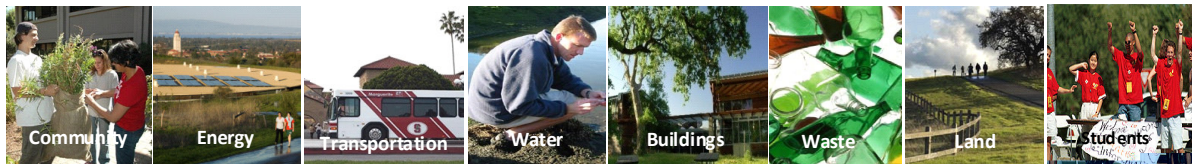


Room Temperature Biological Sample Storage

Stanford University Pilot



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Executive Summary

Stanford University could cut usage of electricity by **forty million kilowatt-hours (kWh)**, reduce its carbon footprint by an estimated **eighteen thousand metric tons** and save **\$16 million dollars** in operating costs over the next ten years by transferring biological samples from frozen storage to room temperature storage technology. (Figure A)

Background: Over 350 laboratories and thousands of researchers across Stanford University are advancing biological and biomedical research generating large collections of biological samples. These samples are both scientifically and financially valuable to the researcher and the university. Often irreplaceable, sample collections at Stanford are growing at an escalating rate. Hundreds of scientific freezers across campus are needed to safely store the current sample collection consuming large amounts of energy, precious research dollars, and valuable space.

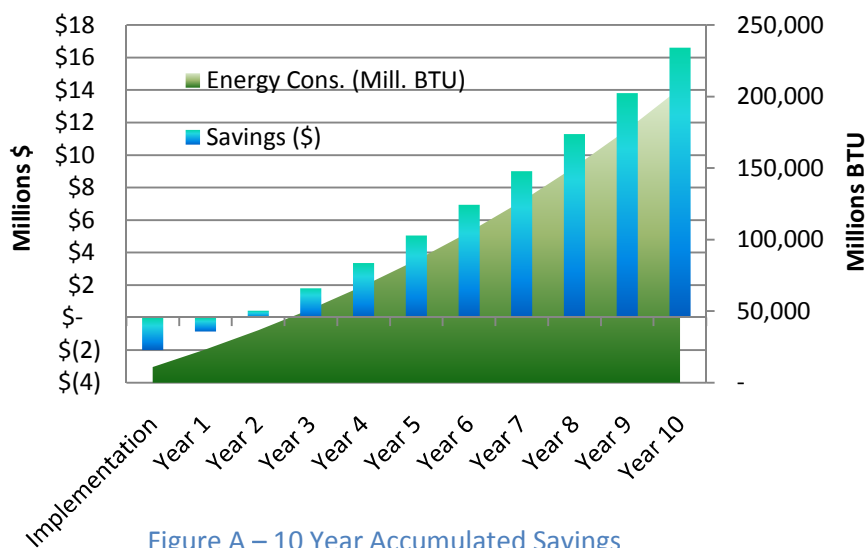


Figure A – 10 Year Accumulated Savings

Objective: The pilot study set out to allow a diverse group of Stanford research laboratories to transfer biological samples from freezers to room temperature storage. The study also intended to evaluate and generate a forecast of environmental, financial and additional benefits of a university-wide program to implement the technology.

Methods: Stanford Sustainability and Energy Management (SEM) recently commissioned and completed a pilot project to estimate potential benefits of room temperature sample storage using a technology developed by San Diego-based Biomatrix™ Inc. Stanford partnered with the company to supply reagents and materials to twelve pilot laboratories from the School of Medicine and Biology Department. A sophisticated forecast model was developed using information from a pilot group of labs, fourteen additional laboratories, other Stanford-specific data, and industry trends to estimate the potential campus-wide benefits.

Key Findings and Conclusions:

- An estimated nine to thirteen million samples (representing 20-25% of the total Stanford sample collection) could be moved from freezers to room temperature technology.
- The initial investment in transferring these samples could be recovered within three to five years under a broad implementation program.
- The program could generate an estimated eleven to twenty million dollars in cost reductions as well as prevent seventeen to twenty thousand tons of CO₂ from entering the environment.
- In addition to direct benefits, transferred samples would be shielded from degradation due to power disruptions, and thousands of square feet of lab space could be liberated for better use. Benefits revealed in this report could be realized immediately and continue to generate savings for many years.

