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Vaccine value chain : an overview and challenges

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***Abstract*— Vaccination, according to the World Health Organization (WHO), is a success story in global health and development that saves millions of lives each year. During the Covid – 19 pandemic, the importance of immunizations in combating Covid – 19 was highlighted, and vaccination was recognized as the most effective technique for paving the way out of the epidemic.**

However, this technique faces a number of challenges, most notably in the vaccine value chain, which has been linked to a number of factors, including market volatility and vaccination demand, which make raw material supply difficult, particularly during pandemics when it is critical to deliver an effective, safe, and high-quality product quickly. Add to it the complexity of production, the difficulty of maintaining the cold chain throughout storage and distribution, quality control and testing, tougher regulatory requirements, and a myriad of other barriers to fulfilling vaccine objectives. As a result, recognizing and resolving difficulties is crucial for establishing a reliable vaccination value chain.

In this article, we will give a general framework of value chain then we will discuss the vaccine value chain, including its characteristics, issues, and obstacles, as well as the context of Covid 19 and prospective advancements.

Keywords*— *Vaccine; Value chain; Covid19; Vaccination

I. INTRODUCTION

Vaccination is a medical procedure that involves the introduction of a specific substance into a healthy organism in order to determine resistance to a disease. It is one of the most effective ways to fight infectious diseases. It lowers the morbidity and mortality associated with infectious diseases that have a high epidemic potential. Furthermore, vaccination is less expensive than diagnosing and treating these infectious diseases [1]. The World Health Organization estimates that existing vaccines prevent approximately 2–3 million deaths per year [2].

Basically, a vaccine is an antigenic preparation whose administration to a susceptible subject induces a specific protective immune response to a given infectious agent, by producing protective antibodies and inducing certain cellular components [5]. According to the WHO (World Health Organization), there are three main approaches to develop a vaccine. Their differences are whether they use a whole virus or bacterium (the whole-microbe approach), just the parts of the germ that trigger the immune system (the subunit approach), or just the genetic material (The genetic approach "nucleic acid vaccine") that provides the instructions for making specific proteins rather than the entire virus.

On November 16, 2019, a virus from the coronavirus family made its first appearance in Wuhan, Hubei Province (Central China). From that point forward, a massive epidemic swept the globe, prompting the World Health Organization (WHO) to declare Covid-19 a "pandemic" on March 11, 2020. Soon after, on April 4, 2020, the WHO reports that over 1 million COVID-19 cases have been confirmed worldwide [3]. Many changes have occurred in people's daily and economic lives, primarily as a result of the fermentation, isolation, and containment strategies that were quickly devised to combat this spreading pandemic. As a consequence, many people have died as a result of this disease, and the total number of people who have died as a result of this disease has surpassed 5,927,600 [4].

In the context of this crisis, everyone is asking, " When will this pandemic end? " But, in order to answer this question, the obvious follow-up question is " How can we stop this pandemic?". The future situation to face is the result of a battle between two forces: on one side, the immune system, and on the other one, the virus and its ability to bypass it. so the only way to strengthen the other side of the immune system is through vaccination

As a result, various vaccination strategies have been employed in order to rapidly develop a safe and effective vaccine to combat the SARS-COV-2 virus, but several challenges remain, particularly with regard to the vaccine value chain. The purpose of this paper is to describe and provide an overview of the vaccine value chain and its challenges while addressing the context of covid 19. A search was conducted to better understand the value chain, especially the vaccine value chain, and the methodology is based on three steps:

- Collection of articles: we entered keywords such as value chain, vaccine value chain, value chain challenges, vaccine value chain challenges, and so on from a variety of sources, including ScienceDirect, Scopus, Web of Science, Taylor & Francis Online, Springer, Emerald Insight, and the National Center for Biotechnology Information (NCBI). In addition, we used the same keyword to run a Google search to find white papers and yearly reports from health-care organizations such as the WHO.
- Selection: The selection was determined based on numerous factors, including the year of publication, the subject of research, the concerns addressed, and the goal of the examination.
- Analysis the selected articles: The articles that made it through the screening process are thoroughly examined.

