Team Results Document
Cornell SensTech

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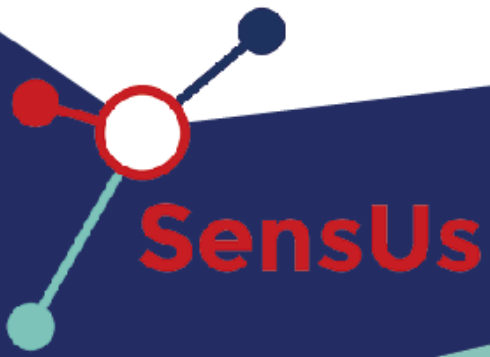

SensUs 2024
Acute Kidney Injury

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1. Abstract

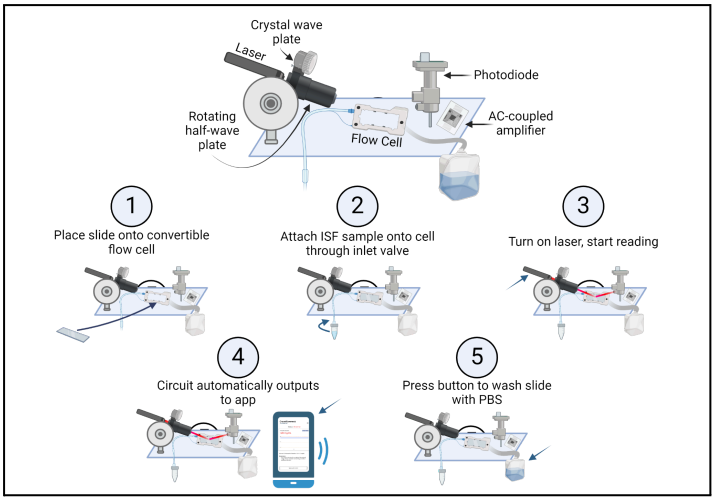
Cornell SensTech presents a detection method for creatinine by combining DNA anti-creatinine aptamers and oblique-incidence reflectivity difference (OIRD) to create a patient-centric biosensor. Interstitial fluid (ISF) is passed through a glass slide in a flow cell where the aptamers are bound to the glass through a silane-PEG-NHS linker. A laser is shone on the glass slide during this process. Following the binding of creatinine, aptamers undergo a conformational change which causes a reflectivity difference in the incident light. The output from the OIRD system is then converted into a comprehensive report on the CreatConnect app for the patient to access in real time. OIRD is a simple, inexpensive, and label-free detection method with great translation potential. The business model at launch, is to form a strategic alliance with an experienced manufacturer and distributor to target sales to healthcare providers and consumers, and supplementing this, will be a subscription model to access app data and results.

2. Biosensor System

2.1 Biosensor Concept Overview

SensTech combines DNA aptamers and oblique-incidence reflectivity difference (OIRD) in a novel biosensing system for the detection of creatinine in interstitial fluid (ISF) for regular renal function monitoring. After scaling down hardware and successfully achieving reliable molecular recognition, the biosensor can be user-friendly and compact.

Figure 1. (Below) A schematic of how a user would use the SensTech biosensor.



The following sections detail how the current biosensor prototype should ideally function before miniaturization of the hardware.

2.2 Molecular Recognition

An anti-creatinine DNA aptamer modified with a 5'-amine group from Creative Biolabs would be bound to a VBR microscope glass slide via a silane-PEG-NHS linker. To attain uniform binding of the linker, the glass would undergo plasma cleaning for 10 minutes to remove all organic contaminants and surface tension. Afterwards, the silane-PEG-NHS linker would incubate on the glass slide and bind through passive conjugation [1]. The functionality of the linker is such that the silane end binds to the glass and the NHS end binds to the anti-creatinine aptamer via an amide bond (Figure 2). When the ISF flows over the glass slide, the creatinine binds to the aptamers. The signal generated by the binding of the creatinine would then be read by the OIRD setup. When bound with creatinine, the aptamers undergo a conformational change. To allow for continuity across measurements, an intermediate wash with phosphate buffered saline (PBS) pH 8 will be required in between readings to unbind creatinine from the aptamers and reset their orientation.

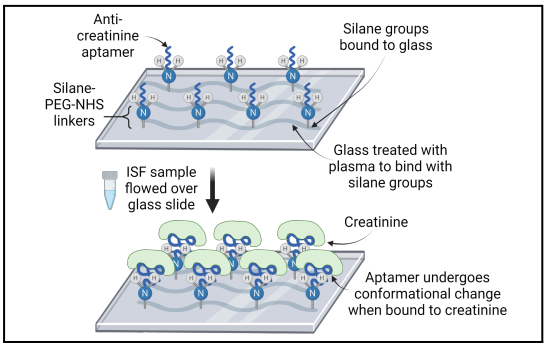


Figure 2. (Left) Plasma cleaned glass slides treated with silane-PEG-NHS linkers connected to aptamers that are ideally perpendicular to the glass slides to capture the creatinine molecules from ISF.

2.3 Physical Transduction

SensTech has chosen to pursue OIRD as an effective measuring technique for aptamer-creatinine surface interaction due to its cost-effectiveness, rapid detection time, and high-sensitivity. OIRD is a more sensitive form of optical ellipsometry used for label-free detection of protein-molecule bindings [2].

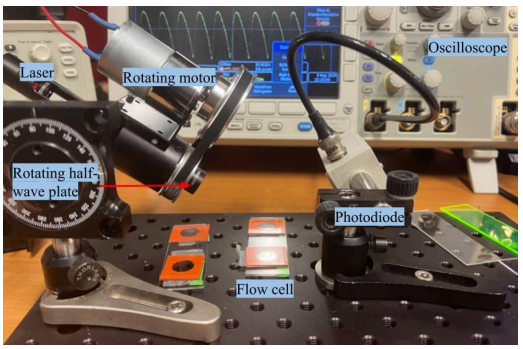
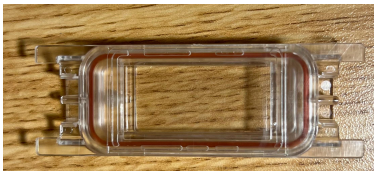


Figure 3. (Right) Schematic of OIRD setup.

OIRD uses a linearly polarized laser beam optical that passes through a phase modulator or a rotating half-wave plate so that the light incident on the surface being probed alternates between S and P polarization. The relative intensities of the reflected light from the

two polarizations varies with the thickness and density of the modified surface layer on the reflective surface. In the prototype setup, a 670 nm laser passes through a motorized revolving half-wave plate that alternates the polarization between S and P. Brewster's angle, which is the ideal angle of incidence and is described by the equation $\Theta = \arctan(n_2/n_1)$, would be necessary to calculate in order to maximize the amount of signal detected by the oscilloscope.



2.4 Cartridge Technology

The treated glass slides would be placed in a convertible flow cell (Figure 4). ISF would flow through the inlet channel and be pumped out into a waste container. After a reading, a PBS wash would then flow in and out.

