the first year (**Table 4**). This figure was based on input from Laboratory Operations personnel, online rent estimates near the Johannesburg airport, and actual costs incurred at the Cape Town HVTN Immunology Laboratory (CHIL), in Cape Town, South Africa.

It was determined that the minimum personnel required to operate a biorepository and to handle the number of specimens anticipated, would need to include a Director, Biorepository Manager, Lead Research Technician, two Research Technicians, and an Administrative Assistant/Receptionist. Other services such as janitorial, IT, and security would likely be outsourced to start.

Other key cost considerations include annual purchased services necessary for equipment maintenance and company-associated legal, human resources, and accounting fees; consumable supplies to include laboratory supplies, protective wear, and liquid nitrogen; staff travel; insurance; occupancy expenses including facility lease/rental, utilities, and maintenance; and other business costs such as tea and coffee for the breakroom or food for special staff events.

**Table 4: Biorepository Annual Operating Expenses in USD.**

| DETAILED BUDGET FOR INITIAL BUDGET PERIOD<br>DIRECT COSTS ONLY | | | | | | FROM<br>07/01/19 | THROUGH<br>06/30/20 | |
|---|---|---|---|---|---|---|---|---|
| NAME | ROLE ON PROJECT | Cal. Mnths | Acad. Mnths | Summer Mnths | INST. BASE SALARY | SALARY REQUESTED | FRINGE BENEFITS | TOTALS |
| TBN | Director | 12.00 | 0.00 | 0.00 | 140,000 | 140,000 | 35,560 | 175,560 |
| TBN | Repository Manager | 12.00 | 0.00 | 0.00 | 95,000 | 95,000 | 24,130 | 119,130 |
| TBN | Lead Research | 12.00 | 0.00 | 0.00 | 35,000 | 35,000 | 8,890 | 43,890 |
| TBN | Research Technician | 12.00 | 0.00 | 0.00 | 25,000 | 25,000 | 6,350 | 31,350 |
| TBN | Research Technician | 12.00 | 0.00 | 0.00 | 25,000 | 25,000 | 6,350 | 31,350 |
| TBN | Admin Assistant | 12.00 | 0.00 | 0.00 | 25,000 | 25,000 | 6,350 | 31,350 |
| **SUBTOTALS** → | | | | | | **$345,000** | **$87,630** | **$432,630** |
| CONSULTANT COSTS | | | | | | | | |
| Purchased Services - General and Equipment Maintenance (HVAC, A/V, Lab Equipment, etc) | | | | | | | 125,000 | |
| Purchased Services - Facility Management (IT, Security, Janitorial, Waste, Drinking Water) | | | | | | | 38,000 | |
| Purchased Services - Legal | | | | | | | 10,000 | |
| Purchased Services - Accounting, Auditing, Banking Fees | | | | | | | 25,000 | |
| | | | | | | | | 198,000 |
| EQUIPMENT *(Itemize)* | | | | | | | | |
| Additional -80C Upright Freezers (5 units) | | | | | | | 75,000 | |
| Additional LN2 Freezers (2 units) | | | | | | | 72,000 | |
| Liquid Nitrogen Bulk Tank Rental | | | | | | | 10,000 | 157,000 |
| SUPPLIES *(Itemize by category)* | | | | | | | | |
| Consumables Supplies | | | | | | | 500,000 | |
| Liquid Nitrogen | | | | | | | 250,000 | |
| | | | | | | | | 750,000 |
| TRAVEL | | | | | | | | |
| Travel/Repository Assistance (x4) | | | | | | | 24,000 | |
| | | | | | | | | 24,000 |
| OTHER EXPENSES *(Itemize by category)* | | | | | | | | |
| Facility Insurance (Property, General Liability) | | | | | | | 60,000 | |
| Occupancy Expenses (Lease, Utilities, Maintenance) | | | | | | | 238,606 | |
| Other Expenses (Tea and coffee for breakroom, food for special events, etc) | | | | | | | 500 | 299,106 |
| **TOTAL DIRECT COSTS FOR INITIAL BUDGET PERIOD** | | | | | | | | **$1,860,736** |
| Indirect Costs (32%) | | | | | | | | **$595,436** |
| **TOTAL COSTS FOR INITIAL BUDGET PERIOD** | | | | | | | | **$2,456,172** |

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Budget justification for the building costs in **Table 4** is as follows:

**PERSONNEL ($432,630)**

**TBN, Director (12 calendar months)**

This position will be responsible for developing start-up operations of the biorepository, overseeing repository management, general operations, personnel supervision, and the Quality Management System. Minimum qualifications are a doctorate and 7+ years of management experience at a biorepository or research laboratory.

