Student Contest Problem 2020

This contest problem is open to Bachelor/Master/PhD level students. The participants have a few months to prepare and submit solutions to the problem (see below) no later than **April 15 2021, 23:59 CET**. Solutions can be prepared by individuals or by teams.

The jury will select the best solution, based on technical and writing skills (scope of the proposal, relevance of assumptions, overall technical consistency, relevant use of Computer Aided Process Engineering tools for simulation & optimization, creativity and quality of the written report. The jury will take also into account the size of the team and its academic level (Bachelor/Master/PhD). If no satisfying solutions is received, the EURECHA SCP committee may decide not to award any prize.

The Award includes:

- First prize: One invitation to attend to the ESCAPE-31, to be held in Istanbul, Turkey, 06-09 June 2021 to present the solution and get the award. First-prize award also includes a money transfer of 1000 EUR, after the ESCAPE event, to cover the travel and accommodation expenses.
- Second prize: One invitation to attend the CAPE Forum, to be held in Istanbul, Turkey, in June 2021 (dates to be defined) to present the solution and get the award. Second-prize award also includes a money transfer of 750 EUR, after the CAPE-forum event, to cover the travel and accommodation expenses.
- Both first and second prizes: the publication of the selected solution on the EURECHA web site (www.wp-cape.eu/index.php/eurecha/).

Submission procedure:

The written report should consist on a **pdf** file written in **English** and not exceeding **15 pages** (including figures).

This **written report**, any **other support file** (Annexes, Spread Sheets, Simulation Input files, etc.), and a support letter from an academic supervisor at your home university, should be packed (zip format) and sent, before the established deadline, as e-mail attachment to eurecha.secretariat@gmail.com.

In the body of this e-mail you **must** include the following information:

• Complete name (for all authors).

• Level (Degree/Master/PhD) and current year of your studies (**for all authors**). If available, please provide a link to a web page at your home institution related to one of the courses you are currently enrolled.

• Complete name and address of your home institution (School/Department/Research Center, etc.). Please provide a link to the web page of your home institution and an official contact to confirm eventually your affiliation/enrolment.

Mobile on-demand (MOD) biopharmaceutical vaccine manufacture

Project description

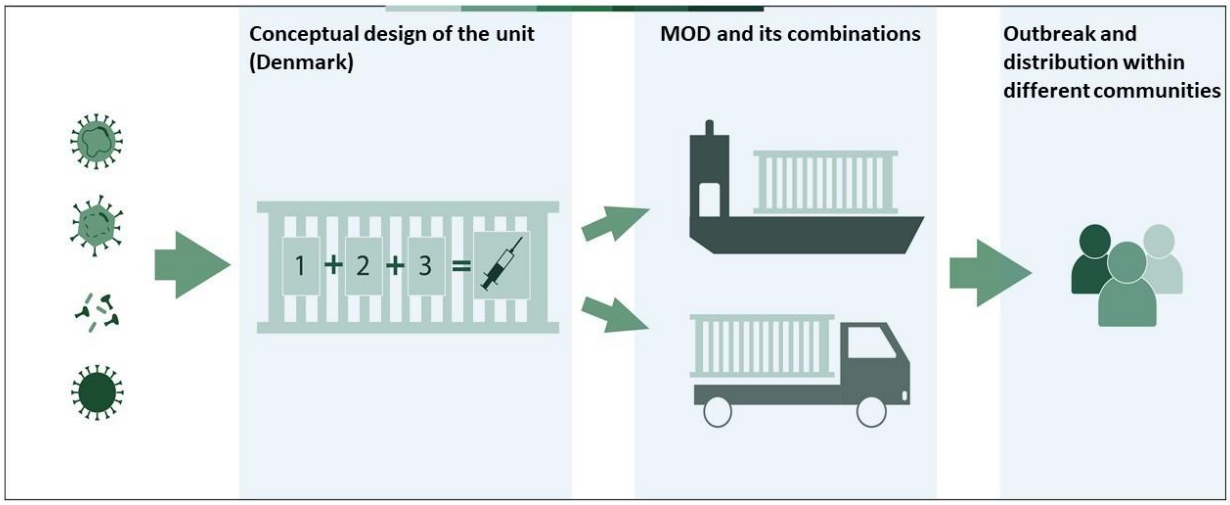
The objective of this project is to design and cost a mobile on-demand biopharmaceutical vaccine production unit such as one that could be used to provide COVID-19 vaccine (when it becomes available) to those in the developing economies with limited access. Once designed, multiple units could be manufactured to send around the world, in particular, to remote areas and lower income countries. An individual unit would be designed to fit into a ship container and could then be transported on an articulated truck from location to location or by river, as required by the local terrain. The unit would be capable of being operated efficiently (preferably in continuous mode, if the production platform allows). A second unit could supply the necessary utilities.

