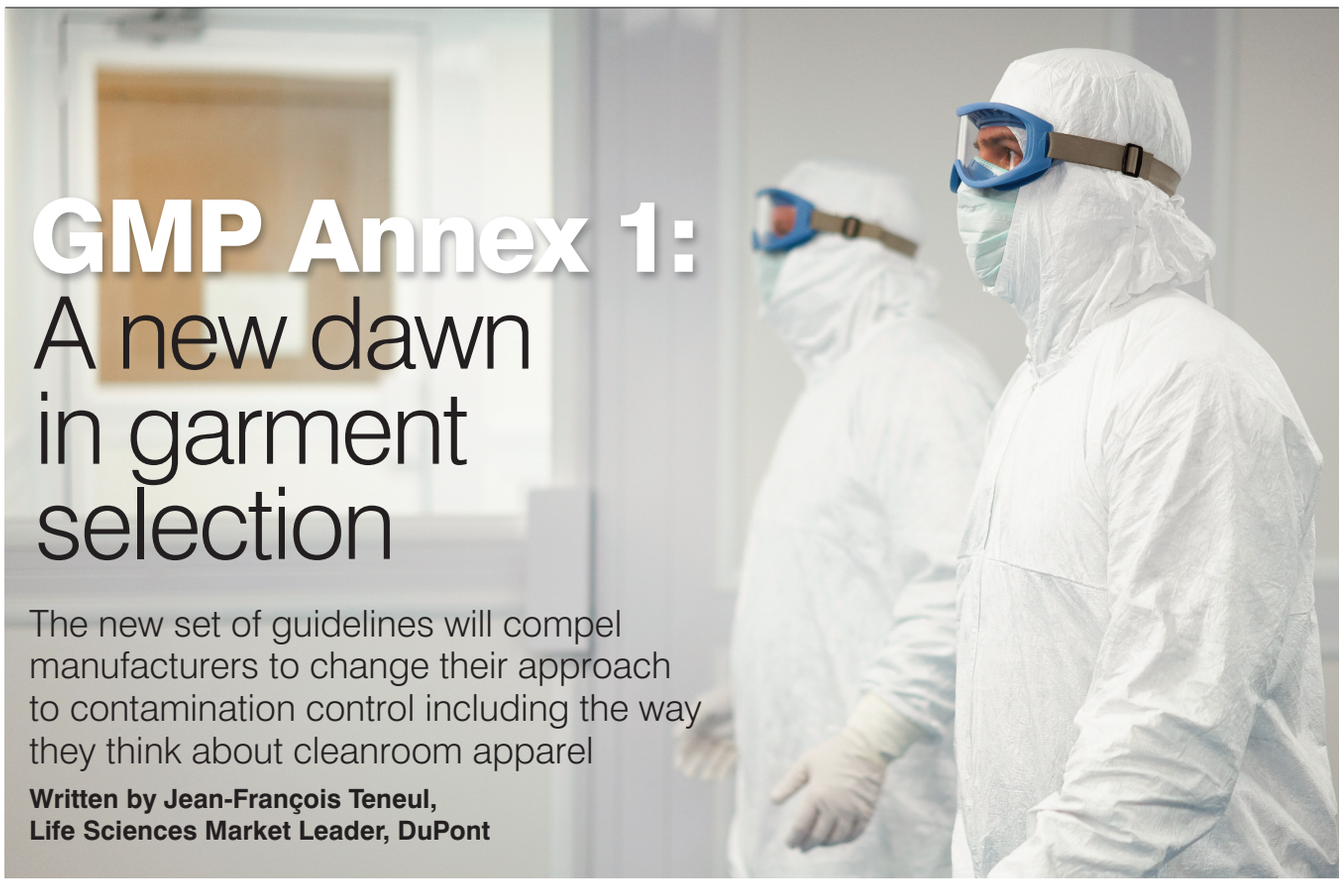

GMP Annex 1: A new dawn in garment selection

The new set of guidelines will compel manufacturers to change their approach to contamination control including the way they think about cleanroom apparel

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The latest version of Annex 1, still in draft, represents a step-change for the industry. Manufacturers of sterile medicines and APIs will be required to take a different approach than in the past and adopt a contamination control strategy that continuously applies QRM principles and proactively identify, scientifically evaluate and effectively control potential risks to quality.

Many elements are involved in such a strategy: the design of the manufacturing site, its equipment and processes; staff training; garment selection; cleaning and disinfection procedures; preventative maintenance; qualifications validations, and monitoring systems. As people are the source of 75% of contamination in a cleanroom, it seems one of the most important factors to understand is the role different types of garments (single-use vs. reusable) can play.

Studies have shown that operators are the primary source of contamination for both microorganisms and particulate matter. From a QRM perspective, it makes more sense to reduce these contamination risks in conjunction with relying on air filtration or cleaning procedures.

Many steps can be taken to control the risks but one of the most important factors is the performance of the cleanroom garment.