Figure 4. Convertible Flow Cell

2.5 Reader Instrument and User Interaction

Performing a Measurement

ISF from the patient would be obtained in a tube and attached to the inlet channel. The pump would be turned on by the patient, allowing the ISF to flow through the treated glass slide.

Reader Instrument

The reading instrument consists of a photodiode, an operational amplifier (op-amp) circuit, and an oscilloscope to visualize the data and convert the photodiode measurement into a reading for the user. The photodiode (Thorlabs DET110) is a high-speed silicon detector sensitive to light in the wavelength range of 350 to 1100 nm. The DET110 photodiode can accurately detect rapid changes in light intensity, which is essential for real-time monitoring of surface interactions. With a responsivity of 0.45 A/W at 650 nm, the photodiode efficiently converts incident light into an electrical signal. The signal from the photodiode would be fed into an op-amp circuit, which amplifies the signal for better accuracy and clarity. This amplified signal would then be interpreted in less than 1 minute by an oscilloscope, which visualizes the information for better readability. In the current stage of development, changes in voltage over time can be measured and read through the oscilloscope, however, through plans to downsize the OIRD setup (see 3.7 Evaluation & Improvements), the oscilloscope would be replaced by an AC-coupled amplifier and a RMS measurement circuit and a Bluetooth PCB circuit would transmit the signal each time ISF is flowed through the cell. This would interface with the biosensor's app, CreatConnect, where the final reading and analysis is presented to the user.

User Interface

CreatConnect would correlate the reflectivity changes with a standardized curve of known creatinine concentrations to calculate the creatinine level of an unknown sample given by the user, and output the result to the user with relevant insights. Users would then be presented with their creatinine measurement history along with a brief explanation. If the app detects an abnormal creatinine level based on the user's typical creatinine baseline, it flags the user, recommending them to schedule another appointment with their provider and push an update to their provider's app. Patients can also view a history of their measurements, enabling them to track changes over time. See Appendix A2 for an in-depth walkthrough of a use case and a mockup of the clinician interface for the app.

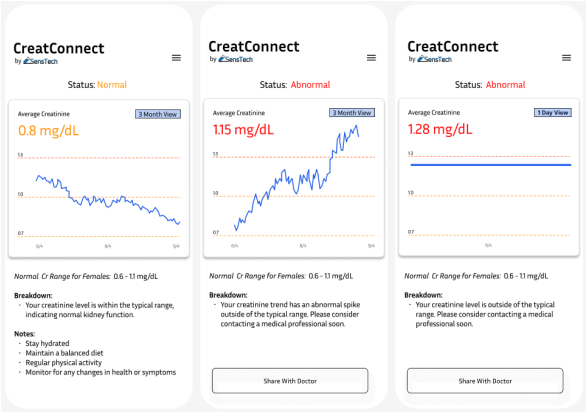


Figure 5. CreatConnect design mockup for the patient interface. Created in Figma.

3. Technological feasibility

3.1 Molecular Recognition Capabilities of the Aptamer

A Biolayer Interferometry (BLI) instrument from Sartorius was used to test for measuring the binding affinity of the aptamer used. The aptamer sequence was found in a paper and modified with a 5'-amine group added and ordered from Integrated DNA Technologies [25]. Biotinylated anti-creatinine aptamer was bound to the streptavidin biosensor tips and the SensTech team tested for creatinine-aptamer binding [4].

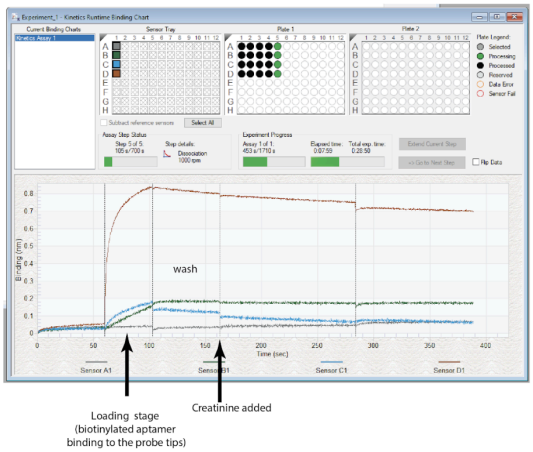


Figure 6. The aptamer was loaded onto the Octet's biosensor tip, run through a buffer wash, and then exposed to 300 µM creatinine. Over the remaining 240 seconds, no changes were observed in the BLI signal indicating either the creatinine was not interacting with the aptamer, or the low molecular weight analyte (creatinine) and any associated conformational change in the aptamer could not be detected.

3.2 Binding of Silane-PEG-NHS Linker to Glass

After plasma cleaning, one milliliter of 1% linker dissolved in DMSO was pipetted onto each slide. While pipetting, the team would look for no surface tension as the goal was to attain as uniform binding as possible. The slide incubated for 1 hour with the linker. Once the linker was attached, a diluted solution of the aptamer was applied.

The results of binding the linker as uniformly as possible is shown below in Figures 7 and 8. A fluorescence marker, cy3-amine, was dropped onto the treated glass to interact with the linker to show binding. In Figure 7, a substantial amount of binding can be seen, however, the binding was not consistently uniform. In Figure 8, you can see an aggregate of the linker bound to the glass demonstrating the variation in uniformity.

Figure 7.

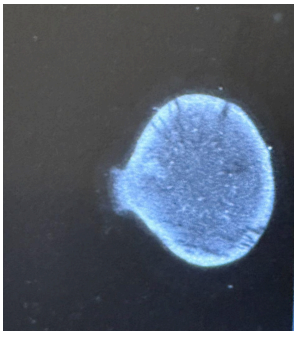


Figure 8.

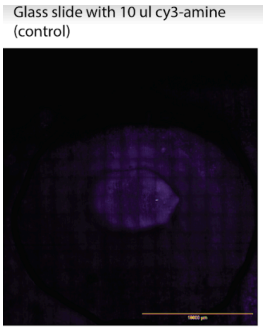


Figure 9.

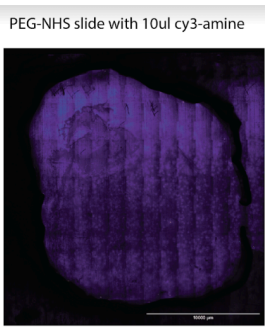
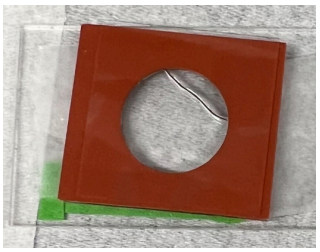


Figure. 10

Another fluorescence experiment in Figures 9 and 10 was done to demonstrate the linker binding successfully to the glass slides to attempt a more uniform distribution.

3.3 Physical Transduction: OIRD Set-up and Testing Data



Another experiment using glass coverslips, the silane-PEG-NHS linker, and the aptamer was used to test the capabilities of the ORID setup as seen in Figure 3. Glass coverslips were chosen to begin downsizing the system and create a mock flow chamber. One glass coverslip was cleaned and untreated, 3 coverslips were treated with the silane-PEG-NHS linker, and 4 coverslips were treated with the linker and the aptamer.

