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Containment and Biosafety of Genetically Modified Organisms (GMOs) in Pharmaceutical Facilities

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Abstract

The rapid advancement of biotechnology has transformed pharmaceutical manufacturing, with genetically modified organisms (GMOs) largely superseding conventional small-molecule synthesis for the production of many modern biopharmaceuticals. By 2024, a wide range of therapeutic products, including gene therapies, recombinant insulin, and monoclonal antibodies, were being manufactured in advanced biological production systems ("bio-factories") utilizing engineered viral vectors and genetically modified host cells such as *Escherichia coli* and Chinese Hamster Ovary (CHO) cells. While these technologies have significantly improved production efficiency, scalability, and therapeutic innovation, they also introduce substantial biosafety and biosecurity concerns. The potential release of genetically modified material into the environment, coupled with occupational exposure risks during bioprocessing, necessitates the implementation of stringent containment strategies throughout the manufacturing lifecycle. This paper critically evaluates the dual-pillar biosafety framework comprising biological containment, which minimizes the survival and propagation of genetically modified organisms outside controlled environments, and physical containment, which relies on engineered facilities, equipment, and operational practices to prevent accidental release. Furthermore, the study examines the international regulatory landscape governing GMO-based pharmaceutical production, with particular emphasis on the biosafety guidelines and regulatory frameworks established by the National Institutes of Health (NIH), the European Medicines Agency (EMA), and the World Health Organization (WHO). Finally, emerging biosafety challenges associated with the transition toward the "Factory of the Future," including highly automated manufacturing platforms and modular bioprocessing technologies, are discussed. The study highlights the need for adaptive regulatory policies, advanced containment strategies, and integrated risk management approaches to ensure the safe, sustainable, and responsible production of next-generation biopharmaceuticals.

Keywords

Genetically Modified Organisms (GMOs);
Biopharmaceutical Manufacturing;
Biological and Physical Containment;
Biosafety Regulations;
Modular Bioprocessing.

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INTRODUCTION

Genetic Modification is a special set of technologies that modify the genetic makeup of living organisms such as plants, animals or bacteria (Young, 2004).GM products are medicines and vaccines, foods and food ingredients, feeds and fibres. Apart from the farmers', genetically modified organisms are beneficial to the societies of the world as the technology is expected to help them attain huge hunger issues among third world countries, which are attributed to the rising population in the world. Biosafety is the principles, technologies and practices for preventing unintentional exposure to pathogens and toxins, or accidental release into the environment (Kumar 2015).

The use of GMOs has revolutionized modern medicine, with a large number of pharmaceutical products containing live-attenuated vaccines, viral vectors and recombinant proteins. But it requires rigid biosafety measures to use these biological agents. The introduction of a new gene into organisms can have different effects in different cells. Also, gene expression pattern can be altered by the single gene introduction. Hence, with the release of GMOs in the environment it's difficult to predicts the risks involved (Prakash *et al.,* 2011 and Batalion, 2000). GMO containment in pharmaceutical facilities is a crucial confluence of environmental stewardship, strict regulatory compliance, and public health safety. It's more than just a requirement for operation.

The Medical GMO Revolution

Genetic material manipulation is intrinsically tied to the origins of contemporary biotechnology. The pharmaceutical business has shifted from chemical synthesis to biological expression methods since the FDA approved recombinant human insulin in 1982. These days, a market worth more than $400 billion is based on genetically modified (GM) bacteria, yeast, and mammalian cell lines.

GMO Categorization and Risk Evaluation

The manipulation of genetic material is an intrinsic part of the origin of modern biotechnology. Since the FDA approval of recombinant human insulin in 1982, the pharmaceutical industry has turned from chemical synthesis towards biological expression methods. Such is the case today for a market that exceeds $400 billion, of which the science is genetically modified (GM) bacteria, yeast and mammalian cell lines.

Levels of Physical Containment

This defence hierarchy is known as physical containment, and there are Biosecurity Levels (BSL) around the world. These levels are a graduated series of controls designed to protect the public and the environment and laboratory workers from biological risks (CDC, 2020).