This article is organized as follows. In Section II, we give an overview about the value chain. In Section III, we will discuss the vaccine value chain. In Section IV, we provide and discuss the current context of covid 19. Finally, we give conclusive remarks and some prospects for improving the vaccine value chain.

II. VALUE CHAIN : CONCEPTUAL FRAMEWOEK

A. Definition

The value chain is a systematic strategy that comprises of numerous actions that attempt to deliver a product or service from its conception, manufacture, and distribution to end customers and usage. Value chain includes producers, inputs suppliers, operation, processors, retailers and buyers. They are supported by a range of technical, business and financial services providers [27].

B. Context and objectives

Developed by Michael Porter (1985), the value chain seeks to deconstruct all of the company's activities in order to determine those that produce value (i.e. those that result in considerable benefits or minimum costs) in favor of focusing on those that offer a competitive advantage. This marketing strategy divides value-creating activities into two categories: primary activities and support activities. The following figure (fig. 1) present Porter's value chain.

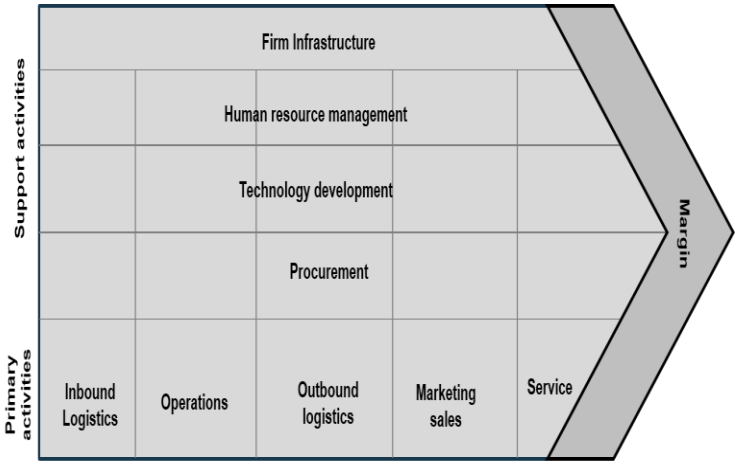

Fig. 1. Michael Porter's value chain.

C. Value chain and activities

1) Primary activities

Activities that contribute to the physical development of a product or service, they are coordinated around the company's strategic competencies [28]. These activities are as follows:

- Inbound operations: Include all actions necessary to receive, store, and distribute inputs, as well as contacts with suppliers.
- Operations: are all of the tasks needed to convert inputs into outputs (products and services).
- Outbound logistics: consist of all operations necessary to collect, store, and distribute the output
- Marketing and sales: activities inform buyers about products and services, induce buyers to purchase them, and facilitate their purchase.
- Service: contains all activities necessary to maintain the product or service operating properly for the buyer after it has been sold and delivered.

2) Support activities

Secondary tasks that are required for the company's proper operation:

- Procurement and purchasing: is the procurement of inputs (or resources) for the firm.
- Human resource management: includes all actions related to recruiting, hiring, training, developing, paying, and (if required) terminating or laying off employees.
- Technology development: refers to the tools, hardware, software, processes, and technical expertise used in the firm's conversion of inputs into outputs.
- Company infrastructure: It includes of services or departments such as accounting, legal, finance, planning, public affairs, government relations, quality assurance, and general management that serve the needs of the firm and connect its numerous elements.

III. VACCINE VALUE CHAIN

A. Definition and presentation

Vaccination is one of the most efficient methods of preventing and/or controlling the spread of infectious diseases. This medical intervention also raises a slew of logistical concerns [9]. The vaccine value chain is a very important key to the success of public immunization and ensuring that the target population is vaccinated, and as shown in the figure (fig. 2), it consists of many parts, including:

1) Suppliers of raw materials : The initial step is to obtain and receive raw materials from suppliers. Vaccine production necessitates the use of numerous components. According to the IFPMA, each vaccine requires over 100 ingredients [10] such as bioreactors, filters, vials, and so on. The list differs depending on the type of vaccine.

