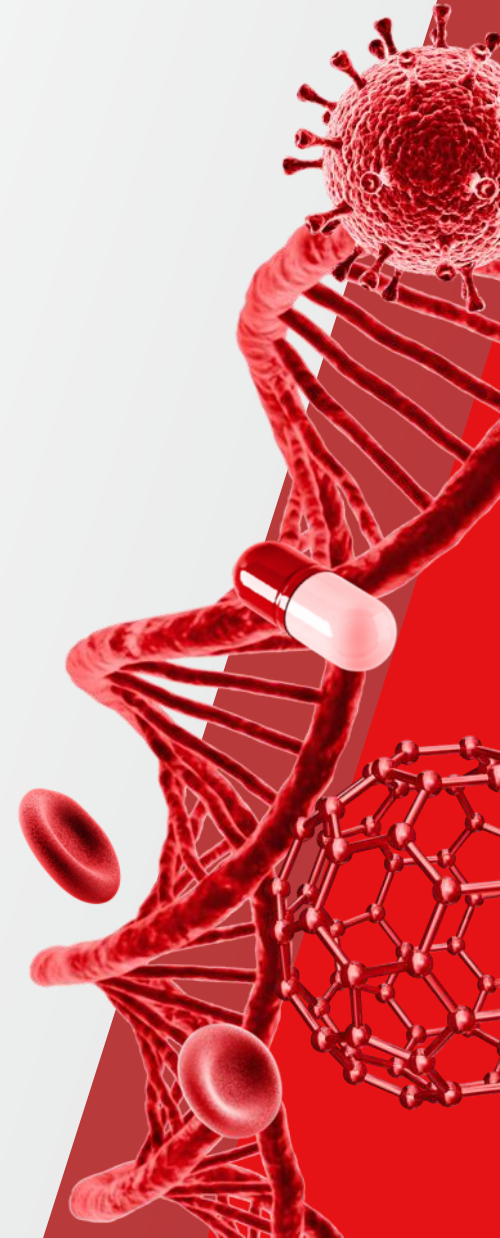


# Risk of Reusables in the Aseptic Processing Area

**Lara Iovino**

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Fisher Scientific, part of Thermo Fisher Scientific  
+1 973 524 4425; [lara.lovino@thermofisher.com](mailto:lara.lovino@thermofisher.com)