Figure 11. (Left) A CoverWell imaging chamber.

A CoverWell imaging chamber with a circular cavity was placed onto a glass slide to simulate a flow chamber (Figure 11). A 65 µL drop of PBS was injected onto the center of the hole and the glass coverslips were placed with the treated side facing toward the PBS. This system was then observed under the laser in the ORID system with the laser angled to a photodiode connected to an oscilloscope for data acquisition. It took about 30 seconds to collect each measurement.

A statistical unpaired, two-tailed t-test was performed to compare the measured values for (1) the empty coverslips versus the linker-treated slips and (2) the linker-treated slides versus the linker-aptamer-treated slips for 3 trials. The p-values were 0.019 and 0.186, respectively. The coverslips treated with only the linker produce a statistically significant change in reflectance compared to the empty coverslips. The second p-value can not be used to determine a statistically significant difference in reflectance between the linker-treated slides and the linker-aptamer-treated slides. This means SensTech's OIRD setup is capable of detection at a molecular level, but further experimentation is needed to determine the setup's limit of detection with aptamers.

3.4 Evaluation & Improvements

Molecular Recognition

SensTech aims to find a DNA sequence that is specific to creatinine, and has already ordered a commercial aptamer to test in September 2024. Addressing this problem is feasible, but it will depend on the SensTech team's financial resources in 2024-25. The Sartorius Octet BLI instrument will be used to test creatinine binding kinetics of new sequences. Further improvements can be done on the uniformity of the linker binding onto the surface by using a syringe pump and plasma cleaning for longer amounts of time. The team also has yet to concretely determine if the aptamer reliably binds to the linker on the glass. This will be one of the top priorities of the team for the upcoming year.

Fluidic Cartridge

The team plans to investigate how many times a glass slide with aptamer can be reused for consecutive measurements to minimize the number of intermediate washes needed.

Reader Instrument

The SensTech team can improve the sensitivity of the laser and signal output by optimizing the angle of incidence and using more sensitive acquisition electronics to further improve the signal-to-noise ratio. The current prototype is large and would require scaling down. The team plans to replace the electric motor that rotates the half-wave plate (Figure 3) with a liquid crystal wave plate to create a more compact instrument. The AC-coupled oscilloscope needed to measure peak-to-peak values can be replaced by a simple AC-coupled amplifier and RMS measurement circuit, or a lock-in acquisition circuit if higher sensitivity is needed, which is significantly smaller and easier to use for the user.

Physical Transduction

Through pairings with other amplifiers, it may be possible to reduce background noise and receive a more accurate signal. The team's initial expectation is that OIRD signals from aptamer-creatinine binding will be large enough to be detected. If the aptamer signal is too weak, OIRD might still be useful for an antibody or tethered enzyme based detection scheme. Instead of an oscilloscope, a simple AC-coupled amplifier and RMS measurement circuit, or a lock-in acquisition circuit can be used to obtain a measured output each time ISF is flowed through the cell. The signal would be transmitted via a BlueTooth PCB circuit to interface with the biosensor's app, CreatConnect, where the final reading is presented to the user.

User Interaction

The current prototype is large and not very user-friendly, and would require scaling down which can be done through further experimentation this year (see: *Reader Instrument*). The proposed user experience through CreatConnect offers real-time monitoring and an accessible button to share data with providers. In practice, it may be challenging to connect users and doctors via SensTech's app, emphasizing the need for: 1. development of a clinician user interface for the CreatConnect app and 2. an effective marketing strategy to promote adoption of SensTech's technology.

4. Originality

4.1 Team Captains

The team is developing a biosensor inspired by OIRD and previous research on covalent attachment of DNA to glass slides [1]. With the help of the supervisor, the team also considered alternate routes. For example, the team tested a creatinine-specific aptamer attached to a fluorophore and a dark quencher (i.e. a molecular beacon), so when creatinine binds, a change in the fluorescence signal might be detected and correlated with creatinine concentration. Preliminary testing using a PTI fluorometer showed no change due specifically to creatinine. The molecular beacon aptamer fluorescence did change dramatically with buffer ionic strength, indicating that even if it did respond to creatinine, the ionic strength of the ISF would most likely overwhelm any changes due to creatinine binding. Due to this, the team decided to move forward with another idea of covalently attaching silane-PEG-NHS linkers to a glass slide (explained in section 2). Originally, the method of glass slides cleaning required piranha solution, but the team opted for a plasma cleaner for safety reasons and a creatinine specific aptamer.

The team also designed a prototype visual of a software display of what the results would look like for patients using the biosensor (section 2.5). The team sees potential in this unique method that combines OIRD, an aptamer, and a user-friendly mobile application.

Lily Blanton (SensTech Team Captain)

Emily Chen (SensTech Team Captain)

4.2 Team Supervisor

The team met on a regular basis to discuss various sensor ideas that they would test. The decision was made to focus on the use of DNA aptamers, since they are inexpensive to create and easy to work with. The team found a publication that showed the sequence for a creatinine specific DNA aptamer [5], and we had a number of modified aptamer variants made with: (1) 5' fluorophore, (2) an internal fluor (Cy3 on nt39), (3) a molecular beacon version (fluorophore on 5' and dark quencher on the 3' end, and (4) 5'- primary amine for conjugation to a silica surface using silane-NHS. In an initial set of experiments we tested the fluorophore and molecular beacon aptamer versions, but never saw a reproducible signal change that correlated with creatinine concentrations. A second detection method we are investigating does not rely on fluorescence, but instead uses aptamers bound to a glass surface and Oblique Incidence Reflectance Difference (OIRD) signals in which the polarization axis of a laser beam is rapidly rotated and the difference in reflected S and P polarizations measured. Fresnel's equations predict how the reflectance of the S and P polarization states changes with the index of refraction differences at the interface. The advantage of OIRD lies in its simplicity. Although our test OIRD setup uses an electric motor to physically rotate a wave plate to alternate between S and P polarizations, this could be replaced by a liquid crystal wave plate to create a more compact instrument. Our prototype system also used an AC-coupled oscilloscope to measure the peak-to-peak values, but this will be replaced by a simple AC-coupled amplifier and RMS measurement circuit, or a lock-in acquisition circuit if higher sensitivity is needed. Our initial expectation is that OIRD signals from aptamer-creatinine binding will be large enough to be detected. If the aptamer signal is too weak, OIRD might still be useful for an antibody or tethered enzyme based detection scheme.