If such a unit is proven to be economically feasible, it could equip the health authorities, humanitarian organizations and global response units to support vulnerable communities in the least developed countries, where the population is scattered over a large and remote area (e.g. Uganda, Afghanistan), refugees and displaced people in camps (e.g. South Sudan, Darfour, Ethiopia), as well as barricaded areas that are in conflict zones (e.g. Yemen). The development of such units facilitates accessibility to safe vaccine doses at affordable prices for these communities. Such units, due to their on-demand design, can be rapidly deployed in a vulnerable community to respond for example to COVID-19 outbreaks, influenza, malaria and other contagious diseases and strengthen the global preparedness to locations where there is not an effective supply chain, expert knowledge, health care infrastructure and economic means to rapidly gain access to state-of-the-art vaccines in the least developed and most vulnerable human communities.

Purpose

The need for vaccines not only raises the challenge about which platform and technology will be most appropriate for manufacture, but also, how it will be possible to manufacture vaccine for a substantial part of the 7 billion people on Earth as well as deliver it to all types of communities including those that are most vulnerable and in the least developed countries. One option could be to develop mobile manufacturing units (mobile factory), which can be moved from outbreak to outbreak to target populations, which are at greatest risk, but not yet with herd immunity. This has particular logic for those living in the poorer, least developed countries to limit travel

of large numbers of people, possibly immigration waves in search of accessing health care, and to provide a vaccine quickly to remote locations. In recent years, the concept of mobile manufacturing units has been proposed for various types of products, but has attracted particular interest in the field of pharmaceutical production.



Background and relevance

The concept of manufacturing pharmaceuticals in multiple small-scale units was first devised around 10 years ago, with multi-national companies such as Bayer and Astra Zeneca as major drivers. At that time, the focus was on developing units which were flexible, compact (intensified) and capable of operating continuously and autonomously (with minimal human intervention). A European Commission funded project around the concept of F3 (Flexible Future Factories) had particular emphasis on small-scale operation, in complete process units (including feed preparation, reaction and product purification) which were the size of ship containers (ISO standard: 2.43 m x 2.59 m x 6.06 m). Each container was linked to a utilities supply board. This makes the system partially mobile, but it still needed suitable utilities. This project gave considerable insight and knowledge into the development of mobile factories (Singh et al 2013), as well as other work which has focused on miniaturized operation (Krühne et al 2014; Wohlgemuth et al 2015; Heintz et al 2016). The focus in all this early work was on small-molecule pharmaceutical manufacturing. In parallel, work at MIT (USA) has also led to the development of units of a domestic refrigerator size, again with a focus on small molecule synthesis (Adamo et al 2016). Nevertheless using microfluidics and well worked out protocols, a mobile on-demand (MOD) pharmacy can now be envisaged (Lewin et al 2016). However, the development of a system suitable for the production of a biopharmaceutical vaccine requires a further level of sophistication (Papathanasiou and Kontoravdi 2020), although the concept has already been

suggested in the laboratory for operation in cell-free biosynthesis mode (Pardee et al 2016), and subsequently yeast-based technology (Crowell et al 2018). More practically, for immediate implementation, a unit capable of operating in a ship container using existing bioproduction platforms and single use technology (e.g., pre-sterilized bags) is required in order to avoid challenges of steam sterilization *in situ*. The robustness of the unit is of paramount importance given where it will be used.