Room Temperature Sample Storage - Pilot Project Report

Stanford University is a recognized leader in sustainability, as acknowledged by the Sustainable Endowments Institute in its 2008 College Sustainability Report Cardⁱ. Even though much has been achieved, a significant opportunity to improve sustainability at Stanford remains untapped within the freezers of its biological and medical laboratories. Stanford houses nearly 2000 freezers in more than 350 laboratories across its campus. Each year these freezers consume an estimated 39,700 Million BTUs (MBTU) of energy, generate 3,600 tons of carbon dioxide (CO₂) and cost \$ 5.6 million to operate.

<p>Stanford University Today</p> <p>350* Laboratories 2000* Freezers 610,000 Square Feet Wet Lab Space *Estimate based on Stanford data</p> <p>Annual Sample Storage Impact</p> <p>40,000 Million BTUs 3,600 metric Tons of CO₂ \$ 5,600,000 operating cost</p>

According to capital equipment records, the University purchases an average of 40 new ultra-low temperature freezers each year to accommodate growth of its biological sample collection and replace aging equipment.ⁱⁱ While maintaining the current sample collection seems daunting, industry experts anticipate the sample generation rate to double in the next two years, driven by an increasing number of samples generated by a growing number of clinical trials, new technology, personalized medicine and stem cell research.

Current Challenges

Energy Use: Stanford’s freezer collection is projected to consume 564,000 MBTU and generate 51,000 metric tons of CO₂ at an accumulated cost of \$69 Million during the next ten years. Figure 1 illustrates the challenge facing Stanford now and over the next ten years due to its reliance on current methods of storing and protecting its biological samples.

Space Utilization: In addition to the escalating cost and energy drain, each freezer occupies 30 square feet of valuable lab space,

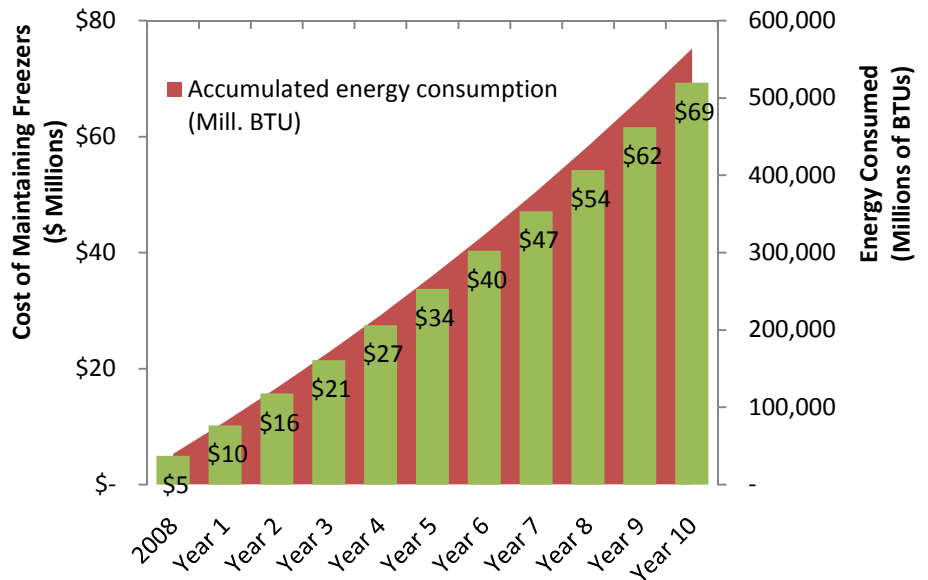


Figure 1 – Ten Year Accumulated Energy and Cost to Maintain Freezer

which is putting pressure on planning for future growth. Assuming the current 5% per year growth rate for the freezer collection, Stanford would have nearly 3,000 freezers in ten years, which would occupy nearly 96,000 square feet of lab space or about one fifth of the total wet lab space, not including support spaceⁱⁱⁱ.

A projection of the growth of Stanford’s freezer collection below in Table 1 is based on a historical growth rate of 5% per year for ultra low freezers. However, the expectations for hiring medical school faculty and expanding current programs could drive the current and future growth rate significantly higher. According to projections from the office of institutional planning, the School of Medicine plans to hire nearly one hundred new research

faculty by 2014 - a 33% increase.^{iv} In addition to an increase in faculty, medical school leadership anticipates an increase in sample generation rate from researchers conducting an increasing number of population studies.

