# Prospectus

**Novel Design of the RTS,S Malaria Process Train Employing Single Use Systems**
(Technical Topic)

**Feasibility Analysis of Supercapacitive Vehicle Adoption**
(STS Topic)

By

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## Introduction to Novel Design of the RTS,S Malaria Process Train Employing Single Use Systems

One of the most prolific problems in sub-Saharan Africa is the rampant contraction of malaria in poverty-stricken regions (Patel 2018). Contracting malaria puts a financial and physical burden on people who are infected as well as those around them (World Health Organization, 2018). Malaria is mainly contracted from mosquito bites that pass on a bloodborne parasite, or plasmodium, and there are few practices that can effectively prevent the infection from occurring. One possible solution would be a vaccine against malaria, such as the RTS,S vaccine produced by Glaxo-Smith-Kline (EMA, 2015). It has been approved for use by the European Medicine Agency (EMA) and could prevent a significant number of cases of malaria if distributed and administered to at-risk communities.

Because the region is so poor, it is beneficial to produce the drug as cheaply as possible, and so different manufacturing strategies are being evaluated to reduce the cost to the consumer or the charities that help pay for the vaccines. One potential method to reduce production costs is to implement a manufacturing process using single use systems (Langer & Rader 2018). Single use systems are gaining popularity in the pharmaceutical manufacturing sector because these systems have the potential to significantly reduce the complexity and cost of manufacturing lines by reducing the amount of necessary cleaning performed on process equipment. The group will set out to model a single use RTS,S production line that can produce the vaccine for $4 per dose as opposed to the current cost of $5 per dose (Kelland, 2015).

**Novel Design of the RTS,S Malaria Process Train Employing Single Use Systems**

In 2017 alone, malaria infections killed around 435,000 people in sub-Saharan Africa (World Health Organization, 2019a). To combat the widespread harm that malaria infections cause to populations in sub-Saharan Africa, the pharmaceutical company GlaxoSmithKline recently released an antimalarial vaccine called Mosquirix. It was approved by the European Medicines Agency (EMA) for market after being put through three phases of clinical trials (European Medicines Agency, 2015). These rigorous trials determined its safety and efficacy in children from sub-Saharan Africa ranging in age from 6 weeks to 17 months after administration of three or four doses. Health care access in this area is inadequate because the poverty rate in sub-Saharan Africa averages 41% (Patel, 2018). The combination of the dosage requirement for this vaccine and the poverty rate in sub-Saharan Africa makes Mosquirix inaccessible in areas where it is most needed. The aim of this technical project is to modify the current manufacturing process of Mosquirix to lower the production costs and implement single use systems, while complying with the EMA standards.

The World Health Organization (WHO) has identified populations that are considerably more susceptible to contracting malaria and has begun distributing Mosquirix through the Malaria Vaccine Implementation Programme (MVIP) (World Health Organization, 2019b). Because the drug is not currently being manufactured for widespread use, the per-dose price is high. It currently costs roughly $5 to manufacture each dose (Galactionova, Bertram, Lauer, & Tediosi, 2015), including a profit margin of 5%, which is reinvested towards malaria research (Kelland, 2015). If the vaccine is to be deployed effectively, it needs to be made more affordable for the Sub-Saharan market. Without cost reduction, we will be unable to provide for the complete target population, leaving millions of lives unprotected against malaria.  Our goal is to achieve production costs of $4 per dose.

The current EMA-approved continuous manufacturing process for Mosquirix begins with the fed-batch fermentation of recombinant yeast cells. The yeast cells are then harvested, disrupted, extracted, and purified using techniques such as ultrafiltration, centrifugation, and chromatography (EMA, 2015). A generic Virus-Like Particle (VLP) production process is illustrated in Figure 1.