2) Manufacturing : The manufacture of vaccines is made up of two parts: the biological part and the pharmaceutical part, it depends on the type of the vaccine but the general process that any vaccine may go through is shown in the diagram (fig. 3 and fig. 4).

3) Control : Quality control is a crucial element in the development process as it already takes up 70% of the manufacturing cycle time [11]. Additionally, there are two types of quality control firstly that carried out by the manufacturer after each stage of production and secondly that carried out by the health authorities to release the product before it is distributed. The article [12] shows a table of the different quality control tests applied during the production of vaccines.

4) Packaging & storage : After vaccine production, the next step is packaging and storage, which necessitates specific conditions to ensure the safety and quality of the vaccines.

5) Distribution and transport : Vaccine distribution and transport is the final step in moving vaccines from manufacturers to their users.

6) Regulatory : Health authorities frame and surround the overall process of vaccine development before it even begins to be manufactured at scale. During the preclinical phase, regulatory authorities establish guidelines on how trials are conducted and give developers permission to conduct human trials.
After this research and development phase, the regulatory agency receives the safety and efficacy data for validation and approval. In addition, regulatory agencies supervise batch release and manufacturing site inspections to ensure that products and facilities continue to meet the same standards [13].

B. Differences between other products' value chain and vaccine value chain

The vaccine value chain is unique due to several factors, including the expertise and knowledge required to develop and manufacture a product like vaccines, as well as the large number of actors, particularly during the clinical trials phase, which necessitates the recruitment of thousands of people, which is not the case for other products because all of the actors are defined, and in some cases the number is extremely small.

Aside from the nature of the product, vaccines are very sensitive, so they require a high level of attention to specific details, which is not the case for other goods. There is also the execution process, which is very complex and requires several steps in the case of vaccines, and it is subject to variations due to rapid changes in the market and demand, particularly during epidemics.

Finally, we must address the regulatory component, which is quite stringent and imposes several constraints on the development of a vaccine, although it is not as stringent for other goods.

C. Challenges of the vaccine value chain

The production of vaccines is very complex and this is due to several factors among which the fragility already of the product which is derived from biological [14] then the need to ensure a high level of security and containment especially during the production phase of the active principle so at the international level there is a classification of bacteria and viruses. In the article [5] you can find the table of this classification in 2016 add to this the obstacles and logistical challenges which makes the availability of vaccines is not immediate in time of need, In the article [16] the author dealt with the case of vaccine shortages in Europe while noting the main causes and recommendations, Furthermore, in this article [17] the author has addressed the same issue of shortages in Europe in order to find out the root causes and strategies to solve it.

The challenges that the vaccine value chain faces are particularly severe in the following areas:

1) Suppliers of raw materials : The most critical factor in vaccine production is to ensure the availability of high quality raw materials as the manufacture of raw materials can be limited in value and sometimes subject to shortages [18].
Furthermore, if the materials are of animal origin, they are thoroughly tested for viral and microbial contamination and are generally sourced from regions free of certain diseases. [14]