Biosafety Level 1 (BSL-1),

The beginning of microbiological work is at the very base of it, the cornerstone. In this situation, the agents involved are well-defined and disease free in healthy adult adults. Think about a typical high school or undergraduate teaching laboratory in which students can try out the baker's yeast or non-pathogenic strains of *E. coli*. The containment is minimal at this level; the risk is very small. No special containment equipment is required and work is generally carried out on open benchtops. But basic hygiene is still crucial. Handwashing sinks should be readily available and there is a tendency to decontaminate the waste

(Richmond and McKinney 1999). It is a public park, but scientific, it's open and accessible, but subject to rules to guarantee safety and order.

The Next Level: BSL-2

The levels of restriction increase as the potential threat increases. Based on BSL-1, Biosafety Level 2 (BSL-2) restricts agents such as *Salmonella* and *Staphylococcus aureus*, associated with human disease with varying levels of severity. These diseases are not usually transmitted in the air, but they have a slight risk of being transmitted when swallowed or touched through the skin. Physical environment is slightly but significantly changed. Sharp measures are carefully monitored during work and access to the lab is limited to prevent accidental infections. The most apparent addition is the use of Personal Protective Equipment (PPE) like lab coats and gloves. Importantly, if there is a chance of splashes or aerosols, BSL-2 mandates that a biosafety cabinet (BSC) be available. One of the main barriers is the ventilated enclosure that filters exhaust air with HEPA filters prior to return to the room. The biohazard icon is used around the world to mark a region where people should be cautious of the germs (WHO, 2020).

BSL-3: The Airborne Danger

A change in engineering and procedures for reaching Biosafety Level 3 (BSL-3) is significant. This level is set aside for both domestic and foreign substances that have the potential to cause fatal illnesses by inhalation. Examples of well-known diseases include tuberculosis and West Nile virus. GMO risk grouping is a preventative measure that compares the receiving organism and the donor organism (from which the genetic material has been derived). A number of crucial elements direct the process:

The structure itself becomes a containment device at BSL-3. In order to prevent air exchange with the hallway, the laboratory must be physically isolated from ordinary traffic, which frequently calls for double-door access systems (interlocking doors). Negative pressure ventilation is the most important engineering control. The clean air is allowed to pass into the laboratory, while the laboratory air is always filtered when it is removed. This ensures that in case of a leakage, air will rush in, ensuring that the pathogens are trapped inside as well (Kozlov, 2018). Also, employee protection is improved. All infectious material work should be conducted in a biosafety cabinet and many times respiratory protection is needed. The psychological toll of working in a BSL-3 is evident as the sound of the ventilator never let's go, the air inside the lab is distinct from the air outside.

BSL-4 is the maximum containment.

The highest level on the pyramid is Biosafety Level 4 (BSL-4). It's covered by the most dangerous and unusual substances that have a high personal risk of deadly disease, often one for which there is no known vaccine or cure. The viruses causing the diseases Lassa fever, Marburg and Ebola are treated here.

The nature of Insert

If the gene made into the GMO encodes a toxin or allergy or an antibiotic resistance marker, the risk is further enhanced. Based on the Cartagena Protocol on Biosafety (Secretariat of the Convention on Biological variety, 2000), the risk assessment should consider "the potential adverse effects of the

living modified organism on the conservation and sustainable use of biological diversity.

Genetic Stability

One area of concern with the potential exists for "horizontal gene transfer," in which altered genes could be transferred to the wild population. Organisms are often grouped together at higher levels when they possess traits that might give them a selectable survival advantage, such as tolerance to drought or herbicides, and thus make them an invasive weed (National Research Council, 2010).

Pathogenicity and Host Range

In case the host organism is a known pathogen, the risk classification should include a consideration of the possibility of a change in the tissue tropism or host range of the organism as a result of the genetic mutation.
There are normally four major risk groups (RG) as established by international guidelines.

- **Risk Group 1:** Microorganisms not known to infect healthy adults. These require routine lab techniques and are considered to be low risk.
- **Risk Group 2:** Agents that can cause human disease but are not normally at risk and have often been treated or prevented.
- **Risk Group 3:** Agents associated with serious human diseases or fatal diseases that have a possible cure or prevention (high individual risk, low community risk).
- **Risk Group 4:** Risk agents that may cause serious or fatal human disease for which there is usually no preventative or therapeutic measure, with a high potential for human infection and disease.