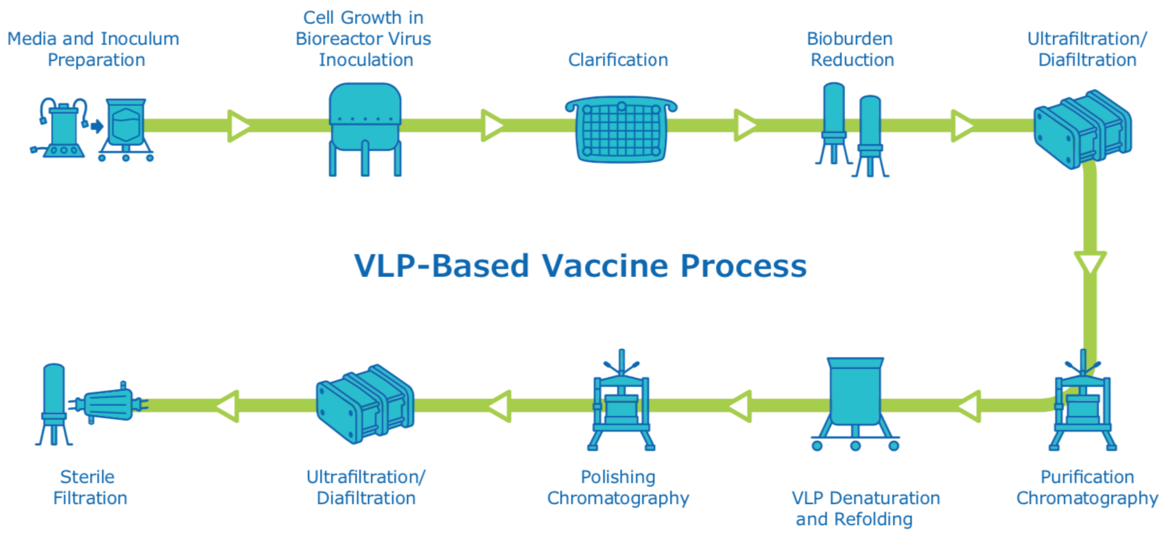


*Figure 1: General Process Flow Diagram for VLP-Based Vaccine Production (EMD Millipore, 2016)*

It is possible to adjust various aspects of the approved process to minimize operating costs. An increasingly popular manufacturing process involves the integration of Single-Use Systems (SUS). Pharmaceutical companies have discovered that SUS lessens overall process costs. SUS implementation can lead to lower facility footprints, smaller capital investment and construction costs, and shorter downtime of equipment resulting from reduced cleaning and sterilization times (Langer, 2018). Additional modifications to the process conditions for the manufacturing process will be considered to decrease the production cost of Mosquirix.

Literature research and data will be the primary informant of the design process, especially regarding VLP production, chromatography, single use components, and sterile filtration. We will design a media inoculum apparatus, bioreactor, clarifier, ultrafiltration and diafiltration skid, chromatography system, and sterile filter. The project will be advised by Eric Anderson, a Professor of Practice at the University of Virginia. The team will also confer with Professors Giorgio Carta and Michael King of the University of Virginia Chemical Engineering Department. We will model the design process with simulation software such as Aspen Plus and MATLAB. Initial process parameters, such as scope and product purity, will be determined during the first semester of the academic year, while the design process will take place during the second semester. The final deliverable will be a technical report that details the fermentation and separation processes, including scale, product yield, cleaning, and scheduling. The technical report will also include an economic analysis calculating cost of startup and operation, production, sales, and research and development to ensure that our process is cheaper than the previously filed Mosquirix manufacturing process. The project will be successful if the designed process is able to produce Mosquirix in a way that is compliant with the published EMA standards and is less costly than the previously published production method.

## Introduction to Feasibility Analysis of Supercapacitive Vehicle Adoption

The use of automobiles powered by gasoline are a significant contributor to the global emissions of greenhouse gases, and in response to the looming threat of climate change, consumers and manufacturers have recently increased their efforts to sell different kinds of electric vehicles (EVs) powered by batteries, hydrogen fuel cells, and natural gas (US EPA, 2018). One possible but relatively unused alternative electric vehicle power source is the supercapacitor. Supercapacitors are similar to batteries in that they are energy and power storage devices, but they are traditionally used in different applications. Their impressively high charging speed but low capacity compared to lithium ion batteries means that they could offer major gains but carry significant drawbacks for consumers (Jain, Kanungo & Tripathi 2018).