Freezers	2008	2013 Forecast	2018 Forecast
Ultra Low Temp freezers -80 C	735	938	1,197
Low Temp Freezers -20 C	1224*	1,562	1,994
Total Freezers	1,959	2,500	3,191
Freezer Footprint (SQ Feet)	58,770	75,007	95,730
Additional Factors not Included Above – Likely to exacerbate freezer growth figures significantly <ul style="list-style-type: none"> • 33% growth expected in medical school faculty by 2014 • Projected increase in sample generation rates due to new technology and population studies • New lab construction space limitations 			
*Estimated number of -20 based on pilot group data			

Table 1 – Predicted Freezer Growth at Stanford

The Opportunity

Given the growth expectations of Stanford’s biological sample collection, which increasingly demands more energy, space and money to maintain, a sustainable alternative is needed to slow freezer demand. Non-freezer-dependant storage technologies are alternatives to current practices that promise to reduce energy consumption, space demands and escalating costs generated by laboratories storing samples in frozen environments.

Stanford University Pilot Study Objective

The objective of this pilot study was to evaluate the potential of room temperature storage to save energy and reduce carbon footprint by allowing Stanford’s researchers to safely store biological samples without the need of freezers.

While room temperature technology has the potential to help reduce Stanford’s dependency on frozen storage, this hypothesis needed to be proven. To this end, the Department of Stanford Sustainability and Energy Management (SEM), initiated a pilot study during the fall of 2008. The Sustainability group partnered with Biomatrix to provide reagents, materials, software and technical support for pilot laboratories.

Room Temperature Sample Storage Technology

The Biomatrix technology evaluated in this study enables safe storage of biological material at room temperature. Called SampleMatrix™, the technology prevents the degradation of biological materials at room temperature, eliminating the need for cold storage and cold shipping. Biomolecules, such as DNA, RNA and bacteria can be stabilized at ambient temperatures providing a cost-effective alternative to storing samples in freezers and cold shipping.

The technology is based on extremophile biology originally identified by Dr. John Crowe, Professor Emeritus UC Davis.^v Using extremophile biology, organisms such as tardigrades and brine shrimp are able to protect their DNA, RNA, proteins, membranes and cellular systems for long-term survival in a dried state or anhydrobiosis (life without water) and later revive by simple rehydration. Biomatrix's technology mimics the natural molecular mechanisms used by these organisms. The technology works by forming a thermo-stable barrier during the drying process to protect samples from degradation during storage at room temperature (Figure 2 and 3).

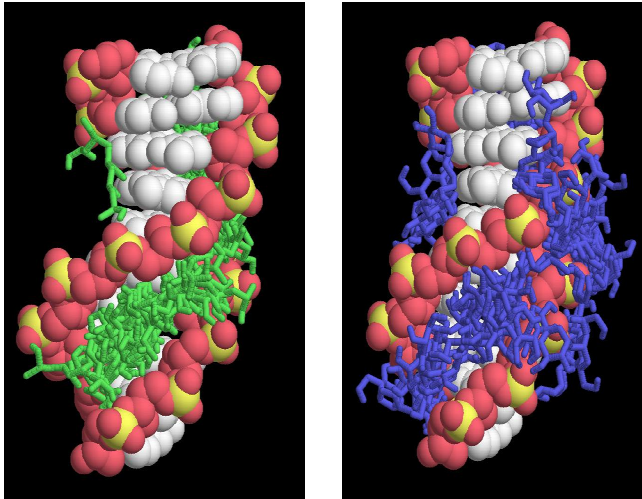


Figure 2 – Structural prediction of SampleMatrix interacting with nucleic acids

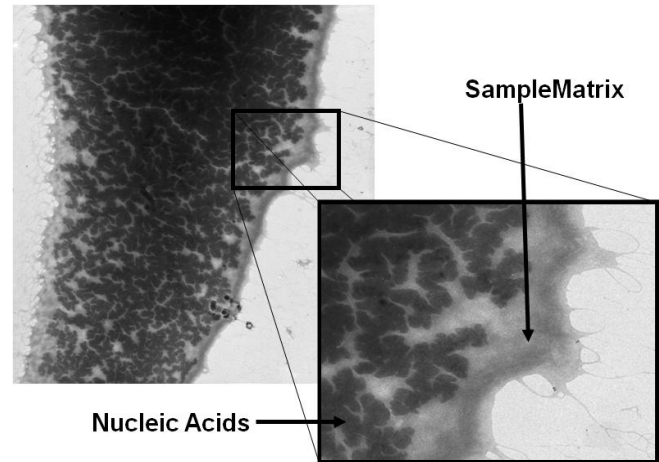


Figure 3 – Electron micrograph of protective thermo-stable barrier.

