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MICROBIOLOGICAL FAILURES DUE TO HUMAN BORNE CONTAMINATION-CLEANROOM GARMENT AND MANAGEMENT GAPS

KEYWORDS

Cleanroom Garments, Construction, Laundry, Gowns, Fraying, Barrier

ACRONYMS

IEST: Institute of Environmental Sciences and Technology
FDA: Food and Drug Administration
ASTM: Refers to a standard maintained by ASTM International
PDA: Parenteral Drug Association
USP: United States Pharmacopeia

ABSTRACT

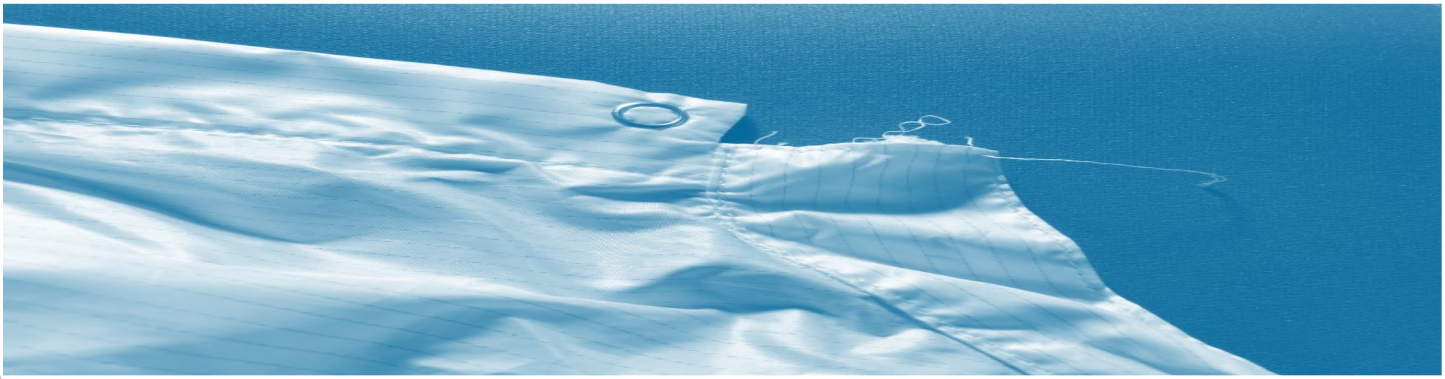
Personnel and their activities are one of the major sources of contamination in a cleanroom. Therefore, making an educated choice for an appropriate gowning system is crucial in limiting human borne contamination that can affect products or processes in the cleanroom. The end user should understand required performance criteria for gowns, test methods, and procedures for gowning system. These should detail; garment use, garment maintenance, as well as develop a quality control program for managing cleanroom garments used in cleanrooms. It is prudent for the end user to understand garment-related factors that may influence the performance of cleanroom operations. Selection, construction, material characteristics, performance, laundering, maintenance, validation, and documentation, as well as test methods should be understood by the end user in order to evaluate relevant properties of gowns for their cleanroom applications.

INSPECTOR'S OBSERVATIONS AND WARNING LETTERS

"Sterile gowns used in the line one filling area during the manufacturing. These gowns were observed to have fraying edges and loose threads"

"Aseptic garments worn in the filling area were also non-integral. We observed 7 sterile gowns with tears or holes; 8 had loose threads."

"Your firm failed to ensure that manufacturing personnel wear clothing appropriate to protect drug product from contamination"