Warren Zipfel (Team Supervisor)

5. Translation potential

Key Progress	Key Activities	Value Proposition	Customer Relations	Customer Segments
- **R&D Investments**: Significant focus on research and development, with projected costs starting at $2 million in 2024, and increasing in subsequent years to support ongoing innovation. - **Strategic Alliance with Phillips-Medisize**: Established a strategic alliance with Phillips-Medisize for manufacturing, ensuring cost-effective production and scalability. - **Patent Strategy**: Implemented a robust patent strategy, including utility and design patents, with plans for international protection as the product matures. - **Clinical Trials**: Ongoing clinical trials aimed at securing FDA approval, a crucial step for market entry and establishing product credibility.	- **Product Development**: Innovative technology to enhance accuracy and user experience. Regulatory - **Compliance**: Strategically navigating the FDA's De Novo classification pathway to ensure full compliance and market readiness. - **Manufacturing & Scaling**: Establishing high-quality manufacturing processes with allies to capitalize on favorable conditions for scaling. - **Marketing & Sales Strategy**: Crafting and executing marketing campaigns to effectively reach key stakeholders. **Key Resources** - **Biosensor Technology**: Leveraging proprietary technology as the cornerstone of ongoing development. - **Skilled Workforce**: Employing experts in research, manufacturing, marketing, etc. - **Advanced Manufacturing Facilities**: Utilizing state-of-the-art facilities for scalable and efficient production. - **Distribution Networks**: Implementing efficient logistics strategies to guarantee delivery.	The value proposition of the product lies in its innovative, creatinine biosensor, which offers fast and accurate results, making it easy for patients to use. This technology improves patient outcomes by enabling early detection and monitoring of chronic kidney disease, reducing the risk of late diagnosis and kidney failure. With a competitive pricing strategy, the product delivers exceptional value to both patients and healthcare providers. Furthermore, it is designed to be covered by Medicare, Medicaid, and private insurance, ensuring broad accessibility for a wide range of patients.	- **Direct Sales**: Cultivating strong relationships with healthcare providers and patients through direct sales efforts and comprehensive education about the product. - **Customer Support**: Providing robust support through the app, enabling users to interpret and take action based on their biosensor readings easily. - **Feedback Loop**: Continuously gathering user feedback to refine and improve the product and app, ensuring ongoing relevance and customer satisfaction. **Channels** - **Healthcare Providers**: Working with hospitals and clinics to facilitate product distribution directly to patients. - **Online Sales**: Expanding reach by offering the biosensor through online platforms, making it accessible to a wider audience. - **Insurance Alliances**: Collaborating with insurers to ensure coverage and simplify the purchasing process for patients.	- **CKD Patients**: The primary target audience, with a focus on those at risk of late-stage diagnosis. - **Healthcare Providers**: Secondary audience, including nephrologists and general practitioners involved in CKD treatment. - **Insurers**: Working with insurance companies to ensure coverage and accessibility for patients.

Cost Structure	Revenue Stream
- **R&D Costs**: Significant initial investment in research and development, with ongoing expenses as technology evolves. - **Manufacturing Costs**: Starting at $83 per unit, with expected reductions as production scales. - **Distribution Costs**: Cover logistics and delivery. - **Marketing & Sales Costs**: Covering salaries, marketing campaigns, and travel expenses.	- **Unit Sales**: Primary revenue stream from selling the biosensor - **SaaS Revenue**: Additional income through an app subscription, offering real-time tracking and result interpretation. - **Insurance Reimbursements**: Revenue generated via insurance coverage, enhancing product accessibility and affordability for patients.

Figure 12. Business Model Canvas

5.1 Introduction

Chronic Kidney Disease in the U.S.

In 2022, more than 1 in 7 adults – about 35.5 million people or 14% of the U.S. population – were estimated to have chronic kidney disease (CKD) according to the Centers for Disease Control and Prevention [24]. Even more concerning is the lack of awareness, with as many as 9 in 10 adults who do not know they have CKD and about 1 in 3 adults do not realize how they have CKD [24].

End-stage CKD affects about 750,000 people in the U.S. annually, with a significant number of cases resulting from undiagnosed or poorly managed earlier stages [23]. The high incidence of late diagnosis not only impacts patient outcomes, but also places a considerable financial burden on the healthcare system due to the costly nature of dialysis and transplant procedures.

Early detection and consistent monitoring are crucial to preventing the progression to kidney failure and improving patient prognosis. The demand for treatment of CKD will grow as the older generations continue to age and awareness of the disease increases. A biosensor product could greatly contribute to the success of treatment plans and slow the progression of the disease.

SensTech's Business Plan Overview

SensTech's business plan is strategically designed to address the critical needs of CKD patients in the U.S. market. By leveraging advanced technology, a contract with Phillips-Medisize, and an efficient manufacturing process located in Arizona, the team aims to deliver a high-quality, affordable product to the U.S. population. The pricing strategy is estimated to be set at $200 per unit, along with a Software as a Service (SaaS) model charging $5 per month for app-based results tracking. SensTech's comprehensive plan includes substantial investments in R&D, meticulous regulatory compliance, and

robust marketing and sales efforts. Through a mix of non-dilutive grants and venture capital funding, SensTech is committed to maximizing stakeholder outcomes by ensuring financial viability, fostering innovation, and improving patient outcomes. The team's goal is to not only achieve profitability, but to also make a significant impact on the management and treatment of CKD.

5.2 Stakeholder Desirability

Customers—High-Risk and Early-Stage CKD Patients

The primary customers are individuals in the U.S. suffering from early-stage CKD, or those at high risk for CKD due to a family history of kidney disease or pre-existing conditions such as diabetes, high blood pressure, or cardiovascular disease. Ideal users are individuals with CKD who are either covered by insurance plans that reimburse for monitoring devices or are willing to pay out-of-pocket for the convenience and improved health management that SensTech's biosensor offers.

Current methods for measuring creatinine levels are time-consuming and often inconvenient, necessitating frequent visits to healthcare facilities for blood tests. Furthermore, these patients are usually working closely with their primary care physicians and specialists to monitor their tendency toward CKD and would respond positively to a specialist who would recommend using this device. The opportunity to monitor their creatinine and detect CKD in the early stages enables them to take corrective actions in diet, lifestyle, and medications promptly, potentially slowing the rate of disease progression. And patients can accomplish this testing at home, without having to fast the day before, go to a crowded blood-drawing laboratory, and wait for results. The patients benefit from a simple system to use, the security of constant monitoring, and the chance for a better quality of life.

Customers—Nephrologists & Endocrinologists

Nephrologists are looking for quality, consistent, and frequent monitoring of their patients' creatinine to help with diagnosing early-stage kidney disease as well as establishing a baseline creatinine level. Endocrinologists also monitor their diabetic patients closely for kidney function. Both specialties would be very interested in a creatinine biosensor to add to their patients' treatments. These physicians would be an influential driver for patients to purchase and use SensTech's biosensor.

Stakeholders

Both physicians and patients are stakeholders as well as the customers and their benefits are described in the previous section.

- Hospital Management – Hospital administrators are looking for ways to improve patient outcomes which can lead to cost savings and higher patient satisfaction. The adoption of the biosensor can streamline laboratory operations and reduce costs associated with invasive tests.
- Insurance Companies and Employers – They seek low-cost ways to diagnose early and reduce severity of long-term chronic diseases such as CKD, delaying the need for costly interventions such as dialysis and/or organ transplantation with accompanying hospitalization.
- Taxpayers – They benefit from reduced healthcare costs minimizing tax increases and providing improved public health outcomes and better allocation of public health resources.