However, recent developments in supercapacitor technology have resulted in triple the energy density of previous supercapacitors, bringing them into a range of potential utility (2018). In order for supercapacitive electric vehicles (SEVs) to become a common choice for consumers, they must be able to satisfy the transportation needs of drivers and be marketable and desirable to them (BERR, 2008). Depending on the context in which consumers are willing to adopt SEVs, it is possible that the nature of public transportation and car ownership could fundamentally change in the more distant future (Zhu et al., 2006). Based on research of supercapacitor technology and review of data on consumer trends and opinions, it will be determined if supercapacitor technology is advanced enough to produce an SEV that would satisfy the needs of an appreciable portion of consumers of the 2020s, and by what actions they could attain a significant presence in the automobile market.

**Feasibility Analysis of Supercapacitive Vehicle Adoption**

The development and adoption of technology can be driven by both the power of the user and the technology itself. As explained by Bruno Latour's actor-network theory, both humans and nonhumans are attributed a certain amount of power in the codevelopment of technology and society (Latour 1992). This is called delegation, or the assignment of agency in how society and technology interact with one another. Both are vested with a level of responsibility that is deemed acceptable by users based on technological constraints and societal values. In order for SEVs to be adopted in the 2020s, it must be established that they can satisfy the needs of drivers with an acceptable amount of effort compared to traditional gasoline powered or electric vehicles.

It is key to establish the goals of automobile drivers as actors when evaluating the feasibility of SEV adoption. Therefore, comprehensively profiling, and analyzing driving habits is essential. These habits include quantitative factors such as average and maximum daily driving distance, time spent driving, and acceptable refueling times or cost. For example, with 17% of drivers exceeding 100 miles/day only twice a year there may be a sizeable market for shorter-range SEVs (Pearre et al. 2011). Additionally, qualitative factors such as geographic location and primary purpose of owning a car (i.e. commute or performance) must be understood. Finally, the desire for more sustainable EVs is an important factor to analyze. By creating a detailed profile of the 2020s driver, the human actor can be fully established and incorporated into an actor network.

SEVs must satisfy certain performance constraints to be a viable option for 2020s drivers. As only the power source is being analyzed, luxury features, appearances, and other non-powertrain characteristics will not be evaluated as a potential difference between traditional EVs and SEVs.  Major driving characteristics like the 300+ mile range of existing EVs will be a major point of comparison (Lambert 2017). The profile of drivers and their needs must be mirrored by the capability analysis of SEVs. For example, with over 90% of drivers exceeding 100 miles of driving in a single day at least once a year, SEVs could struggle to show sufficient utility (Pearre, 2011). It must be proven first and foremost that current supercapacitor technology can provide an energy density and by extension range that is comparable to that of commercially available, early 2020s EVs (Jain, Kanungo & Tripathi 2018). This would establish a meaningful capability of the nonhuman actor. It will also be important to establish the benefits that SEVs offer over gasoline powered vehicles and other EVs to develop a complete understanding of the nonhuman actor's capabilities, such as reduced carbon emissions (Tvinnereim & Ivarsflaten, 2016), fast charging times, and instant torque transfer.