The Basis of Biosafety: Risk Assessment

GMO containment is based on the Risk Group (RG) classification. The analysis must be performed in two steps by Organizations.

1. **Intrinsic risk of the organism:** Pathogenicity, Virulence, Environmental stability.
2. **Properties of the change:** Is the genetic engineering a virulence or resistance to current medical countermeasure?

Risk Assessment and Spill Management

Active risk-management programs are necessary in pharmaceutical production facilities for continued safety. After the change of institutional duties, facilities are required to have an active institutional biosafety committee (IBC), and a dedicated biosafety officer (BSO) to oversee gene handling.

Emergency Spill Protocols

Accidental release of GMO propagative materials or live cells must be contained and cleaned up in accordance with clear and documented procedures at the facilities:

- **Primary Containment Failure:** If a spill does happen inside a cleanroom, operators will use validated disinfectants, (sodium hypochlorite or peracetic acid), to decontaminate surfaces immediately.
- **Secondary Containment Failure:** If the modified material cannot be contained within a facility boundary, emergency personnel will have to collect all physical components and clean up the surfaces of the area where the micro-organisms have been released to stop the spread of micro-organisms in the area.

Physical Containment and Facility Engineering

Physical containment involves the use of structural and mechanical barriers to prevent live GMOs from escaping into the environment.

1. **Closed-System Bioreactors:** Most current pharmaceutical manufacturing facilities use totally closed systems. To avoid aerosolized GMOs from escaping during cultivation and harvesting, large-scale fermenters and single-use bioreactors are sealed with mechanical valves and sterile sampling ports.

2. **HVAC and Air Pressure Cascades:** Pressure differentials are established in heating, ventilation and air conditioning (HVAC) systems to prevent cross-contamination and accidental environmental release. In the case of handling hazardous or modified pathogens, the pressure difference between a cleanroom and adjacent corridors is normally negative. This pressure boundary helps to prevent airborne particles from escaping from the containment area. In addition, exhaust air needs to be filtered with High-Efficiency Particulate Air (HEPA) filters to remove the microscopic biological agent before it is released to the outside.

3. **Waste Inactivation Systems:** Fully decontaminate all effluent streams from a GMO manufacturing area. Automated thermal kill stations or chemical inactivation tanks are used to process liquid waste from bioreactors before it is discharged to public sewers. Single-use biocatalyst bags, single-use tubing are treated by incineration or autoclaving in the plant.

Biological Containment Approaches

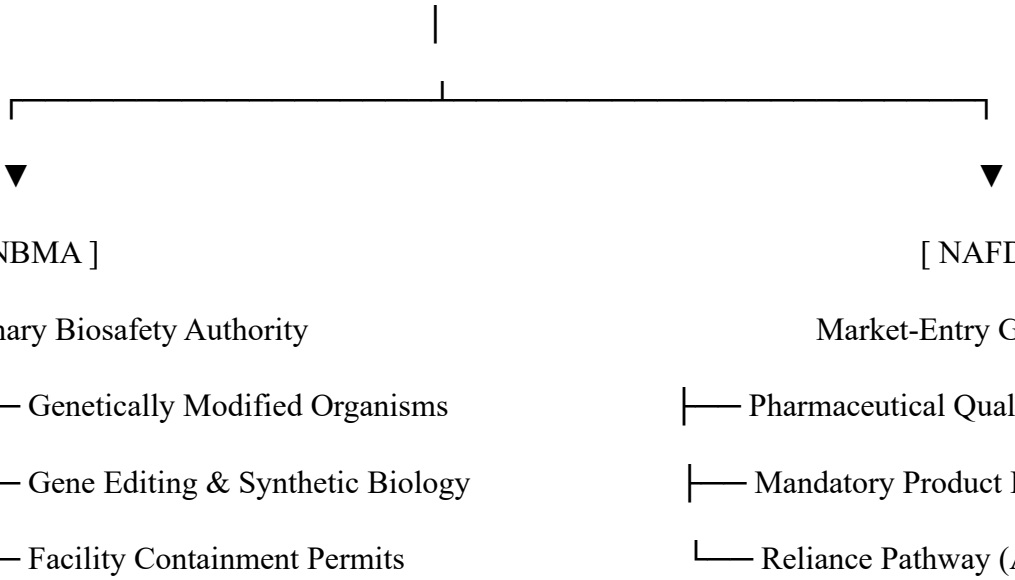
1. **Auxotrophic Mutants:** Production strains that are genetically engineered to have a metabolic defect and thus must be supplemented with a specific, non-naturally occurring nutrient to grow. In the event of an auxotrophic strain escaping from the bioreactor, the strain quickly perishes because of a lack of nutrients.
2. **Self-Inactivating Vectors:** Using viral or plasmid vectors without the ability to replicate the genes. This helps to prevent the vector from being duplicated (duplicated vector DNA) if the vector happens to come in contact with the environmental microbes that are normal.
3. **Attenuated Strains:** Using non-virulent modified genetic frameworks (e.g. replacing Mycobacterium tuberculosis with a safer Mycobacterium smegmatis platform) to reduce the base risk of infection during production.