Not all cleanroom garments are equal

Fabric and garment design should act as a filter to minimise contaminants from the operator, such as skin flakes, hair and sneezing aerosol, from entering the cleanroom.

The garment system plays a crucial role in ensuring that human contamination inside the cleanroom is as low as possible. But not all cleanroom garments are created equal. Some have significantly less filtration efficiency than others, and some can be a source of contamination (e.g. particles, fibres, chemicals and pyrogens).

The garment system play a crucial role in ensuring that human contamination inside the cleanroom is as low as possible

Studies performed for DuPont by an independent laboratory show significant differences between various materials used for cleanroom garments when tested for particle filtration efficiency (PFE) and bacterial filtration efficiency (BFE).

There seems to be a direct correlation between PFE tests and the average fabric pore size. Typically, this is one μ for single-use fabrics; five to six μ for new reusable uncoated polyester fabrics; and up to 30 μ for reusable uncoated polyester fabrics after multiple uses, washing and sterilisation cycles. The smaller the pore size and the more tortuous the path through the fabric, the higher the filtration efficiency, which results in better garment system performance.

Single-use clean and sterile garments have constant filtration efficiency, making quality risk assessment easier compared to reusable garments that have a fluctuating FE during their lifetime due to the flexibility of the woven fabric, as well as the adverse effects of multiple uses, washing and sterilisation cycles.

Many variables in the washing cycle can affect the garment, including water quality and temperature; chemicals used; and air quality in the dryer. With sterilisation, multiple cycles of gamma irradiation have a minimum and maximum kilogray (kGy) dosage, making it very difficult to identify the total number of kGy a garment receives. ▶

Particle shedding is considered the main contamination risk from cleanroom garments. These items of clothing also pose a risk of chemical contamination and pyrogens. Other sources are sewing thread that may be linting; elastics may shed particles when they are stretched; ineffective washing or sterilisation of a used garment; and packaging that may not be validated for cleanroom use.

Particle filtration and shedding from the garment depends on the fabric, its design and manufacturing process, the age of the item and the number of times it has been repaired, washed, dried and sterilised, as well as its packaging and handling throughout the value chain.

In some instances, garments must also protect operators from chemical or biological hazards. Compounding and manipulation of oncology drugs, handling and production of hormones; or manufacturing HPAPI are a few examples of situations that require the use of PPE. But once again, not all cleanroom garments are created equal. Single-use garments offer a higher barrier against chemical and biological hazards compared to the reusable alternative. Due to repeated washing and sterilisation cycles, reusable garments show a decrease in barrier performance over time. That's why it is important not only to understand and assess critical properties, such as PFE, BFE and barrier but to also evaluate, assess, validate and audit the entire value chain and life cycle of the garments.

Value chain assessment

Innovations in garment systems give pharmaceuticals the chance to choose those that best meet their needs and comply with GMP Annex 1. All factors along the value chain should be considered to make an informed decision.

Manufacturing: Rolls of single-use polymer fabric are released under specifications by a sole manufacturer, cut and sewn. Then inspected and released as per SOP. For reusable items, the risk of failure varies considerably across multiple manufacturers, from fibre production, spinning, weaving and then cutting and sewing.

Packaging and transport: Most single-use garments are clean-processed, folded and packaged in a pouch or two, placed in double poly case liners and sealed in a single-use box. A Certificate of Compliance is added during the packing step, and the product has a five-year shelf life. Most reusables are packed in a bag with up to six-month shelf life and then in a reusable crate.

> **Single-use clean and sterile garments have constant filtration efficiency, making quality risk assessment easier**

Evidence of damage is often invisible to the naked eye and this can result in a tear during use, increasing the contamination risk

Sterilisation: Single-use garments are only washed and sterilised before wearing. These garments come with a Certificate of Sterility, and a Certificate of Irradiation is added to the exterior of the box after dose verification. Reusable items are washed and sterilised many times over their life cycle.

Performance in the cleanroom: Single-use garments provide a consistent barrier against particles and microorganisms. Reusable polyester alternatives have a higher risk of contamination due to their high permeability. Frequent washing and sterilisation of reusable garments lead to damaged fabric and larger pores, increasing the release of particles and fibres, as well as contaminants from the operator and other clothing.

Repairing garments: Single-use garments are only worn once. Inadequate repairs on reusable clothes can lead to performance issues. Another concern is knowing when to replace them.

The new GMP Annex 1 revision draft requires that "reusable garments should be replaced based at a set frequency determined by qualification or if the damage is identified". To comply with this requirement, manufacturers must provide evidence of garment performance through a set number of washing cycles and need to standardise and control reprocessing to minimise the risks of garment deterioration.

Evidence of damage is often invisible to the naked eye and this can result in a tear during use, increasing the contamination risk.

DuPont can offer invaluable assistance by providing risk assessment tools and examples of cleanroom garment system validation; supplying documentation such as Certificates of Sterility, and providing traceability of their garments through the value chain.

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