Rules & Regulations

Navigating the regulatory landscape is critical to the success of SensTech's biosensor. This would require working closely with the U.S. Food and Drug Administration (FDA) to understand their regulations and expectations to approve the diagnostic. The regulation finalized on Monday, April 29th, 2024, brings tests developed by laboratories under the control of the FDA. As with any new medical diagnostic introduction, FDA approval requires rigorous testing and validation to demonstrate the safety, accuracy, and efficacy of the biosensor. SensTech will adhere to data privacy laws, such as the U.S. Health Insurance Portability and Accountability Act (HIPAA), to protect Personal Health Information (PHI) as well as Personally Identifiable Information (PII) collected through the CreatConnect app. By maintaining high standards of regulatory compliance, the team aims to build trust with all stakeholders and execute a smooth market entry and prompt product adoption.

Value Proposition—Analysis of Competitors and Their Products

The two tests that physicians currently order for detecting the status of a patient's kidney disease are:

1. Serum Creatinine and Estimated Glomerular Filtration Rate (eGFR) conducted by drawing a fasting patient's blood and analyzing it in a laboratory, and the second is
2. Urine Albumin-to-Creatinine Ratio (uACR), conducted by inserting a test strip into a patient's urine sample. This test is secondary to the creatinine test and done in a lab setting.

The traditional methods above, while accurate, are inconvenient for patients, resulting in poorer compliance to essential testing. Results can take days to be reported and can slow the response to implement treatments. These tests are a one-time measurement, leading to missed diagnoses of CKD.

SensTech's biosensor differentiates itself by offering a highly accurate, user-friendly, monitoring system that patients can use from home. The immediacy of real-time results combined with the convenience of a mobile app for tracking and sharing data set the product apart from any other existing solutions. Additionally, the focus on a seamless user experience and integration with healthcare providers' systems enhances the overall value proposition for all stakeholders involved.

5.3 Business Feasibility

To support the development, manufacturing, and up-scaling of the SensTech's biosensor, the team needs access to advanced technology, skilled researchers, regulatory experts, manufacturing facilities, distribution networks, and marketing expertise.

- *Phillips-Medisize* is a contract design and manufacturing organization with the expertise in supply chain sourcing to support the team's goal of providing a high-quality, scalable biosensor. They have extensive experience in bringing medical devices to market, offering end-to-end solutions from development to distribution. This relationship will ensure that the biosensor is produced at the highest quality standards and is scalable to meet demand.
- *Fish & Richardson,* a well-recognized, international intellectual property law firm, has the appropriate expertise to ensure SensTech's intellectual property is protected and to address any future attempts at infringement of the team's patents.
- *Deloitte's Healthcare and Life Sciences Consulting Group* can help us navigate the regulatory landscape in the U.S. and other countries as the team grows. They can also help with "go-to-market" strategies as SensTech considers sales and distribution.
- *Blue Cross Blue Shield's Association* is a leader in the healthcare insurance industry and insures 1 in 3 Americans. Their consulting involvement will help to facilitate insurance coverage, making SensTech's biosensor accessible to patients.

These strategic alliances will be established through mutually beneficial agreements that outline the responsibilities and expectations for each party. Phillips-Medisize will benefit from a long-term manufacturing contract, while SensTech gains access to their state-of-the-art facilities and expertise. Regular meetings, transparent communication, and performance reviews will be conducted to maintain strong relationships and alignment with SensTech's business goals. All of these allies have international capabilities which would ultimately support SensTech in international expansion.

Key Activities & Safeguards

SensTech's marketing and sales strategy will focus on creating awareness, driving adoption, and ensuring customer satisfaction. This strategy would be implemented when all the regulatory approvals have been obtained, insurance companies are onboard, marketing materials, videos, and online presence are ready to launch, and the product inventory is sufficient to meet supply.

SensTech recommends a phased roll-out based on target audiences in the following sequence:

1. Introduce the biosensor to nephrology MDs at large practices such as Mayo Clinic. SensTech will ask them to be SensTech's product assessment team and to explore how the biosensor could influence the CKD treatment protocols especially for those with early-stage CKD. This might be an opportunity for them to prepare a paper and present the topic at the national American Society of Nephrology Meeting called "Kidney Week." The team would also have a booth at the associated trade show and offer free samples, so interested physicians could test. Nephrologists are truly the opinion leaders in this market and once they are comfortable with the quality and reliability of the biosensor, other medical practices will follow.

2. Provide an educational video program for nephrology patients explaining how deadly CKD can be when untreated. As the nephrologists introduce the product, they can recommend that the patients start by viewing the educational segments, then purchase the monitoring system.
3. Introduce the biosensor to endocrinologists and their patients. The paper can be presented at their annual professional meeting and trade show again with the booth and samples.. The educational program will help the diabetes patients understand the signs of CKD and the risks of not addressing the disease in early stages. This program could reach many of the individuals who might already have CKD and are not aware.
4. Introduce the biosensor to nephrology physician assistants who have their own organization and to other nephrology specialists such as those running the dialysis centers.
5. Create a membership program for patients so if they order the sensors regularly – they receive a discount on future purchases. Also used sensors can be returned to the manufacturing facility for recycling in a postage paid envelope.

Another key element of the roll-out will be a strong sales force to introduce and demonstrate the product to physicians. Ideal hires would be experienced professionals from dialysis centers, and nurses with experience in nephrology.

SensTech's patent strategy involves filing for both utility and design patents to protect the team's biosensor technology and its unique features. The team will engage with a reputable intellectual property law firm, such as Fish & Richardson, to assist with the patent filing and management process. The timeline for SensTech's patent plan is as follows:

- Months 1-3: Conduct a thorough patent landscape analysis to identify existing patents and ensure SensTech's biosensor is unique.
- Months 4-6: Draft and file provisional patents for the core technology and design.
- Months 7-12: File non-provisional patents based on feedback from provisional patent applications.
- Years 2-3: Pursue international patent protection to safeguard SensTech's technology in key markets beyond the U.S.

The regulatory process for a Class II biosensor involves several critical steps, each with specific timelines to ensure the device meets FDA safety and efficacy standards. Initially, engaging with the FDA through a Pre-Submission meeting is crucial to align development plans with regulatory expectations. This phase typically takes 3-6 months. Following this, an Investigational Device Exemption must be obtained before commencing clinical trials, this spans approximately 6 months. The clinical trial phase is segmented into three parts: Phase I focuses on safety and basic functionality and lasts about 6-12 months and Phase II evaluates effectiveness over another 12-24 months. After successful trials, a 510(k) submission is required to demonstrate substantial equivalence to a predicate device with an FDA review period of 3-6 months. Post-market surveillance is necessary to monitor performance and ensure continued compliance. From the Pre-Sub meeting to FDA clearance, the entire process will span 3-5 years, depending on device complexity and regulatory efficiency.