How Regulatory Framework Work in Nigeria

The regulatory system in Nigeria is a multi-tiered, statutory system whereby specialized federal ministries, departments and agencies (MDAs) are responsible for enforcing laws passed by the National Assembly. Concerning biotechnology, pharmaceuticals and regulation of Genetically Modified Organisms (GMOs), Nigeria has a very strict framework of co-operation between biological gatekeepers and the health product regulators.

THE CORE REGULATORY BODIES

NIGERIAN BIOTECH & PHARMA OVERSIGHT



National Biosafety Management Agency (NBMA)

The process of constructing a pharmaceutical manufacturing plant with GMOs or importing a biopharmaceutical product into Nigeria is a multi-step process that an organization has to go through:

Step 1: Involves risk assessment and facility permits that are required (NBMA).

Applicants are required to supply a detailed dossier to the NBMA before a modified organism can be engineered or handled.

- The NBMA utilizes its own Biosafety Risk Analysis Framework, which analyzes the molecular profile of the host organism.
- Agency inspects facility to issue a Containment Permit to ensure engineering safety features such as HEPA filtration, closed system bioreactor, and liquid effluent deactivation stations are in place.

Step 2: The Inter-Agency Collaboration (NBMA-NAFDAC MoU)

The NBMA has primary regulatory responsibility over biotechnology under a formal agreement between the agencies but no permit is issued without the involvement of NAFDAC for human consumption or medical use. NAFDAC then reviews the food and/or pharmaceutical safety profiles once NBMA has confirmed that the biological platform is genetically stable and contained.

Step 3: International Harmonization and Reliance Pathways

The NAFDAC Reliance Guidelines: This was rolled out to facilitate drugs, vaccines and biologicals to follow accelerated pathways. NAFDAC can accelerate the arduous, lengthy review process typically ranging from 120 days to 240 days, and avoid duplicating foreign clinical trials if a product has already been approved by trusted reference organizations in other countries, such as the US FDA, EMA or WHO Pre-qualification.

Global Quality Alignments: However, modern dossiers must be compatible with the highly strict guidelines governing the world (including ICH M13 and ICH E6(R3)), and include strict adherence to Good Clinical Practices (GCP) and international bioequivalence standards.

Step 4: Post-Market Surveillance and Mandatory Labeling

After consumer protection, once approved for the commercial market, consumer choices are legally protected. All GM products have to be labeled strictly by law. Post market monitoring is conducted by both NAFDAC and NBMA along the chain following the distribution of the product for the presence of low level of unconfirmed traits.

Conclusion

To ensure safe production of pharmaceuticals from GMOs, a combination of advanced facility engineering and biological containment controls is needed. By following new international and national biosafety protocols, production workers are protected and the environment is not contaminated. With the advancement of manufacturing technologies toward automated, potent and gene drive systems, facility designs are continually evolving their filtration, pressure monitoring and risk management systems to ensure safe support of biopharmaceutical innovation.

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