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Review Article

Quality Control Challenges and Vaccine Manufacturing

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Abstract

Every year vaccines save millions of lives worldwide resulting in development of global health. The mechanism how vaccines work can be understood that they stimulate or induce the host cells responsible for natural defence system thereby our body can recognize and fight off the target microorganisms including viruses and bacteria. After vaccination once immunity is established, further exposure is detected by immune cells ready to fight disease-causing microorganisms targeted for, and hence preventing from developing sever illness. For helping people by preventing from about 20 disease that could be life threatening, vaccines are available. Immunization is preventing about 3.5-5 million deaths every year. WHO immunization agenda 2030 (IA2030) have the vision and strategy for the decade 2021-2030 for vaccines and immunization.

Keywords: Vaccine, mRNA and pDNA Vaccines, Vector vaccine, Quality control

1. Introduction

Human body is having two types of immune system that is known as innate and adaptive or acquired immune systems. The first line of defence is covered under Innate immune responses against any microorganisms entering our body including viruses. Innate responses are rapid and triggered as soon as cell molecular event for the recognition of pathogen through receptors starts. Innate responses of a host include secretion of different cellular responses including cytokines and interferons, as well as neutrophils, monocytes and macrophages, dendritic cells, and natural killer cells. [1]. There was a great concern during COVID-19 pandemic that whole World faced substantial change and its impact on to the life of human being [2].

Under normal situation development of a new vaccine is not an easy task because it requires team work and decades to complete research including different levels of clinical study phases.

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Exceptionally in year 2020 scientists could able to formulate such vaccines that was not only safe but its production was also fast to meet the demand to fight against COVID-19 within months. Worldwide biological research scientists by working day and night to find out and formulate safe and effective component for inoculation. Trials including preclinical and clinical phase study after formulation were carried out including steps to study the vaccine for its severe adverse effects [3].

2.Types of vaccines

It was really a tough task to develop rapid and multiple COVID-19 vaccines for biomedical research scientists and to produce billions of vaccine doses that was given to large number of populations worldwide [4]. The entry of viral article to the host cell is through the binding of S protein present on viral surface to the host receptor could only be possible through Angiotensin Converting Enzyme 2 (ACE2) [5,6].

2.1 mRNA and pDNA Vaccines

Genetic material (DNA and RNA) can transfer genetic information from parents to children. Like other vaccine Nucleic acid vaccines helps to induce immunity. ZyCoV-D vaccines consist of a circular plasmid DNA

(pDNA) while other includes a messenger RNA (mRNA) molecule coding for a disease-specific antigen that is delivered between two layers of skin. The process for development is simple, cost-effective, and quick as compared to other traditional vaccine processes. Technology advancement have made the process less expensive. Messenger RNA (mRNA) strand is used in RNA vaccines that can code a specific antigen and stimulate the production of antibody. Such vaccine has relatively high capacity, potency and fast development technology [7,8].

2.2 Recombinant Protein Vaccines

Recombinant protein vaccines, a type of subunit vaccine consist of viral or bacterial antigen that are developed through recombinant DNA (rDNA) technology. Entire pathogen production is not required in the development of such vaccine and is therefore considered safe, and is well established in the industry. Delivery of such vaccine is a challenge.

This immunization approach for recombinant protein vaccine portion of recombinant proteins encrypted by DNA that does not have post-vaccination adverse responses [9]. Viral spike "S" proteins are included as antigen component in the development of recombinant protein vaccine [10].

2.3 Viral Vector Vaccines

Cytotoxic-T cell response are induced through vector-based vaccines. In such vaccine the vector used is a viral component the is able to deliver vaccine component in to the host. The process is very tough. Vast product line enables comprehensive workflow packages including time and quality from research to commercial production for Gene Therapies such as viral vectors. They have potential to reduce infectious disease as well as controlling genetic disorder and cancer. In such type of vaccines Viruses are used to introduce killed, attenuated pathogens, or recombinant pathogens in to the host [11]. Adeno virus or pox virus are used as carrier viruses that contain usually S gene/ protein for competing SARS-CoV-2. After administration in the they induce immunity [12].

Short length bioactive peptides generated through the fermentation of bovine milk with Lactic Acid Bacteria are also capable to enhance immune system [13]. The production of such peptides can be enhanced under controlled condition [14-16].

3. Challenges of Quality Control Labs in Vaccine Manufacturing

The Quality Control of vaccines relies from the very beginning on the control of starting materials, complex production process, and final product purification and packaging. In vaccine production process about 70% (estimated)of the production time is dedicated to quality control only. Fortunately, streamlining test processes and technological advances leads to increasing efficiencies of the process. Following are the methods by which one can control quality during vaccine production. Different methods are available and being used by the manufacturer including-

3.1 Rapid methods

Mycoplasma contamination in culture-based manufacturing is a big challenge that can be detected by fast, highly specific, sensitive Microsart® qPCR kits compliant with international guidelines.

3.2 Microbial enumeration

Enumeration of microbial cells that is also known as bioburden testing, is an in-process quality control measure that is used for demonstrating performance and safety at multiple stages of a manufacturing process including up-scaling and down-scaling, from raw materials to final product.

3.3 Membrane filtration

Membrane filtration is very frequently and regulatory-preferred method for microbial enumeration testing of liquids including vaccines. In this method a unique system is used that effortlessly positions the membrane on the agar plate completely touch-free, ready to incubate and can be easily locked thereby reducing the risk of contamination in the product.

3.4 Sterility testing

Sterility is one of the key points for any quality control testing in which QC parameter, ensuring the presence or absence of viable microorganisms' contaminants in the final parenteral products. Aseptic sampling of the sterile canister during the incubation time e.g. Sterisart® devices allow via a septum port, ensuring compliance with global regulations. Octet® Bio-Layer Interferometry (BLI) platform can be used for testing of impurity lot release assays.

3.5 Monitoring of Air quality

Air quality monitoring is a key requirement to maintain microbe free environments in pharmaceutical production with respect to biocontamination control strategies described in related standards and guidelines. Different latest devices including MD8 Airscan® command unit are available that is capable to capture the smallest airborne microorganisms, including viruses, over a short period of time. For enumeration the membrane filter can then be placed on desired standard agar plate for routine incubation at desired temperature and counting is done as per environmental monitoring protocols [17].

Conclusion

Hard work of various team of researchers who worked day and night. Technological advancement in the field

of microbiology, biotechnology, bioinformatics, development, and availability of various software for the analysis of and designing complex molecules made resulted in production and development of effective vaccine in a short period of time during COVID-19 pandemic.

Conflicts of Interest: The authors declare that there are no conflicts of interest

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