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DEPARTMENT OF BIOMEDICAL ENGINEERING

VII Semester

OBT357 BIOTECHNOLOGY IN HEALTH CARE

UNIT- 3 VACCINOLOGY

3.5 Quality Control

- ❖ Quality control (QC) in vaccinology is a critical process that ensures vaccines are safe, effective, and consistent before they reach the public.
- ❖ Given that vaccines are administered to healthy individuals, often including vulnerable populations like infants and the elderly, the standards for safety and efficacy are exceptionally high.
- ❖ QC encompasses rigorous testing and monitoring at every stage of vaccine development and production, from raw materials to the final product.
- ❖ Here we explore the importance, methods, challenges, and advancements in quality control for vaccines, emphasizing its role in safeguarding public health.

3.5.1 Importance of Quality Control in Vaccinology

- ❖ Vaccines are made from living organisms, so they can **easily vary or get contaminated**. Unlike chemical drugs, their structure is very complex and cannot be fully checked by simple chemical tests. That's why special quality control methods are needed.
- ❖ The main goal of quality control (QC) in vaccines is to make sure they are **safe, effective, and consistent.** This is important to keep public trust and to avoid problems like contamination or loss of strength, which could weaken vaccination programs.
- ❖ QC also supports regulatory compliance, ensuring vaccines **meet the requirements** of agencies like the U.S. Food and Drug Administration (FDA), European Medicines Agency (EMA), and World Health Organization (WHO).

3.5.2 Components of Vaccine Quality Control

- QC in vaccinology involves three main pillars: *control of starting materials*, *production processes*, and *the final product*. Each stage requires specific tests tailored to the vaccine type, whether it's a live-attenuated, inactivated, subunit, mRNA, or viral vector vaccine.

- **Control of Starting Materials**: The quality of raw materials, such as cell cultures, viral strains, or chemical reagents, directly impacts the final vaccine. For cell-based vaccines, like influenza vaccines grown in chicken eggs, tests for contaminants like Mycoplasma are critical to prevent infection of the production system. For mRNA vaccines, which use synthetic processes, QC focuses on ensuring the purity of nucleotides and lipid nanoparticles (LNPs).

- **Production Process Control**: The manufacturing process must be tightly controlled to minimize variability and contamination. This includes maintaining sterile environments through environmental monitoring (e.g., air, water, and surface testing) and adhering to Good Manufacturing Practices (GMP). For example, GMP facilities use sophisticated air handling systems to control temperature, humidity, and air quality. Process validation ensures that each step, from upstream (cell culture or antigen production) to downstream (purification and formulation), meets predefined specifications.

- **Final Product Testing**: Before release, vaccines undergo extensive testing to confirm identity, potency, purity, and safety. Analytical methods like mass spectrometry (MS) verify antigen identity and detect impurities, while potency assays, such as immunization-challenge tests in animals, assess immunogenicity. For mRNA vaccines, techniques like capillary electrophoresis (CE) and liquid chromatography (LC) assess mRNA integrity and LNP characteristics. Lot release testing by National Regulatory Authorities (NRAs) further ensures each batch meets approved standards.

3.5.3 Analytical Methods in Vaccine QC

The choice of analytical methods depends on the vaccine platform. For mRNA vaccines, key techniques include:

- **Capillary Electrophoresis (CE)** and **Liquid Chromatography (LC)**: Assess mRNA integrity and purity.
- **Dynamic Light Scattering (DLS)**: Measures LNP size and distribution.
- **Mass Spectrometry (MS)**: Confirms mRNA sequence and detects degradation products.

- For viral vector vaccines, methods like quantitative PCR (qPCR) or droplet digital PCR (ddPCR) quantify viral genomes, while enzyme-linked immunosorbent assays (ELISA) assess functionality.
- Protein subunit vaccines rely on chromatography techniques (e.g., reversed-phase, size-exclusion) for purity and glycan profiling. Emerging methods, such as QuantiGene assays, evaluate gene expression biomarkers for safety, offering faster and more precise alternatives to traditional animal-based testing.

3.5.4 Challenges in Vaccine QC

QC for vaccines faces several challenges:

- **Complexity of Novel Modalities**: New vaccine platforms, like mRNA or viral vectors, lack established regulatory precedents, complicating method validation. Developers must demonstrate robust, reproducible methods across batches and manufacturing sites.
- **Variability and Contamination Risks**: Biological variability in cell cultures or raw materials can affect consistency. Contamination risks, such as Mycoplasma in cell-based vaccines or environmental impurities in mRNA vaccines, require stringent monitoring.
- **Regulatory Harmonization**: Global vaccine distribution demands harmonized QC standards across NRAs, which can be challenging for developing countries with limited resources.
- **Animal Testing Limitations**: Traditional potency tests often rely on animal models, raising ethical concerns and facing statistical limitations. The 3Rs principle (Replacement, Reduction, Refinement) pushes for alternatives like in vitro assays.

3.5.5 Advancements in Vaccine QC

- Recent advancements are transforming vaccine QC. Multi-attribute methods (MAM) using MS allow simultaneous monitoring of multiple critical quality attributes (CQAs), improving efficiency. Real-time release testing (RTRT) and automation reduce variability and speed up batch release, particularly in continuous manufacturing. Machine learning is being explored to analyze complex datasets and predict quality, though regulatory acceptance and data requirements remain hurdles.
- Bioinformatic tools and in silico approaches, such as epitope prediction and toxicity profiling, are also enhancing QC for subunit and nucleic acid vaccines. These methods reduce development time and improve safety assessments. For example, QuantiGene assays have been used to study mRNA biodistribution and safety, providing insights into vaccine behavior without extensive animal testing.

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