After establishing the goals and capabilities of the actors, it must be demonstrated that the relationship between the two is truly a path of minimal effort with a desirable distribution of responsibility. Based on the opinions that drivers have on EVs and their willingness to potentially change their driving habits in order to use SEVs, a mutual delegation of effort and capability or lack thereof can be identified. For example, one of the primary concerns of people interested in switching to EVs is an anxiety over range (Egbue & Long 2012). It is possible that for some groups, SEVs will satisfy their habits when using traditional vehicles. It is also possible that some segments will find SEV use desirable despite making lifestyle changes, and likely that some will find SEV use undesirable because of potential limitations. An investigation into the size of these groups will help support or disprove the feasibility of SEV adoption. It will also be useful to analyze how human actors would perceive radical benefits of SEVs such as rapid charging times (Dameja 2002) instead of focusing on their adaptations to drawbacks. Another major benefit of EVs is the reduced carbon footprint, which is just 40% of that of a traditional vehicle (BERR, 2018). It is possible that certain aspects of SEV ownership will significantly outweigh the perceived effort of driving among consumers.

Finally, the actor profiles and analysis of their interaction can be used to predict the conditions of SEV adoption. If favorable interaction scenarios are identified, these will be the prime candidates for future SEV uses. One prominent example is the success of a pilot program with supercapacitive buses in China that illustrate a successful adoption of SEVs (Zhu et al. 2006). Such analyses require research beyond SEVs, and rely on information on specific interaction scenarios. In this example, peoples' perception of public transit is highly relevant (Steg 2003). One additional consideration is the efficiency gains in traditional vehicles that will continue to stiffen competition for SEVs (US EPA, 2018). As gasoline engines improve, the resistance of switching to SEVs will increase.

**Research Questions and Methods**

The research question I will set out to answer is: Can SEVs feasibly be adopted by early 2020s drivers, and under what circumstances they could effectively enter the market? This question describes the necessary intersection of technological progression and societal values that is the basis of actor-network theory. It will be answered by four primary research topics. First, a profile of drivers in the early 21st century will be established. This will include a qualitative and quantitative analysis of driving habits primarily based on actual driving data from surveys or other studies such as government reports, and help establish the necessary capabilities of a theoretical SEV by defining the needs of the human actor. Second, a primarily quantitative analysis will be conducted on the driving capabilities of theoretical SEVs based on current supercapacitor technology. This will involve research into supercapacitor energy density and how it compares to gasoline and battery-powered options. By projecting the potential capabilities of SEVs, the abilities of the nonhuman actor can be modeled. Third, research will be conducted on the perception drivers have of EVs as well as their perception of modifying their behavior to accommodate their use. Doing so will inform a stance on whether or not SEVs fill a niche that minimizes the mutual responsibility of the actor network. This is the portion of the analysis that will supply an answer to the research question by quantitatively comparing or qualitatively confirming or disproving the ability for SEV technology to satisfy the needs of an appreciable market segment. Fourth, research will branch out to different avenues of SEV adoption to determine their feasibility, such as in taxis or buses. If necessary, the first three steps may be revisited to better inform claims made relating to the fourth step. In summary, my research plan will aim to inform on the respective needs and capabilities of the human and nonhuman actors, their mutual interaction and restrictions, and the settings in which they are conducive to SEV emergence.

**Conclusion: Timeline and Expected Outcomes**

The three core planned deliverables are the collection of enough relevant information to make quantitative and qualitative educated guesses to my research question and begin drafting the thesis to be compiled by the end of the 2019 Fall semester, a first draft of the thesis to be completed by the end of the 2019-2020 winter break, and a final copy to be ready for submission and approval at the end of the Spring 2020 semester. Research will be conducted by asking a new question that supplements the main research question and finding sources that can answer them. Drafting and revising the thesis will be completed on a biweekly basis until I am satisfied with the final draft. The thesis will summarize my research and establish and support a realistic stance on the feasibility of the adoption of SEVs. Exploration of this topic is important because it examines a critical element of the automobile, a ubiquitous sociotechnical artifact.  It should compile the details of the driver-vehicle actor network by sufficiently characterizing the needs of drivers and the abilities of SEVs and analyzing the ease or friction of their interaction. It should also reflect an iterative research process in which possible SEV market penetration scenarios are analyzed and evaluated as realistic or not realistic. Ultimately, the thesis should critically evaluate if the circumstances it presents are permanent or transient, and predict whether its findings are useful in examining EV use will be robust.

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