Sociotechnical Synthesis

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(Executive Summary)

A Deeper Dive into Vaccine Manufacturing

The global COVID-19 pandemic is far from over. To date, there have been 6.2 million deaths from COVID worldwide. Only 15% of the population in low-income countries have received at least one vaccine dose. In high- and upper-middle-income countries, this value is 80% of the population having received at least one dose, showcasing the vaccine distribution inequity. The presence of an unvaccinated population increases the chance of variants emerging as seen with the highly transmissible Omicron variant and its recent subvariant BA.2. One crucial factor contributing to these inequalities is that COVID-19 vaccines based on mRNA technology require storage at -70 degrees Celsius, posing a challenge because many low-income countries do not have the required cold chain infrastructure. Sanofi-GSK and Novavax have developed efficacious subunit vaccines that can be stored in refrigerators, proving that something can be done about this issue.

The technical portion of my thesis produced is designing a manufacturing facility in Cape Town, South Africa to produce a recombinant spike protein-based SARS-CoV-2 vaccine for five years using the Baculovirus Expression Vector System (BEVS) platform for storage at normal refrigeration temperatures. My team and I will be producing four hundred million doses (4 kg antigen) per year. One dose will include a 0.25 mL liquid suspension with 10 µg antigen and 0.25 mL ASO3 (squalene-based emulsion adjuvant), creating a 0.5 mL vaccine dose. The facility will achieve an IRR of $15.6 billion at 15% interest rate. With a fixed capital investment of $50 million, a payout can be expected starting after just 24 days of operating the plant. Charging $15 per dose of vaccine will result in $6 billion in revenue. Accounting for fixed capital costs, operating costs (labor, materials, utilities), and other taxes, our net profit after the first year will be $4.6 billion. Thus, the project is extremely profitable, and we recommend the building of this facility to increase the availability of COVID-19 vaccines in the African continent. The facility will use single-use bioreactors to produce 0.3 kg of intracellular spike protein per batch in baculovirus-infected Sf9 insect cells. Downstream processing will have an overall recovery of 44.5%, yielding 0.1335 kg of purified and formulated spike protein per batch. Between the upstream, downstream, formulation and filling processes, a single batch takes 24 days to complete. To successfully meet our annual production target, thirty batches will be completed each year, with each manufacturing campaign staggered eight days apart. The facility will be operational for 256 days each year, leaving more than enough time to accommodate out-of-spec batches, malfunctioning equipment, and other process deviations.

In my STS research, I focus on the ethical practices of using squalene in vaccines. Vaccines are typically composed of an antigen solution that will eventually be mixed with an adjuvant emulsion to create a single vaccine dose. More recently with COVID-19, vaccines are being formulated with squalene-based adjuvants such as the AS03 manufactured by GSK, which my team uses in our COVID-19 vaccine, which reduces the amount of antigen needed by enhancing the body's immune response to the vaccine through enhancing antigen persistence at the injection site. Squalene (shark liver oil) is an organic substance obtained from sharks, where they must be killed to extract it from their liver. While only 1% of commercially obtained squalene is currently used in vaccines, harvesting sharks for this purpose has serious potential ecological consequences and this number will only continue to rise due to demand. Squalene got its start as being a well-known key ingredient in many high-end cosmetic products, where its oil is highly desired for its moisturizing and restorative properties. With global demand for squalene being so high overall, this results in around 6.6 million sharks captured and killed each year, with many of these sharks becoming endangered. Shark squalene is being used for its cost effectiveness and how easy it is to get. Many pharmaceutical companies such as GSK and Seqirus currently use shark-based squalene adjuvants and there have been claims that COVID vaccines using shark-based squalene adjuvants will kill as many as 500,000 sharks. With many alternatives available such as the semisynthetic pathway through sugar fermentation developed by Amyris and extracting squalene from leftovers of olive oil refining, there is hope of moving away from animal-derived products for the pharmaceutical industry in the near future.

In combination, the technical project and STS research directly impact one another as a closer look should be taken into the ingredients being used in vaccines rather than just picking the most convenient, accessible option available. Given the immediate response that was necessary from all organizations and society involved into the COVID-19 pandemic, a lot can be learned and the use of shark squalene in vaccines is just one huge takeaway that can hopefully be moved away from. It shows just how much room the pharmaceutical industry still must grow and that it will constantly be trying to improve and be more efficient in the processes as more research and findings are discovered every day.