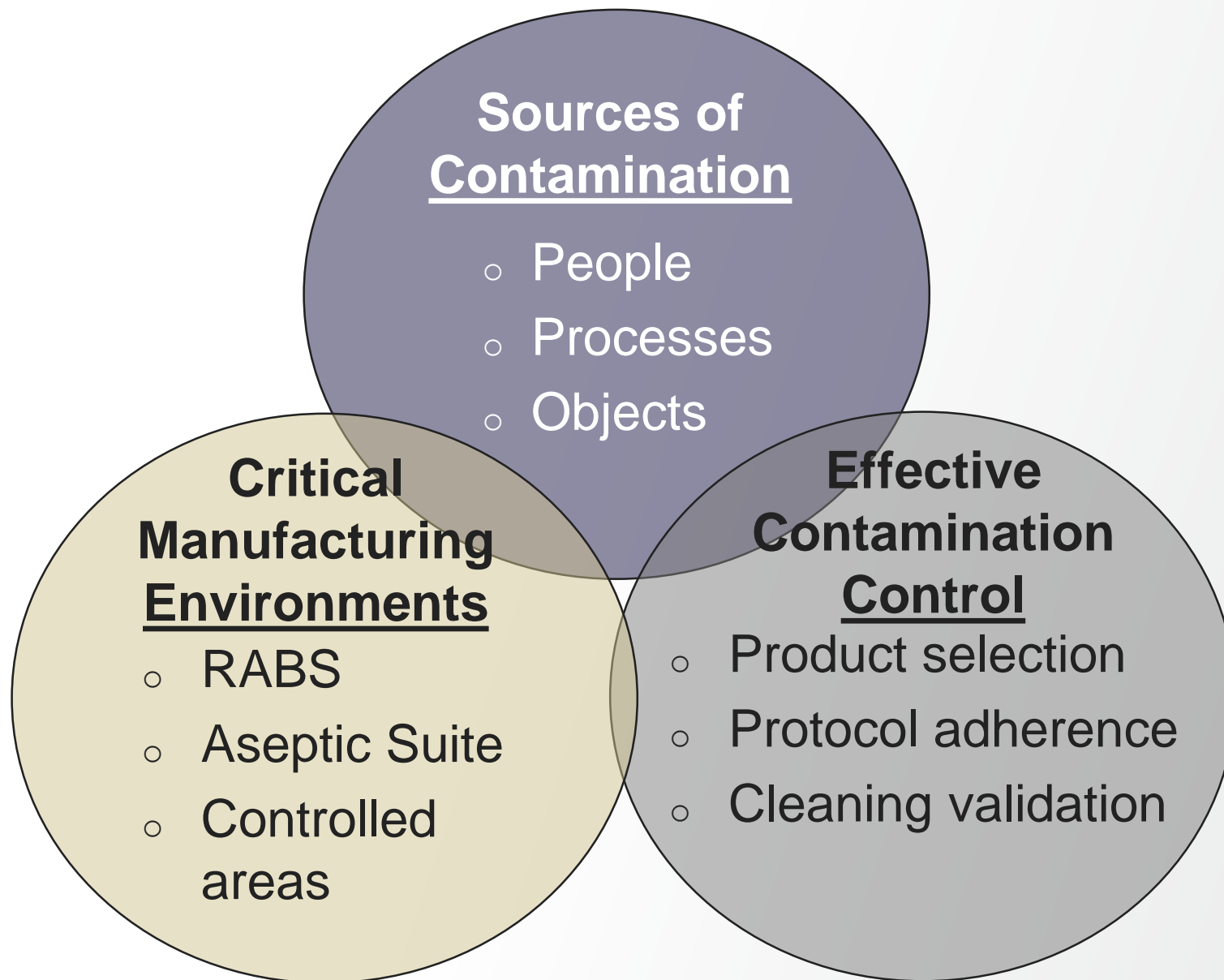
**14 April 2021**



# Where's the Risk – “Photo Hunt” Game



# Risk of Contamination – Sources of Contamination



# FDA 483 Warning Letter Sterile Product Manufacturing site in India - 12/2016

<https://wayback.archive-it.org/7993/20170404201110/https://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2016/ucm534983.htm>

***Your firm failed to ensure that manufacturing personnel wear clothing appropriate to protect drug product from contamination (21 CFR 211.28(a)).***

- *Observed employees working in **gowns had unraveled stitching** extending from hoods, zippers, and pants. Your firm approved these gowns for operations. Employees wore them while manufacturing sterile APIs.*
- *Your response is inadequate...it does not include your assessment of washing, drying, ironing, sterilizing, or other operations that **may contribute to sterile garment damage**. It does not address the **need to limit the number of sterilizations**. ...Excessive sterilizations lead to breakdown of gown fibers.*
- *Your aseptic processing gowns were inadequate to prevent contamination of your sterile products with particles and microorganisms shed from employees' bodies. Your firm must use garments that are suitable for aseptic processing.*

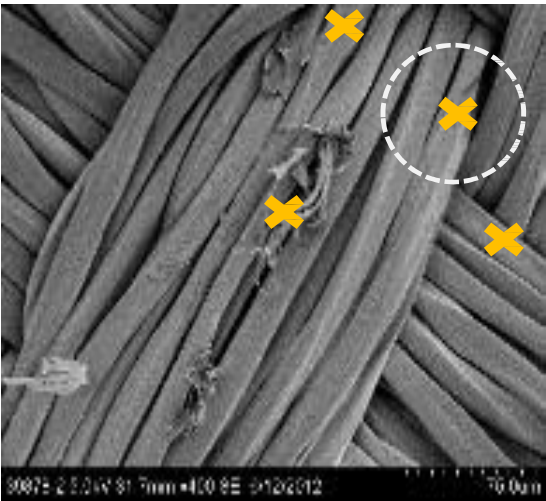
Continued



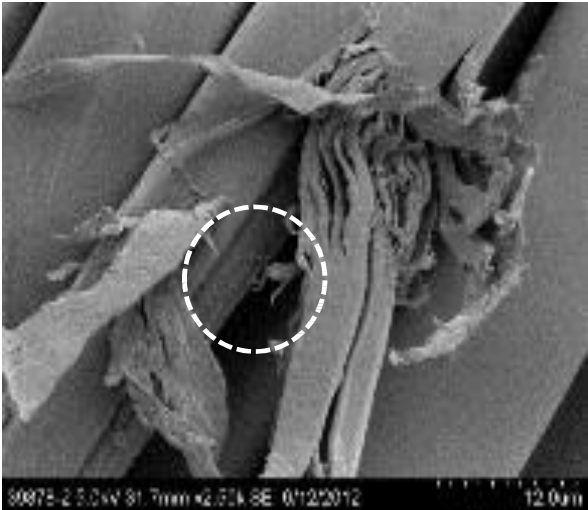
# SEM of Common Cleanroom Coveralls

- How does the material, the laundry & the gamma irradiation process effect particle penetration?