The Biomatrix products evaluated in this pilot provide long-term storage of purified DNA and RNA samples. The technology can easily accommodate a variety of storage containers, thereby facilitating efficient sample transfer from existing collections or the creation of new ones.

Pilot Group Laboratory Selection

Researchers responded enthusiastically to the invitation to participate in the pilot study from the Stanford Dean of Biology and Sr. Associate Dean of Research in the Stanford School of Medicine. The pilot group was established within two weeks, and many additional interested laboratories applied to participate.

Twelve laboratories with a variety of research focus areas were selected from Stanford's School of Medicine and Biology Department. A diverse set of laboratories in the pilot group provided insight into the applicability of the room temperature technology within a variety of laboratory settings. In addition, the group, while not a random sample, does provide a reasonable proxy for making predictions about the broader population of laboratories at Stanford. Labs beyond the core pilot group provided information about sample collections and lab equipment increasing the amount of known data to improve forecast accuracy.

Pilot Participation Group

The pilot group includes laboratories from ten different departments, a microarray core cancer facility, a pediatric psychiatry clinical lab, one tissue bank and one plant biology laboratory. All laboratories have common sample requirements of biological research laboratories with molecular or cellular focus (Table 2).

Laboratory Description	Medical School	Biology
More than 100,000 addressable samples (Core facility and large genomic lab)	1	1
1,000 to 10,000 addressable samples	4	
Less than 1,000 samples	6	
Total sample transfer laboratories	11	1
Laboratories on waiting list (sample collection data only)	13	1
Total laboratories	26	

Table 2 – Pilot Participant Group

Participants provided extensive information about their sample collections, including sample formats and types, freezer storage temperature, sample generation rates, and the number of freezers used to contain each sample collection. The data from the labs provided detail about the samples stored in each lab including the number of candidate samples and provided better understanding of sample management practices.

Data Analysis and Methodology

Nearly one million candidate samples were discovered in the freezers of participating labs in the pilot group. Based on their sample collection, each pilot participant received room temperature storage technology reagents, storage cabinets and sample tracking software from Biomatrica. These materials facilitated the transfer of nearly seventy thousand samples out of the one million addressable samples discovered in the pilot group. Sample collections of twenty-six laboratories were assessed.

Pilot Group	Results
Number of addressable Samples	923,000 (DNA and RNA)
Number of Freezers	34 Ultra-Low (-70°C -80°C)
	59 Low Temperature (-20°C)

Table 3 – Pilot Survey Data

An interactive analysis tool was created using Microsoft Excel™ to provide an accurate model of the costs of frozen storage per biological sample. The model was designed to account for various sample storage formats, sample locations, labor requirements, maintenance requirements and numerous other parameters. All assumptions were verified by reliable industry sources and validated through extensive interviews of Stanford personnel in utilities, facility management group, purchasing and the School of Medicine. Assumptions were further supported through actual data gained from detailed survey responses from the pilot group. Energy and cost savings data from the pilot group were calculated to provide the basis to forecast the campus-wide sample collection. Finally, the projections in the model allowed input of various growth rates to enable generation of conservative, moderate and aggressive scenarios.

The pilot data provided the basis for using the model to make a conservative estimate of the total number of addressable samples on campus. The projection is highly influenced by the predicted distribution of sample container format and was guided by the pilot group sample collection. Using the pilot group data and distribution of sample container format, a prediction of between nine to thirteen million addressable samples

was generated. The container format of these samples is classified into four categories based on the four most common container volumes found in research. The distribution assumptions used in the model are listed in Table 4.