**TBN, Repository Manager (12 calendar months)**

This position will be responsible for managing the Quality Management System, working closely with the Director on all repository operations, and supervision of the research technicians. Minimum qualifications are a university degree and 5+ years of management experience at a biorepository or research laboratory.

**TBN, Lead Research Technician (12 calendar months)**

This position will be responsible for receipt, accessioning, storage, retrieval, packing and shipping, quality control, and data management for biological specimens, and facility and equipment management. This position holds a greater level of responsibility and independence and guides other research technicians. Minimum qualifications are a Med-Tech and 4+ years as a research technician, preferably in a biorepository.

**TBN, Research Technician x2 (12 calendar months each)**

This position will be responsible for receipt, accessioning, storage, retrieval, packing and shipping, quality control, and data management for biological specimens, and/or facility and equipment management. Minimum qualifications include 2+ years as a research technician, preferably in a biorepository.

**TBN, Administrative Assistant (12 calendar months)**

This position will be responsible for all administrative tasks of the biorepository, including front desk duties, answering phones, greeting guests, making travel arrangements, scheduling meetings, placing purchase orders and acting as the central point person for shipping and receiving. Minimum qualifications are 7+ years in an administrative assistant or manager role.

**CONSULTANT COSTS**

**Purchased Services – General and Equipment Maintenance ($125,000)**

Request funds for HVAC, audio-visual (A/V), laboratory equipment, electrical/UPS, fire panel, secure access systems (e.g. key-access doors and security cameras), emergency generator and automatic transfer switch support services and general maintenance.

**Purchased Services – Facilities Management ($38,000)**

Request funds for facilities management services including IT and network support, security, janitorial, biohazard waste disposal, and drinking water supplier.

**Purchased Services – Legal ($10,000)**

Request funds for legal services and representation for company start-up operations, human resources support and material development, general in-country representation for FHCRC, and managing all necessary registrations and company document filings. This cost will likely decrease after the initial start-up year.

**Purchased Services – Accounting ($25,000)**

Request funds for accounting, monthly VAT filings with SARS, financial audit, and banking fees.

**EQUIPMENT**

**-80ºC Upright Freezers ($75,000)**

Request funds for five -80ºC upright freezers ($15,000 each) to store additional anticipated samples.

**Liquid Nitrogen Freezers ($72,000)**

Request funds for two liquid nitrogen freezers ($36,000 each) to store additional anticipated samples.

**Liquid Nitrogen Bulk Tank ($10,000)**

Request funds for monthly rental of three liquid nitrogen bulk tanks to support 12-15 liquid nitrogen freezers.

**SUPPLIES**

**Consumable Supplies ($500,000)**

Request funds for consumables supplies such as chemicals, reagents, protective gear, and laboratory supplies (e.g. pipettes, media, cleaners and detergents, specimen transfer bags, test tubes, etc.)

**Liquid Nitrogen ($250,000)**

Request funds for weekly liquid nitrogen refills for bulk storage tanks required to support 12-15 liquid nitrogen freezers.

**TRAVEL**

**Travel/Repository Assistance ($24,000)**

Request funds for travel for the Director and Repository Manager to attend HVTN Conference(s) in Seattle, WA (2 trips) and research technicians to fly between Seattle, WA and South Africa for initial training on systems and processes (2 trips).

**OTHER EXPENSES**

**Facility Insurance ($60,000)**

Request funds for general liability and property insurance, and political risk insurance necessary to continue or shut-down operations over a 3 month period in the event political unrest impedes regular operations.