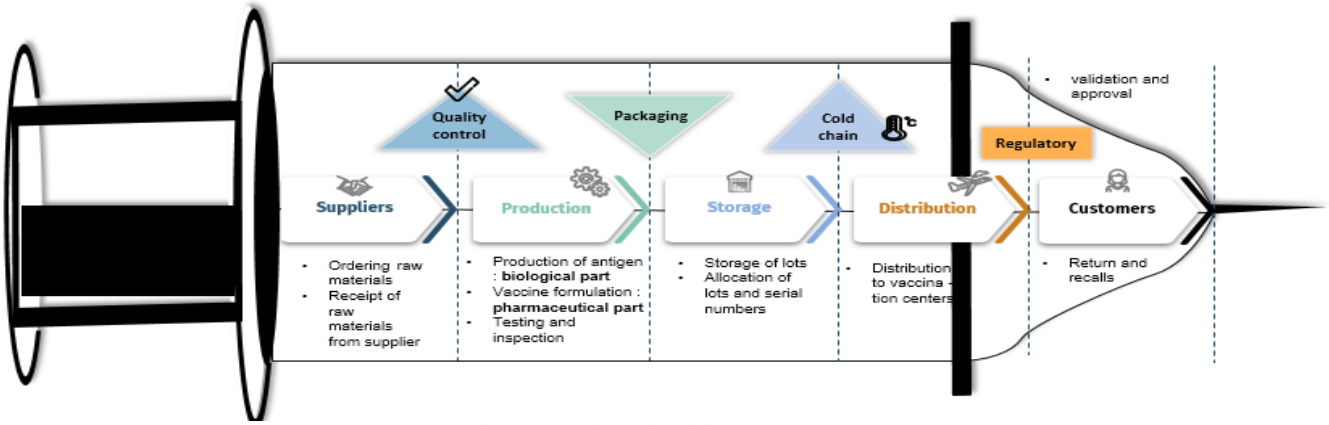

Fig. 2. Vaccine value chain process.

Therefore, In the article [19] the author mentions that suppliers of vaccine manufacturers have to apply quality systems that prove that they meet certain standards. ISO certification, good manufacturing practices for production sites and registration of culture media with a "certificate of conformity" from the European Directorate for the Quality of Medicines and Health Care are reliable quality systems for vaccine production. Besides, Suppliers must ensure that each batch of raw materials used in a product that will be used for the manufacture of vaccines meets the required level of safety and traceability.

2) Manufacturing : The production of vaccines is a rather special process as it requires a lot of time, resources and knowledge therefore it is very much framed by several regulations that guide and validate the transition from one stage to another. The production of vaccines is very complex and this is because of many reasons including the complexity of the production process as mentioned in the article [18] each change in the process (e.g. new facilities, production equipment, changes in raw materials) will lead to the emergence of new regulations and this is an obstacle for vaccine manufacturers to make improvements to the process as well as to modernize it.

3) Packaging and storage : A vaccine can be manufactured, but without proper packaging and storage throughout the value chain, vaccination will not be possible [20]. Vaccines are biological substances that are sensitive to external factors. Thus, their safety and efficacy decrease when they are stored at temperatures outside their optimal temperature ranges or in light. Storage management of vaccines is implemented through an adapted cold chain [21]. The cold chain is a system that ensures the quality and efficacy of vaccines from the time of manufacture to the point of use. It consists of equipment, people and must meet standards and procedures. Storage is therefore done in cold rooms or specialized refrigerators. Of course, all these devices are equipped with regulation, temperature control and continuous air circulation to ensure the even distribution of the temperature.

4) Distribution and transport : As you know, vaccines are fragile and complex products, that's why during their distribution and transportation it is very important to maintain the cold chain to guarantee their quality. The distribution of doses is carried out in cold rooms, refrigerators and freezers, isothermal boxes, and sometimes refrigerated vehicles [21].

IV. THE CONTEXT OF COVID – 19

Several companies have successfully developed COVID-19 vaccines in less than 12 months, an extraordinary achievement, given it typically takes a decade or longer to develop new vaccines [22].

In order to achieve this goal, it was necessary to mobilize significant research resources and then to carry out simultaneously clinical trials (phases I, II and III), investigations into production capacity and securing the value of raw materials so that manufacturing could begin as soon as possible after the trial phase. Regulatory procedures have also been accelerated, the time required to authorize the launch of clinical trials on vaccines has been reduced to about ten days in certain cases [11].

Therefore, despite the supposedly rapid development of vaccines against covid 19 there were several issues that researchers were trying to identify and resolve including vaccine acceptance and in the article [23] the author tried to estimate the acceptance rate of the COVID-19 vaccine and to identify the predictive factors associated with vaccine acceptance. In addition, the article [24] discusses factors that affect the effectiveness of real-life covid 19 vaccination, including logistical issues related to vaccine availability and distribution, as well as immunization strategies. In parallel, new variants of SARS-CoV-2 are also discussed.