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INTRODUCTION

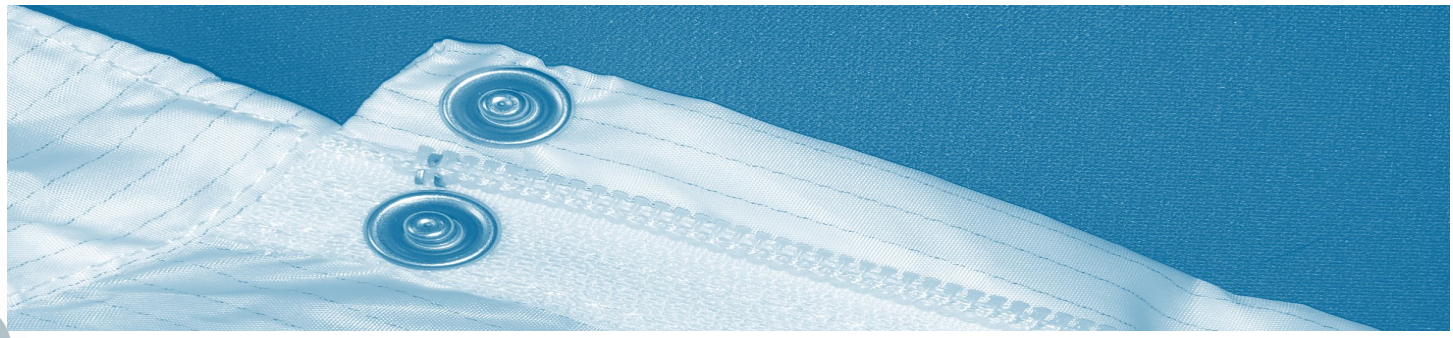
Importance of the role of gowns in contamination control cannot be emphasized enough; it is crucial to understand that the human body is a reservoir of microorganisms which are consistently shed into the environment. These microorganisms belong to all groups of bacteria; Gram positive and negative cocci, Gram positive and negative rods, yeast as well as mold. These organisms can contaminate a sterile product but can also lead to false positive results in laboratory such as sterility testing. The major functions of cleanroom garments include protection of cleanroom environment and subsequently the product against contamination by people, protection of cleanroom personnel against solid or liquid hazardous substances and biological hazards, dissipate electrostatic charge, not generate contamination and allow heat exchange for the comfort of personnel. If not chosen and managed properly these functions will not be performed.

CLEANROOM CLOTHING REQUIREMENTS

Per EU GMP, "The clothing and its quality should be appropriate for the process and the Grade of the working area. It should be worn in such a way as to protect the product from contamination.
Per 21 CFR 211.28, "Personnel engaged in manufacture, processing, packaging or holding of drug product should wear clean clothing appropriate for duties they perform."
Per FDA's Guidance for Sterile Drug Products…2004 "An aseptic barrier gown should provide a barrier between the body and the sterilized materials, and prevent contamination from particles generated by, and microorganism shed from, the body. Gowns should be non-shedding and should cover skin and hair."
ISO 14644-5 Cleanroom Operation notes in part 4.2 Cleanroom Clothing, that the environment and the product shall be protected from contamination generated by the personnel and their clothing. In order to maximize containment the choice of barrier fabric, the clothing style, and the extent of coverage of personnel by the garment shall be established. It is also pointed out that cleanroom clothing shall be made of minimal linting fabrics and materials resisting breakdown and not shedding additional contamination. The necessary cleaning, processing and packaging shall be defined.

GAP IN UNDERSTANDING CLEANROOM GARMENTS

Acquiring cleanroom garments is usually processed by the purchasing department, where cost is the priority. Long term contracts are established with the gown supplier or gown laundry service for price reduction. Quality agreements are often not established, and even if they are they are in general terms. Service level agreements cannot be established unless the purchasing agent understands the importance of gown processing to meet consistent quality of gowns and how critical it is to cleanroom contamination control.
Pharmaceutical industry turns to FDA guidances, USP and PDA or other Journals for information, however critical information related to gown choice and management is only found in IEST's best practices and various ASTM International standards and a hand full of publications or texts.



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WHAT SHOULD BE CONSIDERED WHEN CHOOSING CLEANROOM GOWNS

Fabric

Understanding the fabric and the filtration efficacy is important depending upon the environment the gown will be used in; this is extremely critical for aseptic facilities. In general there are three types of materials cleanroom gowns are made from.

Woven fabrics

Woven fabrics are typically used in the construction of garment systems, including body coverings, head coverings, face coverings and footwear, for use in all classifications of controlled environments. The yarns used in the manufacture of woven fabrics intended for use in cleanroom garment systems are typically made of continuous, multifilament polyester.

Knit fabrics

Knit fabrics are made from multifilament polyester yarns similar to those used in making woven fabrics. Knit fabrics do not provide a stable filtration medium for body-covering garments. Hence, knit fabrics are not recommended for use in cleanrooms.

Nonwoven fabrics

The third fabric type used in the construction of cleanroom garment systems is nonwoven fabric. Nonwoven fabrics run the gamut from loosely organized bonded strands to tightly arranged films and membranes. Many cleanroom garments made from nonwoven fabrics are thought of as single-use or limited-reuse products (1).