The team is committed to minimizing the environmental impact of SensTech's biosensor. This includes using eco-friendly materials, optimizing manufacturing processes to reduce waste, and developing a recyclable product. This also includes adherence to the Fair Labor and Standards Act, and creating a safe working environment for all employees involved per Occupational Safety and Health Administration standards.

SensTech's distribution channels will include direct sales to healthcare providers, relationships with pharmacies, and an online platform for direct-to-consumer sales. This multi-faceted approach makes SensTech's biosensor easily accessible to patients, and the team's customer relationship management system will help maintain engagement and satisfaction.

5.4 Financial Viability

To fund the development of SensTech's creatinine biosensor, the team can explore a mix of non-dilutive and dilutive funding opportunities. Non-dilutive funding sources include grants from

Cornell University, such as the Cornell Technology Acceleration and Maturation fund, which supports early-stage research. Additionally, New York State offers various grants. Federally, SensTech can apply for Small Business Innovation Research and Small Business Technology Transfer grants, which provide significant non-dilutive capital for research and development. Other non-dilutive grants can be sourced from foundations and industry organizations dedicated to advancing medical technology. Regarding dilutive funding, venture capital firms specializing in medical devices and health technology offer substantial investment opportunities with strategic industry insights and connections, as well as corporate venture capital arms of major healthcare companies. Diverse funding streams can create robust financial backing for SensTech's project while minimizing equity dilution.

SensTech's strategic alliance with Phillips-Medisize will significantly streamline the production and distribution of the biosensor. By locating the team's manufacturing plant in Arizona, SensTech can take advantage of favorable taxation and a vibrant innovative ecosystem, resulting in an estimated manufacturing cost of $55/unit according to other industry averages. Assembly costs, including space, labor, and training, will add an additional $15/unit, while distribution expenses for shipping, warehousing, and transportation will be around $3/unit. Marketing and sales costs, encompassing sales salaries, marketing campaigns, and travel, will amount to about $10/unit. Initially, the total landed cost per unit will be $85, with an expectation to reduce this to $55 over the coming years as efficiencies improve. To ensure a sustainable business model that maximizes return on investment, supports ongoing R&D, and expands SensTech's reach across the U.S., the team plans to price the biosensor at $200/unit. Additionally, a SaaS model will be used for the accompanying app, CreatConnect, which tracks biosensor results in real-time. The app will be available for a subscription fee of $5/month, providing continuous support and data management for users.

Profit & Loss Statement

The team's financial projections for the creatinine biosensor are based on a comprehensive assessment of costs, revenue potential, and strategic pricing. The initial costs involve significant investments in R&D, with $2 million allocated in 2025, increasing incrementally until 2029 to account for extensive clinical trials, FDA regulatory compliance, and product refinement. The anticipated ramp-up in sales

	2024	F2025	F2026	F2027	F2028	
Revenue ($)	$ -	$ -	$ -	$ -	$ -	
R&D Costs ($)	$ 2,000.00	$ 1,500,000.00	$ 2,000,000.00	$ 2,500,000.00	$ 3,000,000.00	
Manufacturing Costs ($)	$ -	$ -	$ -	$ -	$ -	
Distribution Costs ($)	$ -	$ -	$ -	$ -	$ -	
Marketing Costs ($)	$ -	$ -	$ -	$ -	$ -	
Sales Team Costs ($)	$ -	$ -	$ -	$ -	$ -	
Operational Costs ($)	$ -	$ 500,000.00	$ 700,000.00	$ 700,000.00	$ 700,000.00	
Total Costs ($)	$ 2,000.00	$ 2,000,000.00	$ 2,700,000.00	$ 3,200,000.00	$ 3,700,000.00	
Net Profit ($)	$ (2,000.00)	$ (2,000,000.00)	$ (2,700,000.00)	$ (3,200,000.00)	$ (3,700,000.00)	

Profit & Loss Statement	F2029	F2030	F2031	F2032	F2033	F2034
Revenue ($)	$ -	$ -	$ 5,000,000.00	$11,000,000.00	$23,000,000.00	$49,000,000.00
R&D Costs ($)	$ 4,000,000.00	$ 5,000,000.00	$ 1,000,000.00	$ 1,000,000.00	$ 1,000,000.00	$ 1,000,000.00
Manufacturing Costs ($)	$ -	$ -	$ 2,000,000.00	$ 4,000,000.00	$ 8,000,000.00	$16,000,000.00
Distribution Costs ($)	$ -	$ -	$ 500,000.00	$ 1,000,000.00	$ 1,500,000.00	$ 2,000,000.00
Marketing Costs ($)	$ -	$ 1,000,000.00	$ 2,000,000.00	$ 3,000,000.00	$ 1,000,000.00	$ 1,000,000.00
Sales Team Costs ($)	$ -	$ 250,000.00	$ 750,000.00	$ 1,000,000.00	$ 1,000,000.00	$ 1,000,000.00
Operational Costs ($)	$ 1,000,000.00	$ 1,200,000.00	$ 1,500,000.00	$ 1,500,000.00	$ 1,500,000.00	$ 1,500,000.00
Total Costs ($)	$ 5,000,000.00	$ 7,450,000.00	$ 7,750,000.00	$11,500,000.00	$14,000,000.00	$22,500,000.00
Net Profit ($)	$ (5,000,000.00)	$ (7,450,000.00)	$ (2,750,000.00)	$ (500,000.00)	$ 9,000,000.00	$26,500,000.00

Figure 13. Profit/Loss Spreadsheet

from $5 million in 2031 to $49 million by 2034 reflects the team's market penetration strategy and growing consumer base. The operational costs include a detailed breakdown of manufacturing, distribution, marketing, sales, and operational expenses, with a clear path towards profitability from 2033, as the team projects a net profit of $9 million. By 2034, with a projected net profit of $26.5 million, the financial model demonstrates the biosensor's potential for significant financial success. As the team leverages economies of scale, product-led marketing, and deepens ties with allies, suppliers, and distributors, the team's landed costs should fall and margins will grow. After 2034, exponential growth is expected as patients, healthcare professionals, and other stakeholders grow their confidence and awareness for SensTech's product.

6. Team and Support

Supervisor and Coach:

Nadine Padillo – The team coach who provided guidance and advice from her own experiences (she participated in the SensUs 2021 competition) by meeting with the research and development team frequently throughout the year.
Dr. Warren Zipfel – The supervisor of the team who aided in experimental design, execution, and overall guidance. Also, provided lab space and frequently met with the team to go over the biosensor.

Team Captains:

Lily Blanton – President of the team who was responsible for SensUs communication and Google Classroom submissions. She was also on the wet lab subteam working in the lab and contributing to write ups and submissions.
Emily Chen – Vice president of the team who was responsible for team organization and obtaining project team status at Cornell University. She was also on the wet lab subteam working in the lab and contributing to write ups and submissions.