**Occupancy Expenses ($238,606)**

Request funds for lease, utility, and building maintenance expenses covered under agreement with landlord.

**Other Expenses ($500)**

Request small amount for additional expenses to keep and maintain staff morale, such as coffee and tea for the breakroom and food for special staff meetings or events.

**INDIRECT COSTS ($595,436)**

The offsite indirect cost rate for FHCRC activities is 32%. This supports facilities and administration expenses related to FHCRC oversight and support of the international biorepository including finance, accounts payable and receivable, purchasing, human resources, IT, general counsel, facilities support, etc.

### 6.4 Comparison to Existing Practices

As discussed, one-time costs of building a biorepository in South Africa are estimated to be $6,349,746 USD with annual operating expenses around $2,456,172 USD. Once the facility is up and running the annual operating expenses are of the biggest concern, and are projected to grow with the annual South African cost of living index rates (CIPX), historically at or under 7%.

If current data remains unchanged, existing and projected annual commercial repository costs will reach approximately $10.6 million USD in 2024 and grow at an estimated rate of 7% per year (rate of increase for past 5 years) thereafter. **Figure 4** shows a comparison of expenses for utilizing the commercial repository versus building and operating an independent facility. All costs are assumed to increase by 7% annually, based on the historical rates of the South African cost of living index (CPIX).

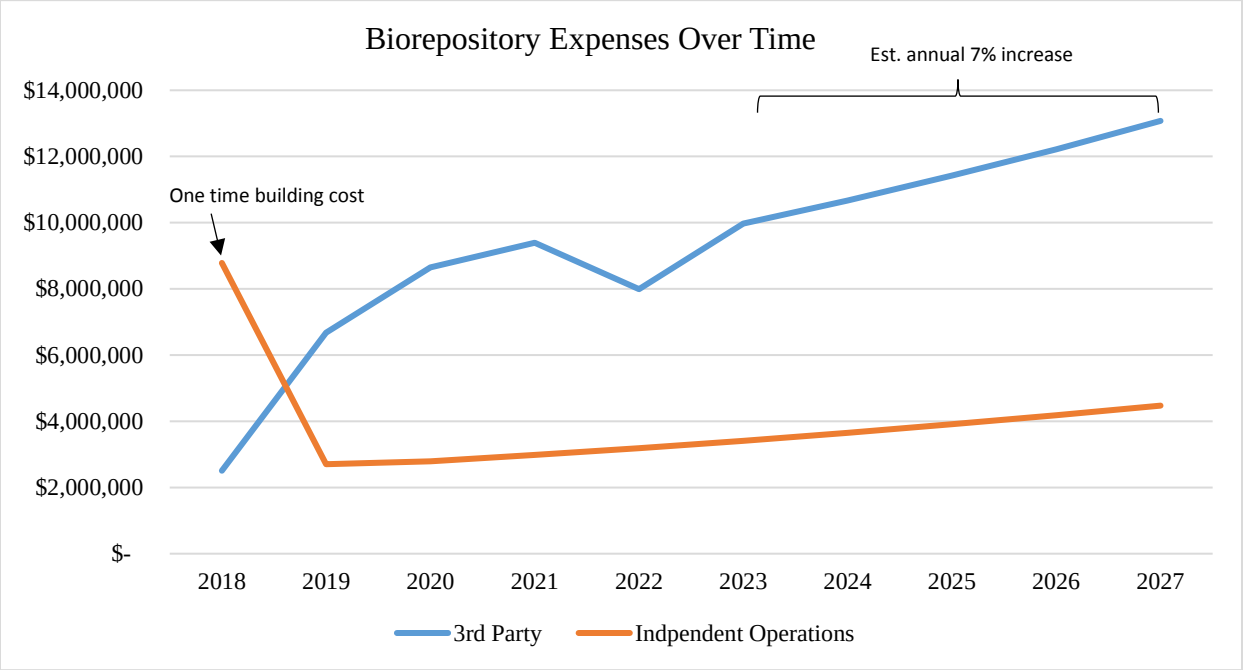


**Figure 4. Comparison of Biorepository Expenses over Time**.

Cost estimates for utilizing the commercial repository for the life of active HVTN studies at a minimum will likely total in excess of $29 million. If an independent biorepository is pursued, with the ongoing cost savings of operating an independent facility, the initial one-time building expenses would be recouped by Year 4 of operations.