Garment sizes

Garments are generally available in generic sizes by letter (e.g. S=small, M=medium, etc.); however, the end user should be aware that sizes may vary among different manufacturers or suppliers. Wearing the wrong size gown can generate contamination, either by bellowing effect with larger than required gowns, and causing discomfort and garment tears when tight fitting gowns are worn. To ensure a correct fit, sizing samples should be used before ordering.

Choice of wrist cuffs and leg cuffs

Cuffs are available in knit, elastic, elastic with thumb loop, snap, or open varieties, or any combination of these designs. Knit cuffs provide a comfortable, snug fit around the wrist or ankle, however, due to the porous nature of a knit fabric, cuffs made of this type of material

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What should be considered when choosing cleanroom gowns (continued)

Material properties and testing

Depending on the specific application, evaluation of fabrics intended for use in cleanrooms may include tests for the following characteristics. A variety of ASTM International standards are used by the gown manufacturer to test each of the aspects below.

- cleanliness and cleanability
- electrostatic properties
- biological properties
- durability
- comfort
- opacity
- particle filtration efficiency
- microbial penetration
- chemical compatibility
- fluid resistance

Certain properties of the component fabric and materials may provide information on wear characteristics under laboratory or simulated conditions. These tests are defined in various ASTM standards as well as IEST CC003 (1). This information may be helpful in comparative evaluation, but the true durability of a garment can be measured only under real-use conditions over a significant amount of time. In addition, garment system components and construction should be compatible with the intended method of sterilization over the expected life of the garment. A sample garment should be sterilized and then evaluated for degradation. Some durability tests include abrasion resistance, tensile strength, and tearing strength. Additionally particle generation is measured on new garments using the body box testing as well as Helmke drum test (1). The Helmke Drum test also helps define the number of laundry cycles the garment is capable of withstanding. The Helmke drum test method is used to quantify particles dislodged from garments (4,5,6).

Other areas to evaluate to ensure that the garment does not get compromised over multiple laundry cycles and starts fraying is the sealing of raw edges of material by overlock, or sealing. The thread, the sealing of edges, and stich length is also defined by various ASTM Standards.

Entrapment areas are attached and stitched features of the garment that can trap unwanted contamination and debris. These include pockets, pager tabs, belts, pleats, fold over collars, folded cuffs, unnecessary seams, sewn-on emblems, sewn-on logos, and pen tabs (1). These types of features should be avoided in gowns used in critical areas of the cleanroom, especially in aseptic facilities. Pockets, linings, zippers, and other supplementary items used in the manufacture of garments should be compatible with cleaning and sterilizing methods. These should be installed on the garment in a way that minimizes the entrapments that can become a reservoir for

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Points to Consider During Garment Processing

The purpose of cleaning or laundering is to restore a soiled garment to acceptable performance for its intended application. The various techniques and methods used in processing cleanroom apparel and accessories may greatly influence the overall performance of the gowning system. Each user may require particular defined controls, such as specific pre-cleaning procedures or segregation from other gowns for preventing cross contamination.
The end user should ensure through an audit process that the processing of gowns through the laundry service does not compromise garments over their useful life. The audit should include the following checks, and not just a paper audit. This includes procedures from the time soiled garments are picked till delivery of cleaned/sterilized garments.

Soil sorting of garments and Inspection
Soil sorting of garments and Inspection at the processing/laundry facility should utilize both visual and tactile inspection steps to uncover damage to the garment including erased markings of identification before the garment is released for further laundering and sterilization . Garments that are badly damaged or unrepairable should be removed from distribution. This information should be tracked through a computerized tracking system.

Garments should be inspected for but may not be limited to:

- Excessive wear
- Puckering
- Cuts, tears, undone stitching
- Loose threads at seams
- Stains
- Fiber breaks
- Shrinkage
- Integrity of elastic, seams, bindings, and snaps
- Holes in high wear areas typically near knees and elbows
- Loose threads at seams
- Zipper function
- Buckles, operational snaps
- Tufts of filaments emanating from the seams

Air cleanliness in garment processing facilities
All processing of garments, such as laundering, testing, and initial packaging should be performed in a cleanroom that meets the specified air cleanliness class in accordance with *ISO 14644-1* and is consistent with the final use of the garment system (1).

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Points to Consider During Garment Processing (continued)

Processing of garments

Garments may be cleaned by either washing with purified water, or by dry cleaning, or by a combination of both. After garments are washed, they may be rinsed with purified, deionized (DI) water, reverse osmosis (RO) water, or both, to reduce the nonvolatile residues on the garments. The appropriate cleaning process will depend on the needs of the user, and should be a part of the agreement between the user and the garment processor (1).