Activities

There are several scenarios for the manufacture of a suitable vaccine, which ultimately will be dependent upon which are successful in clinical trials. This project aims at techno-economic analysis of MOD production units based on alternative platform technologies for the production of the vaccine. These are produced through different biotechnological platforms e.g. CHO cells, yeast, mRNA. These could be produced as intercellular or extracellular products in which case the latter is preferable. For at least one of these platforms, the following activities will be performed:

1. Define a flowsheet to produce the product.

   The process flowsheet is the sequence of unit operations that are necessary to carry out vaccine manufacturing. A flowsheet is designed based on both upstream and downstream process knowledge, gathered through literature search and discussion with SCP contact (Seyed Soheil Mansouri, Assistant Professor, Technical University of Denmark, seso@kt.dtu.dk). Therefore, a feasible process alternative that includes production units, utilities and waste management is devised. In this task, the process flowsheet for a selected vaccine production route (at least one) is defined and the technologies associated with it are identified as well as their current technology readiness level. The technology readiness level associated in this task is essential as it will determine the minimum required costs for a scalable solution during design and costing of final process design.

2. Size the flowsheet and process equipment to fit into a ship container size.

   Here, students will define how to miniaturize the units operations, feed supply and piping. This will be carried out using a model-based strategy such that once the final dose of a vaccine is determined, then the process can be adjusted. Thereby, a benchmark dose will be selected that is most plausible for the vaccine type considered. Note that, an objective of this design is to arrive at a solution that can fit in a standard sized ship container. The reason for this is to provide the scalability of the project in a

very short time. The goal is to enable a rapid increase in production capacity by having many containers producing at the time. This will add an additional degree of flexibility to adequately respond to vaccine need depending on the size of vulnerable community to be vaccinated and its infrastructure. For example, for a small population with limited supply chain distribution network infrastructures, a container or a number of them placed in vicinity of the target community may suffice. On the other hand, for a larger population that has a working supply chain distribution network, the process can be quickly scaled up on a ship that docks in a port and does centralized on-demand production, with product easily transported to other ports if needed. Alternatively, the plant is transported on a truck trailer to further destination on land. The key point is to minimize human mobility.

3. Design and impact of a single unit (mass and energy balance).

   Here the process design will be finalized, and mass and energy balances will be completed. Once the detailed mass and energy balances are available, a comprehensive economic and sustainability assessment will be conducted. One of the features of this unit should be that it will not cause any environmental issues, especially if single use devices, which are typically made from plastics, are being used. Therefore, life cycle assessment and waste management strategies may be considered (optional). Furthermore, the issues related to handling waste, providing utilities, product testing, and quality assurance should be mapped and evaluated.

4. Economic evaluation of the manufacture of multiple units.

   The economics of the process are driven by on-demand necessities. Thereby, comparison of the feasibility of decentralized production (with a more manageable supply chain) using MOD with centralized production by large manufacturers is a driving force for their realization. Indeed, centralized production by large manufacturers and creating a global supply chain from one or a few production sites to provide vaccines in least developed countries and vulnerable populations is challenging. This is mainly due to a more complex and costly supply chain network given the lack of local and global logistics for such centralized productions as opposed to a MOD with a more local and targeted distribution network. Note however, the production cost of the unit given its humanitarian nature is intended to be still cost competitive. A costing study of the MOD units should be conducted to identify and discuss largest economical barriers in comparison with centralized production.

5. Design operation and control of the unit (optional).

   Control and operation of such mobile production unit in remote areas and lack of technical support creates a challenge for safe production of vaccine. To address these challenges, a control and monitoring strategy may be developed based on global positioning system (GPS), internet of things (IoT), and data-driven approaches for control and operation of such mobile unit from a control center. However, on-site quality assurance and product testing may still require personnel and their automation and remote control may be challenging. However, procedures for this would be envisaged for rapid training of local personnel. Another feature of this unit is that it has to be a sealed container with minimum required human intervention, manipulation, maintenance and handling. This will pose an extra challenge in degree of sophistication for control and operation of this unit. Note, however, that this degree of sophistication needs not to be beyond what is necessary to keep the MOD production and operation expenses (CAPEX and OPEX) as low as possible. Moreover, the investments in global control center and its location need to be addressed. The global control center could be placed on the carrier (in this case a ship) or on land in specific geographical location.

Acknowledgements

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