Container Format Temperature	High Density	Medium High	Medium Low	Low Density
Ultra Low (-80)	4%	6%	57%	0%
Low (-20 C)	4%	6%	23%	0%
Energy Consumption Per Sample	Low ←—————→ High			

Table 4 – Campus-wide Projection of Container Format Distribution

High density sample containers occupy smaller volumes per sample and therefore consume less energy per sample volume than low density container formats. The model was designed to allocate energy consumption of a sample by format; therefore careful consideration had to be given to the format distribution of the pilot group. The distribution percentages of the pilot group guided a reasonable distribution for the predicted number of samples on campus. Evidence that the percentages in Table 3 are conservative was provided by a previous freezer study conducted in the School of Medicine in 2007, which found that nearly 90% of samples in ultra-low temperature freezers were in medium-low category.^{vi} If the percentage of samples at lower density is closer to 90%, then the potential savings for Stanford could increase dramatically due to the energy required to store a greater number of lower density samples.

An important benefit to non-frozen storage is the freedom to store samples at higher density than in the frozen environment, which can generate even greater savings. Within the frozen environment, samples are often stored in individual tubes, which are typically much more costly and less efficient than storing multiple samples in a higher density plate type format. Researchers favor this less efficient energy format because they try to limit the number of “freeze-thaw” cycles for each sample. When samples are stored in a higher density format such as a ninety-six well plate for example, the other ninety-five samples are thawed when a researcher needs to use only one sample. Therefore, most research laboratories favor individual tubes for frozen storage. However, samples stored in ambient temperature can be individually accessed without any effect to neighboring samples within a single storage plate. Moving individual tube samples out of frozen storage to room temperature in a higher density format therefore increases the amount of savings gained.

Since projections in the model rely heavily upon the container formats of samples in the pilot group and many of the samples in the pilot group tended to store in high density containers, then the projected savings gained by a campus-wide program may be understated. Therefore, a program that takes advantage of the freedom that room temperature storage provides researchers to store samples in higher density container formats could realize even greater savings.

Cost, Savings and Results

According to model calculations, transferring the addressable samples in the pilot group alone would save Stanford an estimated 108 Million BTU of energy, reduce CO₂ emissions by eleven tons and save nearly \$17,000 every year by reducing capital equipment and operational costs for six freezers.

The pilot group also provided insight into the potential magnitude of the savings in energy, CO₂ emissions and operating costs that could be brought about by moving samples out of frozen storage on a campus-wide scale. Extensive interviews of pilot participants provided the data foundation to estimate the number of candidate samples stored across campus. Stanford personnel provided capital equipment counts, costs, purchase information and trends, research faculty numbers and wet lab square footage to validate our estimates and make accurate predictions about future growth.

Stanford Campus-wide Potential	
Addressable Samples	9 – 13 million
CO ₂	900 – 1100 Metric T/year
Electricity	2.0 – 2.4 million kWh/year
Chilled Water (space cooling)	340 – 400 thousand T-hr/year
Total energy	10 – 12 thousand MBTU/year
Cost savings	\$1.2 – 1.4 million/year

Based on the calculations within the forecast model, Stanford research laboratories currently contain between nine and thirteen million samples that could be transferred to room temperature storage. Transferring this collection could save more than two million kWh of electricity, nearly four hundred thousand ton-hr of chilled water needed to cool space, and reduce the carbon footprint by as much as eleven hundred metric tons of CO₂ annually (Table 5).

The value becomes even more evident over ten years. Using a conservative annual sample growth rate of 10%, Stanford could reduce estimated forty million kWh and nearly seven million ton-hrs of chilled water by placing current and newly generated biological samples into room temperature storage (Figure 4 and 5).

This potential energy reduction would reduce the University’s carbon footprint by an estimated fifteen thousand metric tons over the same period. Savings of this magnitude could help slow the escalating energy and space demand challenges of maintaining the current freezer-based system.

In addition to the significant environmental benefits, shifting samples to room temperature dramatically reduces costs. The samples that could be transferred to