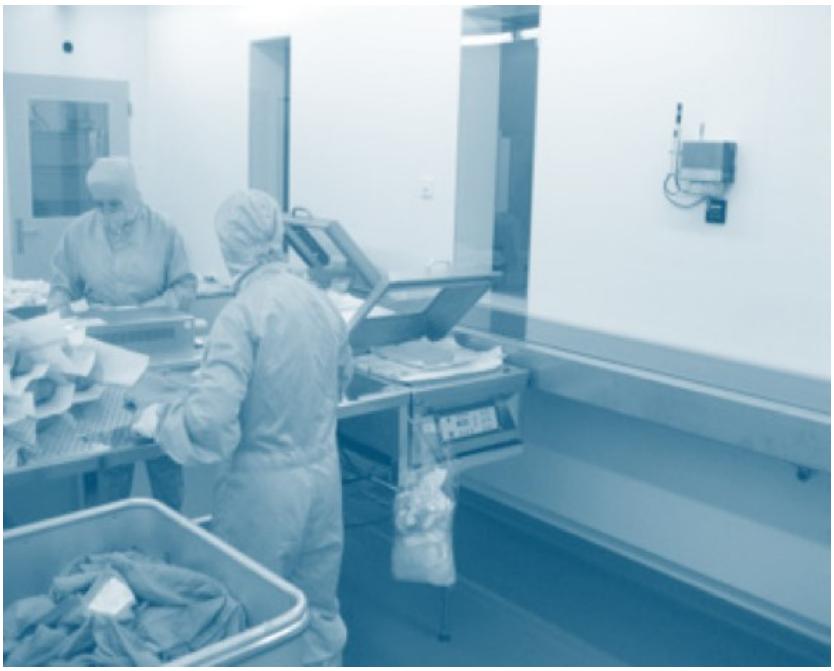
Garment tracking systems

This barrier property of cleanroom garments can be degraded gradually with each laundry cycle, which creates the need for a process to track the number of cycles to which a garment has been subjected. This is where the Helmke Drum Test can be used to determine the maximum number of laundries a specific garment type can withstand (5).

Laundering procedures

Use of harsh chemicals and high temperatures during washing and drying may damage the fabrics resulting in particle generation and fraying of garments.

To avoid shrinkage (undue wrinkling and seam puckering), wash temperatures should range from 32 ° C to 60 °C . Water quality should reflect the most stringent requirements of the clients served. Detergents used should be nonionic surfactants. Product is tumble-dried at a moderate temperature (typically no more than 60 °C) and gradually cooled at the end of the cycle to avoid fabric shock (1).



Packaging and shipment of garments

All garments should be over bagged to protect extraneous material, or contaminants, or otherwise adversely affect product cleanliness or cause odor.

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CONCLUSION

It should be the responsibility of the quality department to develop a plan and procedures for procurement and management of gown supplies.

The first step is to analyze the needs and precisely, determine what type of gowns and accessories would be required depending upon the contamination control needs. This includes the materials, design, and change frequency. This may include a survey or initial audits of gown suppliers and laundry services to ensure that they meet the requirements and standards.

The second step would be to establishment specifications or formal documentation outlining the requirements resulting from the first step above. This formal system will set a standard against which the quality of the cleanroom garment program will be judged during the program's lifetime. Vendor surveillance and audits of prospective vendors' facilities and capabilities should be judged against the garment program specifications already established.

ABOUT THE AUTHOR

Ziva Abraham is the President and Founder of Microrite, Inc., a California based consulting firm providing consulting and training services to pharmaceuticals, biotechnology, medical devices and in vitro diagnostics in the areas of quality assurance, quality control, microbiology, and validation. Ziva has over 25 years of academic, research, clinical and industrial experience in microbiology, and quality assurance. Ziva has received her Master's Degree in microbiology and has worked on developing microbial insecticides using entomogenous bacteria and fungi towards her doctoral research. Her career also includes founding and managing clinical laboratories for Maccabi Medical in Israel. She has trained personnel from various industries in microbiology techniques and methods. She uses her extensive experience to teach why assessing risk of microbial contamination should be in the forefront of any company that has products for human/veterinary use. Her experience in clinical laboratories has provided her with the framework to understand the effects of microbial contamination in products from a patient safety perspective.

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