Risk Assessment of Biohazardous Drugs

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Introduction

The implementation of United States Pharmacopeia (USP) 800 in healthcare created a new resolve to conduct thorough risk assessments of healthcare formularies to ensure the safe handling of hazardous drugs.

The role of this assessment was to:

- identify drugs with hazardous properties.
- conduct toxicokinetic assessments of identified drugs.
- determine the potential health consequences of exposure.
- conduct an exposure assessment for each identified drug.
- evaluate the overall exposure risks (risk matrix).
- classify drugs that meet assessment criteria as hazardous.
- establish appropriate training for at-risk personnel.
- mitigate exposure through feasible and appropriate controls.

As the pharmaceutical industry is investing heavily in the development of novel biologics[7,8,9,10] to treat and/or correct human disease, it is imperative that the healthcare industry be prepared to utilize the same assessment criteria to mitigate the exposure and health risks associated with a biologic's BioHazardous properties.

TABLE 1: Novel biologics found in FDA approved drugs or in investigational products used in human clinical trials.

VIRUSES	BACTERIA	OTHER
Adenovirus[1, 3]	(BCG) Bacille Calmette-Guérin	Gene Therapies[7,8]
Polio[6]		RNA Therapies[7,8]
Herpes Simplex 1[1,3]	*Listeria monocytogenes*[5]	DNA Therapies[7,8]
Vaccinia[1,3]	*Salmonella typhimurium*[2]	Cellular Therapies[7]
Vesicular Stomatitis[3]	*Staphylococcus epidermidis*[4]	Chimeric Viruses
Adeno-associated		Bacteriophage
Coxsackieviruses[1]		
Maraba[1]		
Reovirus[1,3]		
Lentivirus		
Newcastle Disease[3]		

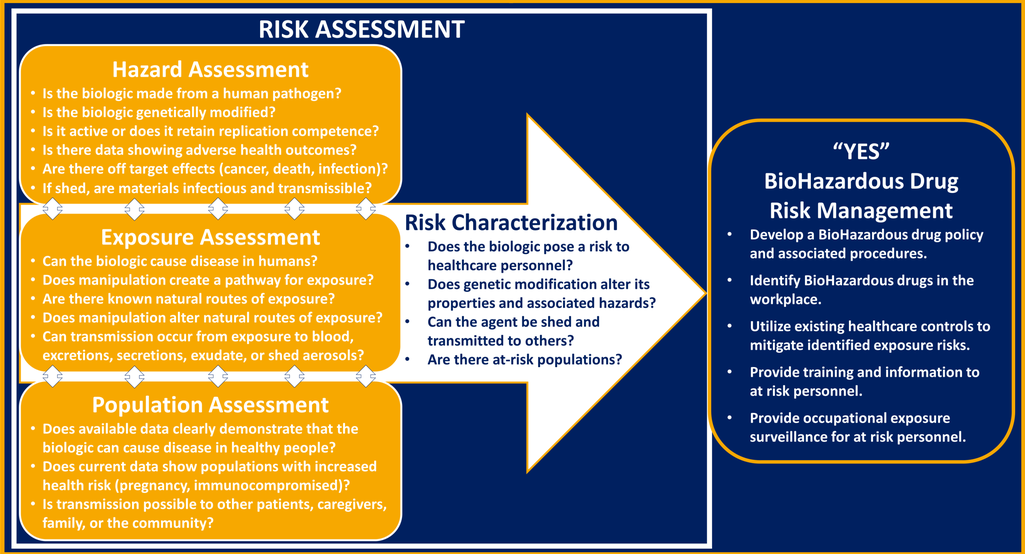
Note: The viruses and bacteria listed may be genetically modified or unmodified, replication-competent or incompetent, and may carry and express a transgene (e.g., SARs-CoV2 spike protein).

Research Question

Based on the absence of consistent guidance from Pharma, USP, NIOSH, or the FDA on proper handling practices for biologics with biohazardous properties, should pharmacists be prepared to conduct internal risk assessments of novel biotherapeutics and investigational products? Additionally, if a biologic is found to possess biohazardous properties, should the biologic be classified as a BioHazardous drug?

Method

Utilizing a modified NIOSH exposure assessment graphic[11], each novel biologic (Table 1) was evaluated to determine if it meets the listed criteria to be classified as a BioHazardous Drug. The risk factors considered are based on notable adverse events, FDA clinical holds[12], pharmaceutical/sponsor recommended precautions, known biohazardous properties, and health risks associated with these biologics.



Results

Table 2 presents the results of the risk assessment analysis of the novel biologics listed in Table 1. Note that this assessment did not account for genetic modification or other means of bacterial or viral attenuation, selective tissue replication, or tropism.

Table 2: Risk Assessment Classification – BioHazardous Drug

Criteria Met	Criteria Not Met	Further Study Needed
Adenovirus, Polio, HSV1, Vaccinia, Coxsackievirus, Lentivirus, BCG, Listeria, Salmonella, Staphylococcus	Gene Therapies, DNA Therapies, RNA Therapies, Cellular Therapies, Newcastle Disease Virus	Adeno-Associated Virus, Vesicular Stomatitis, Reovirus, Chimeric Viruses, Bacteria Phage, Maraba Virus

Discussion

The results of this simple risk assessment exercise indicate that a group of biologics listed in Table 1 could be classified as BioHazardous Drugs (Table 2) warranting the consideration of additional controls, education, and oversight. Additionally, understanding the risk associated with some of these biologics requires more study and those that do not currently meet the assessment criteria should be periodically reassessed.

Conclusion

Human clinical research utilizing novel biologics to treat and/or correct disease is rapidly advancing with the FDA approving seven (7) new cell and gene therapies in 2023. Based on this track record, it is anticipated that drugs, classified here as BioHazardous, will eventually transition from investigational to standard of care treatments. As these drugs pose unique health and exposure risks to pharmacy personnel, pharmacies to include specialty, outpatient, and retail pharmacies will need to establish appropriate risk assessment, characterization, and management strategies to protect their personnel, patients, visitors, and the community.

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