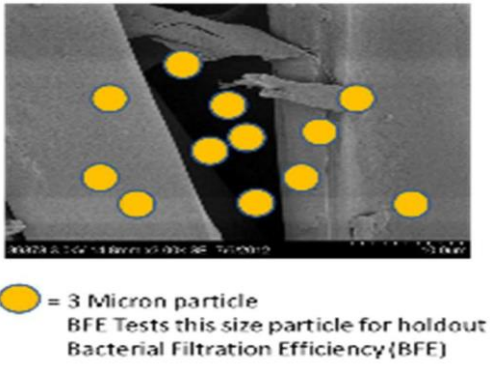
75 microns



12 microns



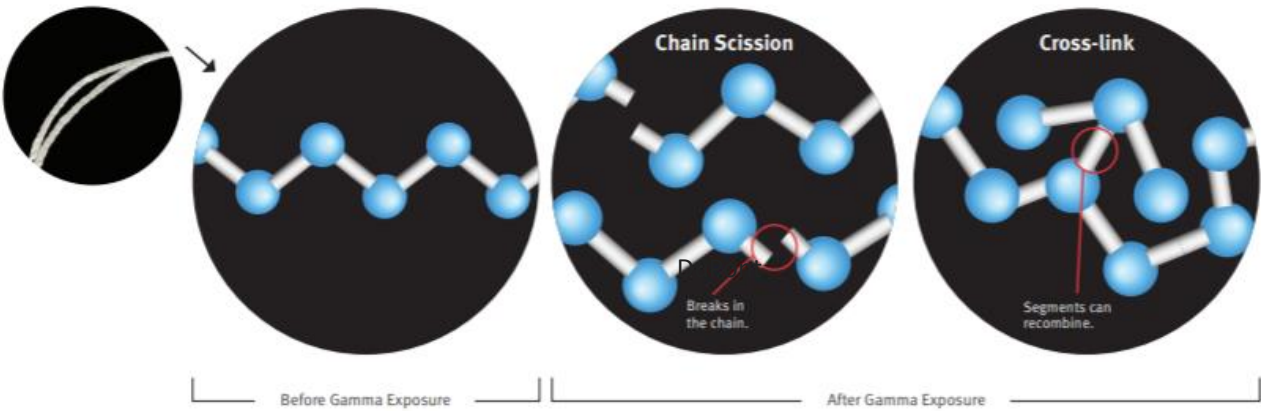
10 microns



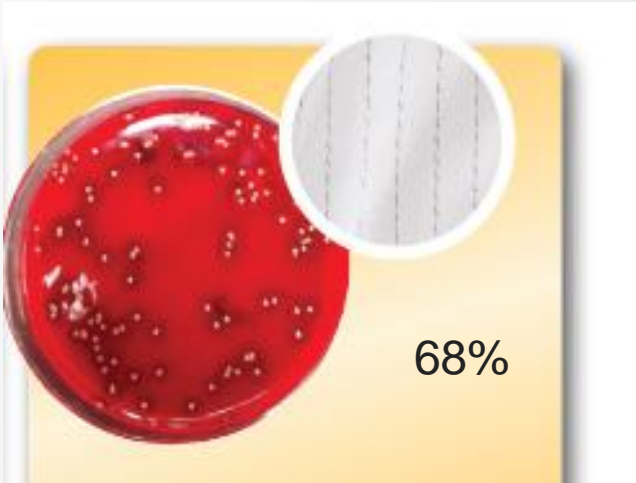