### 6.5 Special Considerations for Operating International Facility

As with any new business endeavor, there are special considerations to consider, especially when crossing international boundaries. Experts interviewed as part of this Capstone project reflected on specific barriers and risks, as well as benefits to embarking on the creation of a biorepository in South Africa, established and operated by a U.S. non-profit organization.

#### 6.5.1 Barriers and Risks

Biorepositories are complex facilities that involve many components, any of which create a risk to successful operation. Barriers and risks identified in the expert interviews, include:

- Compliance with both South African and U.S. regulations
- Appropriate handling of hazardous gases – suggest doing HAZOP inspection and achieving ISO9000 or SANAS certification
- Optics – Americans coming into the country and taking away business from an established company
- Loss of goodwill with current South African partners – taking business away from a company (i.e. commercial repository) with good standing in the local community; the transition must be handled with care
- Understanding and communicating with key players in the local industry – this may include the Human Heredity & Health in Africa (H3Africa) Consortium,[89] Stellenbosch University Immunology Research Group (SUN-IRG), and KwaZulu Natal Research Institute for TB and HIV (K-RITH) now the African Health Research Institute.[90]

[89] https://www.h3africa.org/
[90] https://www.ahri.org/

- Specimen loss/damage – important to maintain quality
- Improper handling, lack of redundancy, back-up systems and personnel able to respond to facility alarms
- Politics around handling and shipping of biological specimens
- Ensuring chain of custody – proper shipping is really important to minimize risk/damage to specimens
- Consistent and reliable infrastructure – IT, electricity, supply delivery
- Staff retention – it is difficult to retain skilled personnel once trained, especially internationally
- Facility that is upgradeable – has the ability to expand space as needed
- Funding sponsor considerations – if the facility is used for more than HVTN work, what considerations need to be given to the sponsors (i.e. NIH) and how would priorities be managed?
- Security
- Civil/Political unrest
- Distance management and communication
- Network-funder relationship and required audits – DAIDS/vaccine developers audit may require implementation of unanticipated improvements and processes

### 6.5.2 Rewards and Benefits

Understanding the potential savings by building and operating an independent biorepository could be a large enough economic driver to justify engaging in such an endeavor; however, experts reported additional benefits for consideration as follows:

- The ease of transferring HVTN samples – everything falls within the scope of the HVTN to fix and set-up properly, unless multi-network
- Control of costs
- Ability to make more funds available for clinical trials – main annual budgets that cover long term specimen storage are usually fixed
- Opportunity to develop South African staff in certain skills
- Potential savings in transport time and associated risks
- Better quality control

**6.6 Discussion**

Embarking on the development of a biorepository in South Africa is not a task to take lightly. As hypothesized, there is a clear cost savings associated with running an independent facility to handle HVTN biological specimens. There would be high upfront capital costs, but general operations would be far less than a third party for-profit facility, and initial building expenses would be recouped in savings in four years of operations based on the analyses provided here. However, great care would need to be taken in the development of such an operation. Space and location would need to be carefully chosen in a safe area with reliable infrastructure. The facility would need to be near an airport to ensure specimen shipment/delivery from clinical trial sites within recommended timeframes as needed; preferably located near multiple forms of transportation. Relationships with local partners and other key organizations would need to be carefully handled and maintained to reflect the contributions such a facility has to the local society, training South African people in highly sought laboratory and repository skills and freeing funds to be redirected into life-saving HIV vaccine research.

However, despite the cost savings and other benefits, there are many risks and barriers that must be seriously considered. A huge administrative burden and associated liability would be acquired to ensure the biorepository meets all of the necessary local and international regulations. Great attention must be given to training and maintaining personnel, which can be particularly difficult when working with a non-profit salary scale and competing with for-profit industries. There is a great risk of losing goodwill from the local community given the optics associated with taking business or personnel away from an established company or other South African partners. Civil and political unrest is another consideration to be weighed, especially with the recent call for and resignation of President Zuma and new ruling political party. Overseeing the management of such a facility from the United States could also pose problems; such that good communication must be prioritized and optimized on a continual basis.

There was further disagreement among styles of freezers to be purchased, -80$^{o}$C upright or chest freezers, resulting in a decision that must be made in consideration of space and funding restrictions versus maintaining the highest sample quality. Additional research likely needs to be given to this topic alone.

When consulted, experts seemed to discuss the risks in greater detail and spent less time addressing the benefits, though investigators may see a great benefit in the ability to do more science with awarded funds. After considering all of the data, the ultimate question is, what cost savings is worth navigating the risks and barriers?

# Chapter 7. Recommendations and Conclusion

## 7.1 Recommendations

**Recommendation 1:** Funding for this endeavor, not addressed as part of this Capstone project, must be determined before any decisions can be made.

Federal funds typically do not support such large capital endeavors, nor is it clear who will pay for ongoing storage costs once active studies have closed. The need for future funding sources to support long term biospecimen storage, as acquired through U.S. Federally funded research grants, is a problem that will not be alleviated on its own. As more research is conducted globally and institutions face political and cultural restrictions with shipping samples outside of the country or off the continent, there could be a need to also engage with local governments to help support such costs, though ownership and liability for collected biospecimens is another factor to consider and could impact these relationships.

**Recommendation 2:** Re-engage the U.S. Federal government (i.e. National Institutes of Health) to fund a central biorepository in support of all studies by all groups taking place on the African continent, or at least sub-Saharan Africa.

There is already a federally supported model in the U.S. that could be extended to Africa, whether it is contracting with an existing commercial biorepository or constructing and operating a new biorepository, and would therefore work with multiple networks.

**Recommendation 3:** The HVTN should investigate further options, such as cost sharing with the HPTN.

Cost sharing with the HPTN may decrease operating expenses and increase the consistency of specimen management across networks. The HPTN conducts trials throughout Africa and may find benefit from utilizing a non-profit centralized biorepository in South Africa,

moving away from local on-site storage. Should this be pursued a calculation of the cost of storing and handling each sample would need to be determined and appropriately accounted for, so not to impact the non-profit status of the FHCRC South African subsidiary company.

**Recommendation 4:** Processes and policies should be implemented regarding the destruction of samples, ultimately reducing projected long-term storage costs.

It is not realistic to maintain every sample that is collected, though there is always a risk to future research questions when a sample is destroyed. Updating and seeing-through sample destruction practices could be a solution to slow the growing long-term storage cost burden. The most expensive specimen is the one collected early and kept in storage for a long time.

### 7.2 Conclusion

The construction and operations of an independent biorepository in South Africa is a complex multi-variable endeavor that ultimately has no perfect approach. The data collected and analyzed here seem to indicate that there would be significant financial savings, and it may be a favorable option for further pursuit. However, embarking on this operation would be a large initial funding issue and complicated administrative and logistical undertaking, presenting risks to established partnerships and a liability for maintaining compliance with local, country-specific, U.S., and international regulations.

Upon further investigations into cost-sharing and the identification of long-term funding sources, if the HVTN is willing and able to navigate the risks and barriers, then it would appear to be feasible to move forward with constructing and operating an independent biorepository.

## Bibliography


Abayomi, A., Christoffels, A., Grewal, R., Karam, L., Rossouw, C., Staunton, C., Swanepoel, C. and van Rooyen, B. "Challenges of Biobanking in South Africa to Facilitate Indigenous Research in an Environment Burdened with Human Immunodeficiency Virus, Tuberculosis, and Emerging Noncommunicable Diseases." *Biopreservation and Biobanking* 11, no. 6 (2013). DOI:10.1089/bio.2013.0049

Barnabe, M. *Peripheral blood mononuclear cells: PBMC isolation, preservation, and culture.* May 30, 2017. Accessed February 17, 2018. https://blog.quartzy.com/2017/05/30/peripheral-blood-mononuclear-cells-pbmc-isolation-preservation-culture

Campbell, L. D., Astrin, J.J, Brody, R., DeSouza, Y., Giri, J. G., Patel, A. A., Rawley-Payne, M., Rush, A., and Sieffert, N. eds. *ISBER Best Practices: Recommendations for Repositories, Fourth Edition*. N.p.: International Society for Biological and Environmental Repositories (ISBER), 2018

HIV Vaccine Trials Network [HVTN]. *About.* n.d. Accessed February 17, 2018. https://www.hvtn.org/en/about.html

HIV Vaccine Trials Network [HVTN]. *International Sites.* n.d. Accessed March 17, 2018. http://www.hvtn.org/en/hvtn-international-sites.html

Hughes, E.J. *Biobank-repository operations and best practices* [PowerPoint Presentation]. 2015

Mirambeau, A. M. "CDC Coffee Break: Conducting a Cost Analysis." Lecture, January 8, 2013. Accessed February 17, 2018. https://www.cdc.gov/dhdsp/pubs/docs/cb_january_2013.pdf

National Cancer Institute [NCI]. *NCI best practices for biospecimen resources*. March 2016. Accessed February 17, 2018. https://biospecimens.cancer.gov/bestpractices/2016-NCIBestPractices.pdf

National Research Council (US) Panel on Collecting, Storing, Accessing, and Protecting Biological Specimens and Biodata in Social Surveys. *Conducting Biosocial Surveys: Collecting, Storing, Accessing, and Protecting Biospecimens and Biodata*. Washington, DC: National Academies Press (US), 2010. Accessed January 23, 2018. doi:10.17226/12942

Organization for Economic Co-Operation and Development (OECD). *OECD Best Practice Guidelines for Biological Resource Centres.* Paris, France: OECD Publishing, 2007. Accessed February 18, 2018. http://www.oecd.org/sti/biotech/38777417.pdf

Staunton, C. and Moodley, K. "Challenges in biobank governance in Sub-Saharan Africa." BMC Medical Ethics 14, no. 35 (September 11, 2013). Accessed February 17, 2018. doi:10.1186/1472-6939-14-35

## Appendix 1. Questionnaire

### Oral Interview Questionnaire

I am a research administrator for the HIV Vaccine Trials Network (HVTN) at Fred Hutchinson Cancer Research Center (FHCRC). I am also a student in the Master of Science Program in Research Administration at Johns Hopkins University. I will be collecting data to analyze the feasibility of building and operating a biospecimen repository in South Africa. I will be using the results of this questionnaire to not only fulfill the requirements of my master's degree but also to present the results of this project to HVTN management for them to evaluate the feasibility of building and operating such a repository.

**A Feasibility Study: Building and Operating a Biospecimen Repository in South Africa**

Information captured through this oral interview questionnaire will be utilized in the creation of a feasibility study to examine and analyze whether it is economically feasible to build and operate a biospecimen repository in South Africa. This study will also provide recommendations to administrators and research investigators that they may use in planning and costing out their studies.

Full Name (First, Last):_____ Date:_____

Position or Title:_____

Institution: _____

**Questions**:

1. Have you ever built or participated in building a biospecimen repository?

    ☐ No

    ☐ Yes

2. Have you ever operated, participated in or have direct knowledge of the operations of a biospecimen repository?

    ☐ No

    ☐ Yes

**If you answered No to questions 1 and 2 please do not proceed with the questionnaire.**

3. If you answered yes to question 1, what was your role?

    ☐ Facilities Manager

    ☐ Architect/Project Manager

    ☐ Repository Manager

    ☐ Repository Program/Project Manager

    ☐ Repository Technician

    ☐ Consultant

    ☐ Informatics Specialist

    ☐ IRB Administrator/Member

    ☐ Pathologist

    ☐ Research Scientist

    ☐ Grant Manager/Analyst

    ☐ General Counsel

    ☐ Others (please specify):

    _____

    _____

4. If you answered yes to question 2, what was your role?

    - ☐ Facilities Manager
    - ☐ Architect/Project Manager
    - ☐ Repository Manager
    - ☐ Repository Program/Project Manager
    - ☐ Repository Technician
    - ☐ Consultant
    - ☐ Informatics Specialist
    - ☐ IRB Administrator/Member
    - ☐ Pathologist
    - ☐ Research Scientist
    - ☐ Grant Manager/Analyst
    - ☐ General Counsel
    - ☐ Others (please specify):

      _____

      _____

5. Based on your role and experience, what components of building and operating a biospecimen repository do you consider to be most important to include in a cost analysis?

    - ☐ Physical Facilities
        - o Lease
        - o Utilities (i.e., water, electricity, etc)
        - o HVAC systems

- Lighting
- Flooring
- Security systems
- Back-up power
- Fire prevention systems
- Geographic location relative to sample collection sites and emergency back-up
- Other:

_____

_____

☐ Specimen Processing and Storage Equipment

- Freezers
- Cabinets
- Liquid handling machines
- Cryostats
- Nucleic acid extractors
- Vendor calibration (periodic)
- Other:

_____

_____

☐ Laboratory Information Management System

- Software
- Licenses

- Maintenance
- Other:

_____

_____

☐ Equipment maintenance/repair/replacement

☐ Staffing and Administrative Costs

- Payroll
- Benefits
- Consultant fees
- IT support

☐ Consumables, Operating Supplies and Gases

- Buffers
- Reagents
- Chemicals
- Disposables
- Disinfectants
- Safety supplies
- Personal protective wear
- Liquid nitrogen
- Other:_____

_____

☐ Minor Equipment

- Monitoring equipment

- Barcode scanners
- Computers
- Office equipment
- Telecommunications

☐ Service Contracts for Equipment Maintenance and Disaster Recovery

☐ Certification and/or Accreditation Fees

☐ Other Quality Management Fees

☐ Transferring Collections

☐ Other (please describe):

_____

_____

6. What special considerations must be given to operating such a facility in a foreign country?

☐ Skilled staff

☐ Export controls

☐ U.S./foreign regulations

☐ Ethical considerations

☐ Legal considerations

☐ Policy considerations

☐ Financial sustainability

☐ Currency fluctuations

☐ Data security/Protection of confidentiality

☐ Informed consent

- ☐ Energy/constant power source
- ☐ HVAC systems
- ☐ Technical and logistical issues
- ☐ Quality control
- ☐ Efficient transport logistics
- ☐ Availability of liquid nitrogen and dry ice
- ☐ Location of repository in terms of climate
- ☐ Internet connectivity
- ☐ Other (please specify):

_____

_____

7. To the best of your knowledge, what type of documentation is required to build and operate a biospecimen repository in South Africa?

- ☐ Business license
- ☐ Architectural approval from city
- ☐ Approval from the State? Identify the government areas they have in South Aftica
- ☐ Environmental impact statement
- ☐ Other (please specify):

_____

_____

8. Please describe the biggest barriers/risks to establishing a biospecimen repository in a foreign country, or specifically South Africa?

_____

_____

9. Please describe the greatest rewards/benefits to establishing a biospecimen repository in a foreign country, or specifically South Africa?

_____

_____

10. Are there any resources (i.e., articles, books, websites, people, etc.) you would recommend that would be relevant or helpful to this project?

_____

_____

## Biography

Emily Higbee, born in Seattle, Washington, graduated with a Bachelor of Science degree in Biology from the University of Washington in 2007. Following graduation, she began working at the Fred Hutchinson Cancer Research Center (FHCRC) in 2008 where she combined her administrative experience with her love of science. Emily began her research administration career at FHCRC as an Administrative Coordinator for the HIV Vaccine Trials Network (HVTN), and after holding several roles within the Vaccine and Infectious Disease Division, she is now the Program Manager and Secretary for FHCRC's South African subsidiary company that supports the HVTN's multi-site, large scale clinical trials throughout sub-Saharan Africa. Emily loves to travel, camp, and read, but spends most of her free time with her husband and children at their home in Washington State.