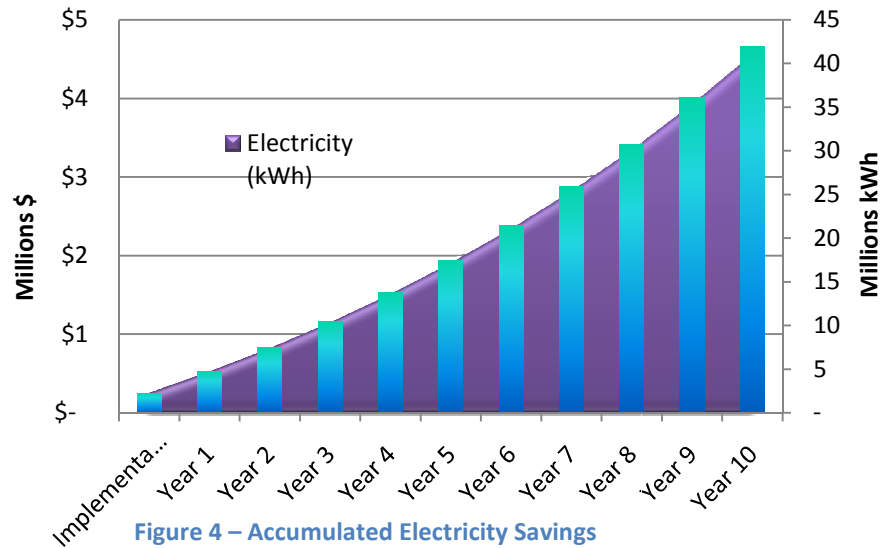


Figure 4 – Accumulated Electricity Savings

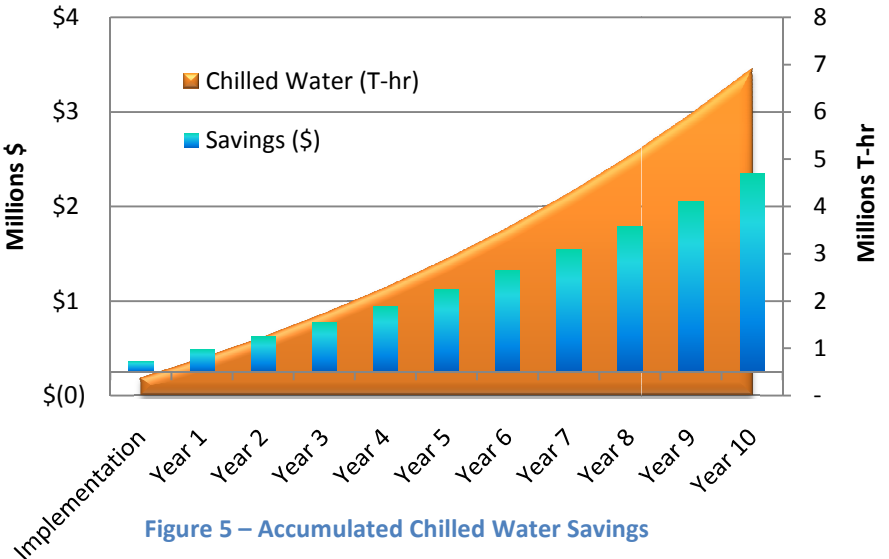


Figure 5 – Accumulated Chilled Water Savings

room temperature storage today, along with the samples projected to be generated by research over the next decade (assuming a 10% per year sample generation rate), would cost over thirty million dollars to maintain in freezers. Using room temperature sample storage, Stanford could realize a net savings of more than sixteen million dollars over the next decade and recover its initial investment within three to five years (Figures 6). Greater savings and freezer reduction could be realized as new products become available, such as those Biomatrix is developing to allow storage of blood, serum and protein samples at room temperature.

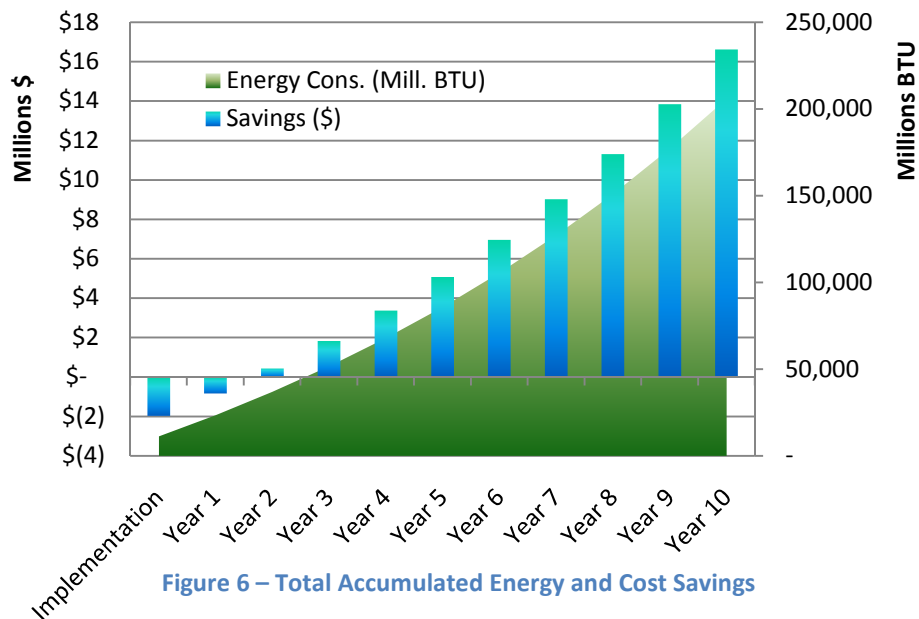


Figure 6 – Total Accumulated Energy and Cost Savings

The projected savings fall into several categories (Figure 7). Energy savings from electricity and chilled water account for nearly 27% of the total. Capital equipment and maintenance account for 40% of the projected savings, and 28% of the savings is generated from reclaiming the space occupied by each freezer. Space costs are internally allocated, and cost per square foot is determined by an internal charge-out rate. To avoid the possibility of overstating energy savings, all electricity and chilled water costs normally allocated to wet lab space at Stanford are *not* included in the space cost per square foot used in the savings projection. Total savings remain significant at nearly one million dollars annually and close to eleven million dollars over ten years even when space savings are excluded altogether. Further, the period required to recover the initial investment in transferring samples only lengthens by one year when space is not given a monetary value. While space charges are an internal transfer, the value of space is an important consideration, particularly with cost of new construction and, as stated previously, the number of faculty is expected to increase along with the pace of sample generation.

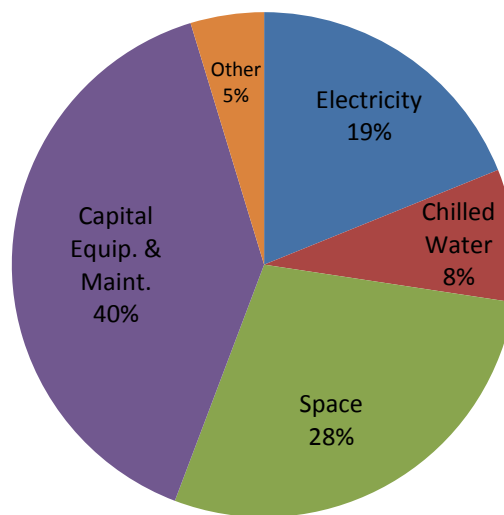


Figure 7 – Cost Savings by Category

Additional Benefit - Reducing Sample Risk

Beyond the significant amount of space allocated and despite the huge investment Stanford makes every year to keep biological samples in a frozen environments, the samples themselves are currently at risk. The Stanford collection is vulnerable to catastrophic events such as earthquakes, fires and severe weather as well as more mundane equipment failure and accidents. Equipment failures are so common that investigators and departments purchase excess freezer capacity to accommodate regular disruptions.

Sample loss is not only a setback to science, but also a monetary loss to the university. Even before any research is performed by scientists, clinical samples need to be acquired and the acquisition cost can be significant. Clinical sample acquisition costs range from \$1,000 per sample and can reach as high as \$10,000 for samples with specialized selection criteria.^{vii} Once samples are acquired and research commences, their value increases over time as new analysis technologies are developed and discoveries are made in a particular disease area.^{viii} Beyond the energy and cost savings, moving valuable samples to room temperature will help reduce the risk of sample loss due to catastrophic events and other threats. Using costs from clinical researcher experience and an estimate of the number of clinical samples of various types, the approximate value of the Stanford sample collection based on the sample acquisition costs could be nearly three billion dollars (Table 5).

Value per sample	% of collection	collection value
\$2,500-10,000	1%	\$1.21 Billion
\$500-2,500	9%	\$0.56 Billion
\$100-500	40%	\$0.79 Billion
\$0-100	50%	\$0.26 Billion
Total	100%	\$2.82 Billion

Table 5 – Estimated Value of Stanford Sample Collection

Summary

- Analysis of the Stanford sample collection through the pilot study revealed the substantial amount of energy and expense required to protect Stanford’s current biological sample collection from degradation using freezers. On a campus-wide scale the university will spend \$68 million over the next decade to maintain and add to its freezer collection to protect valuable samples, not including costs to build freezer farms.
- Implementation of room temperature storage across the Stanford campus could not only reduce energy consumption and greenhouse gas emissions, but also save money, conserve valuable lab space and reduce disaster risk of the current sample collection.
- Benefits could begin to accrue immediately as compared to projects with long construction timelines that need to occur before a single kilowatt-hour is saved.
- The magnitude of cost savings is dependent on the rate of adoption, as well as the anticipated sample generation growth rate.
- In addition, integration of room temperature storage technologies into current research workflows could reduce expense and risk of cold transportation. It could also provide a cost-effective solution for offsite back-up to further protect valuable sample collections.

Recommendations for Implementation

The benefits of room temperature storage are significant, and capturing them will require a careful, well-thought-out strategy to increase adoption and remove any obstacles. The pilot study and participating laboratories provided valuable insights into the potential adoption of a broad program as well as obstacles that would need to be addressed for successful implementation. Many of the most important observations from the pilot to guide the design and development of an implementation plan are documented in Table 6.

Observations	Critical Success Factors
Enthusiastic response from researchers	Interest in sustainable storage alternatives at all levels
Labs are slow to transfer samples	Labor support needed for successful implementation
Perception by principal investigators that energy and cost savings benefit the department, not the lab	Need to properly incentivize labs to support sample transfer
Value of samples is high and important	Samples are irreplaceable - value is very important and much higher than the cost of storage
Large numbers of DNA and RNA housed at ultra-low temperature	Many samples on campus eligible for room temperature storage
Frozen environments are hard to work in; locating samples difficult, frequent thaws put samples at risk	Room temperature storage improves productivity and flexibility in the work environment

Table 6 – Pilot observations and conclusions

Translating the pilot study to a successful program will require a strong commitment from leadership within the School of Medicine and Biology Department as well as a support from the Sustainability and Energy Management Group.

Next Steps

- Conduct detailed survey of laboratory sample collections on campus
- Collaborate with the School of Medicine and Biology Department to align incentives as well as establish political support within the organization
- Understand how sample transfer can be translated into freezer purchase reduction or shutoff
- Create appropriate incentives for departments, principal investigators and individual researchers to motivate adoption
- Develop program with larger service laboratories or core facilities to facilitate and support consistent sample transfer and management
- Include formalized process for organizational change to take advantage of easy sample transfer and education opportunities such as retiring professors, new hires, and post-doctoral and PhD turnover
- Provide consistent information around program incentives and benefits, publish success and establish feedback mechanisms
- Identify a manager and staff to develop implementation plan for large scale sample transfer

Study Scope and Limitations:

The forecast in this study provides an estimate of Stanford’s biological sample collection based on data obtained from a subset of the entire population. While the number of pilot labs is sufficient to provide an accurate prediction of the benefits and costs of a room temperature program they do not provide a statistical random sample and are subject to selection bias. The group is intended to provide a diverse sample which could represent the Stanford population of research laboratories.

Many of the assumptions in this prediction are based on conservative assumptions and therefore may underestimate the savings potential of a room temperature program. Study results are based on currently

available technology and should be updated as new technology enables a greater number of sample types to be stored at room temperature.

Other room temperature storage technologies do exist; however, the scope of this pilot did not include evaluation of these products. In order to accurately forecast the benefits of other technologies, additional product specific information would be needed, including transfer protocols and labor time, product costs, supporting equipment costs, storage sample formats and addressable sample types. During the pilot study many benefits were uncovered in addition to those generated by moving samples out of freezers which could be studied in greater depth to quantify these benefits in greater measure.

Information Inquiries:

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ⁱ Stanford Press Release, September 24, 2008, *Stanford scores high for sustainability in national study*, <http://news-service.stanford.edu/pr/2008/pr-card-092408.html>

ⁱⁱ Cathy Booth, Laboratory Management, Molecular and Cellular Physiology Department Stanford University

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^{iv} David Obrien, Office of Institutional Planning, Stanford School of Medicine

^v Crowe JH, et al., (1999). *Ann. Rev. Physiol.* 1998;60:73-103

^{vi} Don Rust, Health and Safety Management, Stanford School of Medicine

^{vii} Personal conversation, Dr. Joachim Hallmayer, Pediatric Psychiatry, Stanford School of Medicine, December 12, 2008

^{viii} Personal conversation, Dr. David Hirschberg, Director Human Immune Monitoring Center, Stanford School of Medicine, December 16, 2008