Research & Development:

Puloma Bishnu – One of the leads responsible for coordinating meetings with Nadine and contributing to write ups throughout the year. Led research & development meetings September - December going over literature review and brainstorming an idea to pursue. She is next year's president.
Adelin Chan – On the wet lab subteam working in the lab and contributing to write ups and submissions. She is next year's vice president.
Alexander Harris – On the wet lab subteam working in the lab and contributing to write ups and submissions. He is next year's wet lab subteam lead.
Aleksandra Marjanovic – One of the leads responsible for coordinating meetings across research & development as well as contributing to write-ups and submissions. Also led work on hardware and data collection.
Larson Ortiz – On the dry lab subteam working in the lab and contributing to write ups and submissions.
Spoorthi Patil – One of the leads who was responsible for coordinating meetings with Dr. Zipfel and Nadine. Led research & development meetings throughout the year going over literature review, working on experiments, and writing reports. Also delegated tasks across the subteam.
Tanay Vedartham – On the dry lab subteam working in the lab and contributing to write ups and submissions.
Alice Wei – On the dry lab subteam working in the lab and contributing to write ups and submissions. She is next year's dry lab team lead.

Business & Outreach:

Grace Chu – Current business and outreach subteam lead responsible for coordinating team activities. Responsible for overseeing semester & annual plans along with completing any necessary deliverables.
Jad Kassir – Previous business and outreach subteam lead responsible for developing the business plan and entrepreneurship deliverables. He also supports fundraising and financing activities.
Dylan Park – Subteam member responsible for helping leads with social media posts, socials, website, and fundraisers.
Kevin Zhang – On the business and outreach subteam responsible with managing the club finances and administrative needs, including CampusGroup. He also supports the subteam with any tasks that need to be completed.

7. Final Remarks

The SensTech team plans on experimenting with more aptamers to test if they are specific enough to creatinine. If it is not, the team plans to explore antibodies as a potential biorecognition element. Additionally, the team wants to pursue a full-fledged proof of concept where the hardware of the device is fully optimized, with the app properly linked and able to produce a user-friendly output. Working on this endeavor while discerning the best way to detect creatinine on a surface will be the main project for the next year.

The team would like to thank Dr. Zipfel and Nadine Padillo for advising throughout this entire process, from getting the team approved to enter the competition to actually testing and experimenting in the lab. The progress SensTech has made as a team to raise money, obtain lab spaces, and become officially recognized as a research team on campus has been incredible and is a testament to the cooperative efforts that the team and advisors have made to ensure the team's success. Lastly, the team would like to thank the SensUs committee for granting us the opportunity to compete for the first time. The SensTech team is incredibly excited to see where this next year will go!

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Appendix

A1 User Costs

	Year 1	Year 2	…	Year 5
1 year subscription for CreatConnect App	$60	$60	$60	$60
CreatConnect Biosensor	$200	-	-	-
Total Lifetime Cost After Year X (Uninsured)	$260	$320	…	$620
60% Health Plan Coverage	$104	$128	…	$248
80% Health Plan Coverage	$52	$64	…	$124

Figure A1. Money spent out of pocket after X number of years on the CreatConnect biosensor + app system with varying insurance coverages.

A2 Customer Journey

App Interface (Patient)

Upon opening the app, the patient chooses if they are a Stage 1, Stage 2, Stage 3 (Early) CKD patient or an At-Risk patient. This will determine the reference ranges used for reports in the app for both user and doctor.

A2.1 At-Risk Patient

Jane is a 47 year old female dealing with obesity, hypertension, and diabetes with a family history of kidney disease. Her primary care provider informs her that she is at high risk for CKD and will need to monitor her creatinine levels on a regular basis. She is referred and ultimately has an appointment with an endocrinologist. The clinician recommends she utilizes CreatConnect, an easy to use device that takes a drop of her blood and outputs her creatinine level in 30 seconds in the CreatConnect app on her phone. She'll be able to monitor her average creatinine level on a weekly, monthly, and yearly basis and share her data with her endocrinologist at every appointment with the tap of a button.

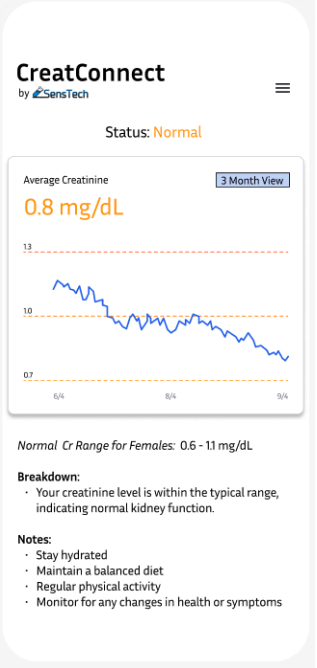


Figure A2. (Right) The app screen for a patient who has a normal Cr status over the course of 3 months. Created in Figma.

Jane decides to check her creatinine level for today (Figure A3). This is not the first time Jane has seen an abnormal result. She has not scheduled an appointment because it is hard to get time off of work and wanted to wait to see if her levels got worse. She decides to check her creatinine levels from the past 3 months (Figure A4).

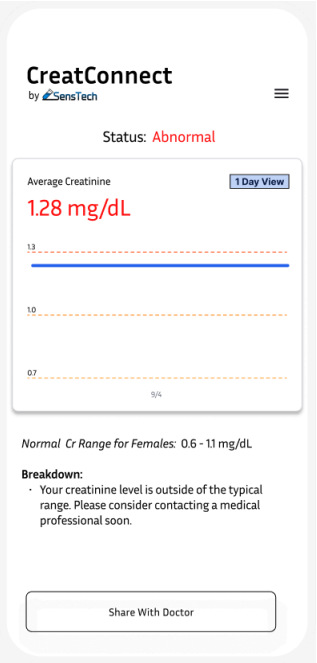


Figure A3. Daily view of Cr level.

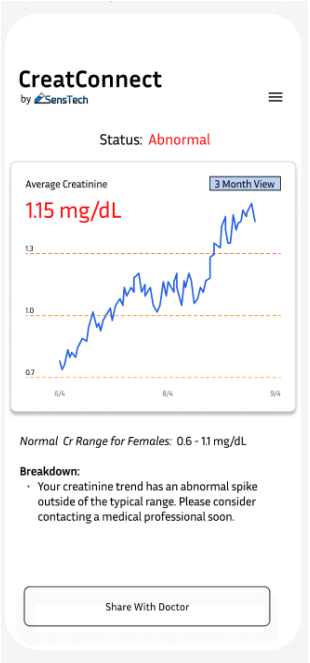


Figure A4. 3-month view of Cr levels.

Jane notices that it has been some time that she has been recording abnormal results and her creatinine levels have been trending upwards. This raises serious concern for Jane and she decides to promptly schedule an appointment with her endocrinologist. She sends an alert for her medical profile to her endocrinologist using the "Share With Doctor" button. Her provider will now be able to quickly pull up the specific abnormal result Jane was concerned about during their visit.

App Interface (Doctor)

The endocrinologist meets with Jane Doe for their appointment, where Jane explains that she scheduled the appointment because she noticed abnormal creatinine levels for some time. The clinician pulls up the app on their work phone and clicks Jane Doe under Abnormal Alerts (Figure A5) and is brought to the page that Jane sent an alert for (Figure A6).

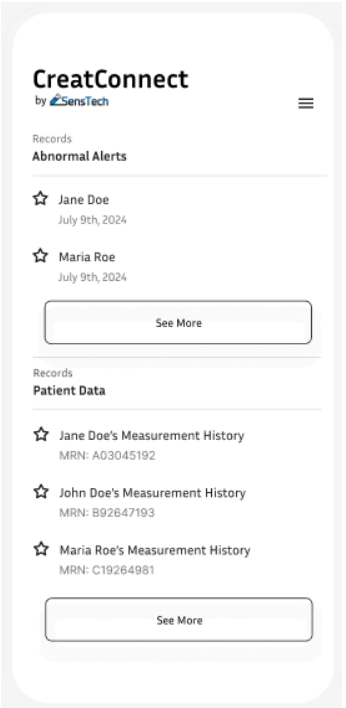


Figure A5. (Left) Physician homepage.

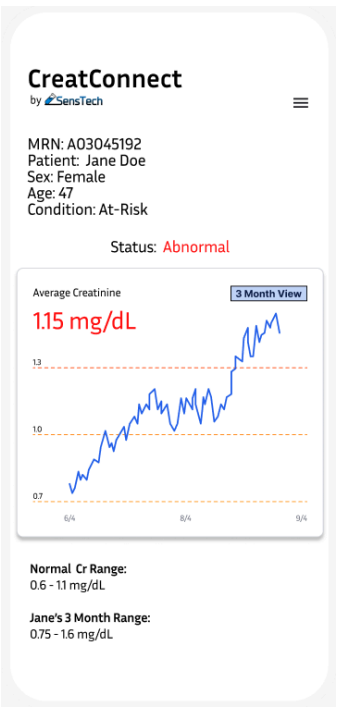
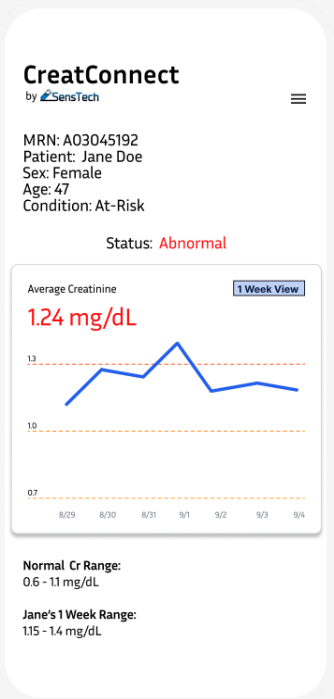


Figure A6. (Right) Result sent by user to clinician.

The endocrinologist notices the uptick in creatinine levels past the normal range that had occurred recently, and decides to look at the weekly view for the past recent week (Figure A7).



Based on these abnormal levels, the clinician orders blood work which confirms the results from CreatConnect. The clinician diagnoses Jane with Stage 1 CKD and works with her to develop a maintenance plan to prevent progression of the disease.

A2.2 Stage 1 CKD Patient

Jane continues to use CreatConnect to monitor how her creatinine levels change as she starts on the plan she made with her endocrinologist. Because she is already diagnosed with Stage 1 CKD, her baseline range will always be outside the normal range of creatinine for females. She goes to Settings to switch her condition from "At-Risk" to "Stage 1 CKD." Now, whenever she checks her creatinine level, it will be compared against the creatinine range for Stage 1 CKD patients, and can monitor if her levels increase past the upper limit of the typical creatinine range.

Figure A7. (Left) Weekly view of Cr level.

A4 SWOT Analysis

Along with the ideation and fabrication of the biosensor, a SWOT analysis is necessary in order to strategically evaluate SensTech's position in the market and growth potential. By identifying **S**trengths, the team can utilize their unique skills and gain a competitive edge in the industry. Understanding **W**eaknesses allows the team to not only address possible shortcomings but also improve different aspects. By analyzing **O**pportunities, the team can continue to adapt to technological or market changes and push for growth. Lastly, recognizing **T**hreats prepares the team to navigate challenges from the market, competitors and regulatory changes. By conducting this thorough analysis, SensTech is able to optimize strategies, make better decisions, and be more successful in the market.

Strengths

1. Cornell SensTech is composed of 14 students from 7 different majors. Having individuals from business, biomedical engineering, information science, and various other disciplines allows the team to not only have a wider skill set when problem solving but also provide unique perspectives when improving certain aspects of the biosensor. One example of this was a dry lab member introducing new ideas utilizing his computer science background that aimed to improve the user experience across research and development. As most of the team has more experience in scientific research, this was an extremely valuable perspective.
2. As of late Spring 2024, Cornell SensTech was established as a College of Engineering (CoE) student project team with conditional status. By moving from an independent club to a student project team, the team is able to access the resources of the CoE such as workshops, meetings with project team advisors, networking with established project teams, and future funding. This past year, the team raised a majority of their funds through fundraising so being able to request funds in the future will allow the team to have access to more materials.
3. Cornell SensTech was recently established as a club in 2023 and has come a long way since the original founding four members. The team has come across many ups and downs throughout their journey but have continually been resilient and emphasize the idea of redirectioning rather than allowing hurdles to stop them.

Weaknesses

1. Being a new team is a double-edged sword because despite SensTech members facing challenges head-on, the team has focused a lot of its efforts this past year in setting up a

strong foundation such as establishing lab spaces, club culture and an accountability system which has led to less time being spent on the development of the biosensor.
2. Half of the team members will be in their final year at Cornell in 2024-25 so the team has to retrain new members and this may temporarily slow down progress.
3. Despite the biosensor being ideated, the creation of the biosensor is in its preliminary steps and will have to go through many iterations before it is presentable in the market or to stakeholders.

Opportunities

1. Since CKD is a prevalent issue and a reliable continuous biosensor that detects creatinine is lacking in the market, this creates a need for SensTech's biosensor.
2. By working with CoE project team faculty, the team is planning on using their resources for setting up a budget and reaching out to potential company sponsors. By collaborating with allies in and surrounding Ithaca, NY, the team can potentially fundraise for biosensor development.
3. This year, SensTech mainly reached out to on-campus resources to establish a presence on campus; because of this, the team did not have as much bandwidth to create a strong relationship with companies from the SensTech Alliance meetings.

Threats

1. There are many papers and resources talking about OIRD and anti-creatinine DNA aptamers, but little work has been published on combining these two technologies to create a biosensor. With such a novel idea, the team has and will continue to encounter many challenges that have not been navigated before.
2. The patient may have trouble obtaining interstitial fluid from themselves and would possibly require some training to do so.
3. Although the team is experimenting with a novel idea, the biosensor setup currently would require an oscilloscope and for users to understand how to use the device.