V. PROSPECTS

The Vaccine Value Chain (VVC) will improve as a result of current trends toward the use of AI in the advent of smart solutions. For example, the implementation of Industry 4.0 designs based on sensors, IoT, and cyber-physical systems that connect machines, equipment, suppliers, and customers. This will consist of simple machinery and self-maintenance at the plant level, comprehensive connections between firms along the supply chain [30].

In the other hand, AI technologies can be used to address cost and waste in VVC, as it highlighted in the survey [29] where 63 percent of executives saw a gain in revenues and 44 percent saw a decrease in expenses as a direct result of implementing AI in their supply chains The rise in revenue was mostly ascribed to the use of pricing, demand and sales forecasting, propensity to buy prediction, and customer-service analytics [30].

The rapid development of vaccines against the SARS COV 2 virus (The vaccine value chain process has been shortened from 5-10 years to 6-9 during the pandemic) led us to think of making a duplication on all types of vaccines in order to reduce the time that is usually identified as "long". In the paper [26], a review of the applications of artificial intelligence in the context of coronavirus was made.

VI. CONCLUSION

Vaccination has long protected many people from many diseases, or at least from the most severe forms of some dangerous diseases.

In this paper, we present the vaccine value chain, its main components, and the challenges discussed in the literature in each section, as well as the background of Covid 19 and future developments.

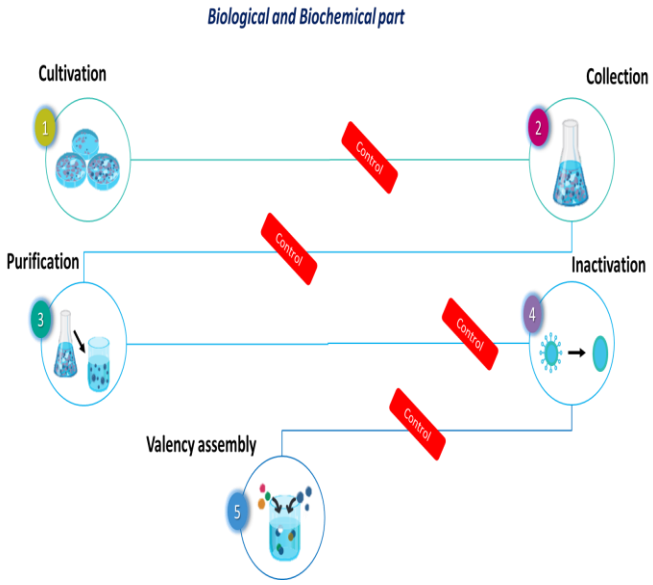

Fig. 3. Biological part of production.

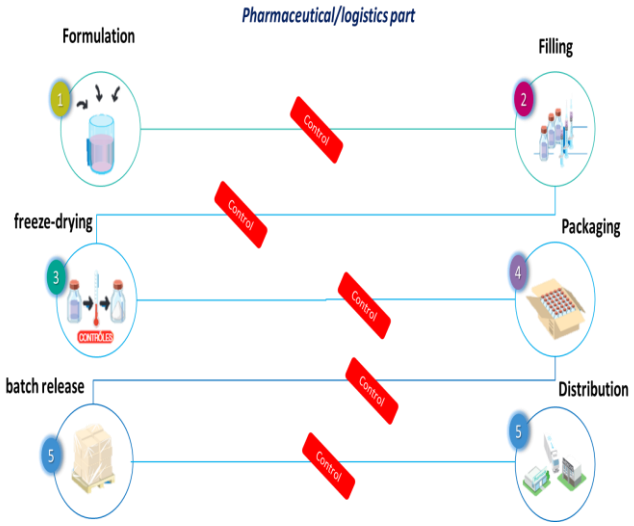

Fig. 4. Pharmaceutical part of production.

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