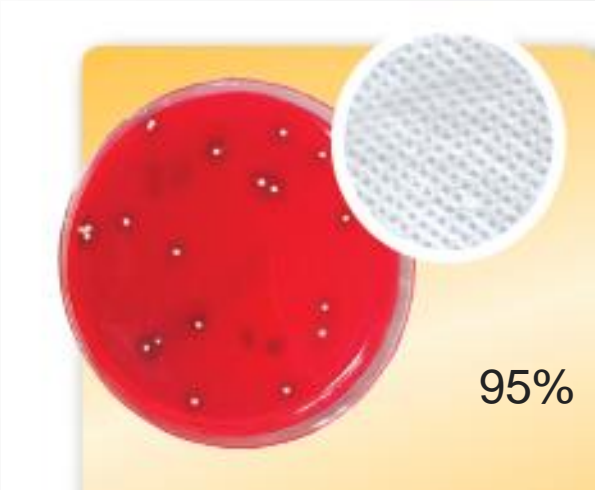
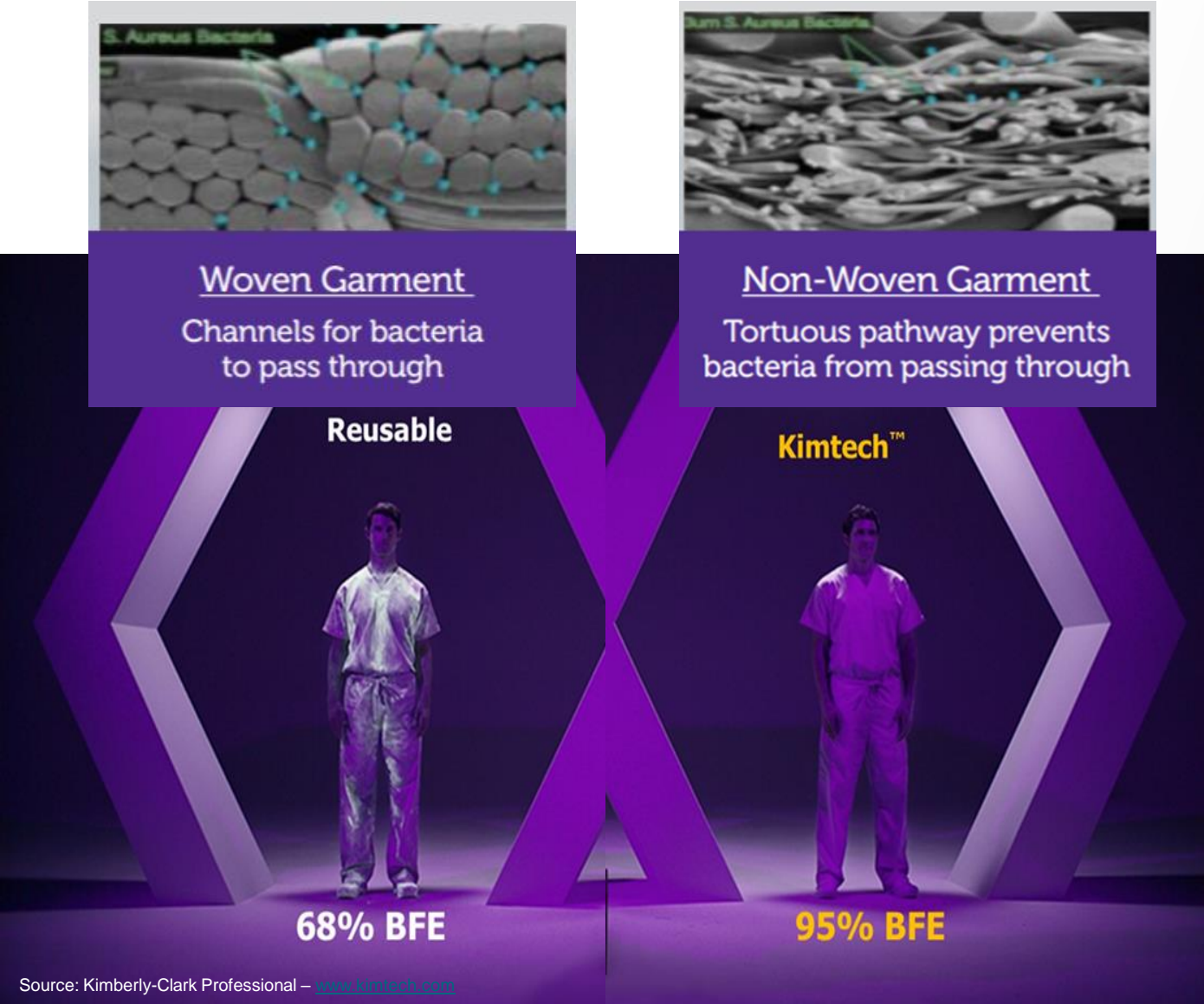
Note: (SEM) samples only a very small area. