Thesis Project Portfolio

Design of an mRNA Vaccine Manufacturing Platform to Target *M. Tuberculosis*

The Price of Insulin: Who Gets to Decide?

An Undergraduate Thesis

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Sociotechnical Synthesis

The main motivation behind my technical and STS projects is to improve healthcare accessibility. With my technical project, the goal is to design an mRNA vaccine manufacturing facility to treat tuberculosis worldwide. By modeling the production blocks and understanding economic implications, I designed a process that reached demand for tuberculosis treatment both domestically and internationally. My STS research project looks to explain the increase of insulin prices in the United States. By going through current policy, I look to find where accountability should be held to ensure insulin accessibility for all patients.

My technical report outlines the design and operational framework for an mRNA vaccine manufacturing facility, specifically targeting *Mycobacterium tuberculosis*. The facility is designed to produce 10 million doses of vaccine annually. The production process involves mRNA synthesis, lipid nanoparticle (LNP) encapsulation, purification, and sterile filtration, ensuring high product quality and regulatory compliance. The vaccine is intended for healthcare workers and travelers in the U.S., as well as high-incidence regions such as Southeast Asia and Africa, which account for 70% of global TB cases. The facility will produce 576 grams of mRNA annually to be sent to external fill-to-finish operations, sufficient for 10 million vaccine doses. This includes allowances for fill-to-finish losses and ensures consistent supply to domestic and international markets. During the process, *in vitro* transcription is employed to produce mRNA strands using a T7 RNA polymerase system. A co-transcriptional capping process ensures high efficiency and stability of the mRNA product. The mRNA is encapsulated in lipid nanoparticles using a confined impinging jet mixer, providing protection against degradation and facilitating cellular delivery. Sequential chromatography steps— affinity chromatography and anion exchange chromatography— remove impurities, achieving a final mRNA yield of 38%.

Finally, two filtration steps ensure sterility and bioburden reduction, with minimal product loss. The production design ensures that demand is met and accessibility is further increased by marketing vaccine doses as less expensive compared to domestic prices for developing countries with high-incidence. My project ensures an efficient treatment platform for a highly prevalent disease, while also removing access barriers during the distribution process. The facility adheres to stringent regulatory standards for Good Manufacturing Practices (GMP). Processes are designed to meet FDA and WHO guidelines for vaccine production, ensuring safety, efficacy, and environmental sustainability. This facility represents a significant advancement in vaccine manufacturing technology. By leveraging modular mRNA synthesis processes and scalable LNP encapsulation techniques, it addresses the urgent need for an effective TB vaccine while maintaining flexibility for future applications against other infectious diseases.

My STS report examines the policy oversights behind the increasing prices of insulin in the United States. Through policy analysis of the 2022 Inflation Reduction Act (IRA), I show how the IRA and other past policies have systematically excluded those not insured by Medicare and failed to hold the organizations that drive the increase in insulin prices accountable. Specifically, I show how past economic analysis reveals that pharmaceutical benefit managers (PBMs) have consistently been profiting more as insulin prices increase, with drug manufacturers decreasing their shares over the same time period. PBMs have gained immense power in the drug distribution process through negotiating rebates and fees and through vertical integration. Without proper accountability, this power will go unchecked and prices of insulin will only increase. I propose that the reason that full accountability is not held is due to political visibility; policy has historically targeted drug manufacturers and the infamous “Big Pharma,” since it is a more visible component of the drug distribution process. However, with little

information being shared on the role of PBMs to voters, it is hard to motion for bipartisan support of laws that protect voters from discrepancies of which they are unaware. To counteract this issue, I propose that those representing the public ensure that voters are educated and aware of the role of PBMs in drug prices to increase support of bipartisan acts such as the Patients Before Middlemen (PBM) Act.

My STS and technical reports have given me the opportunity to look for improvements and reform on both scientific and political levels. The technical report deepened my understanding of the unit operations involved within the vaccine manufacturing process along with the costs of upkeep, raw materials, labor, and utilities. I now understand all of the moving parts of the manufacturing process and the costs necessary to uphold the process and reach production demand. In determining the value of the vaccine domestically and internationally, my STS report demonstrated the importance of prioritizing accessibility over profit. On the other hand, my STS report allowed me to recognize the healthcare accessibility I often take for granted. In learning more about the experience of marginalized patients accessing insulin, I realize I underestimated the access to treatment my family and I have. My technical report gave me insight into the relative cost of manufacturing, which allowed me to narrow down outside factors affecting insulin price, since the price of manufacturing has stayed relatively the same over the past years. Both projects changed my perspective as a scientist and a voter, showing me the importance of technologies and policies that prioritize the wellbeing of others rather than profitability.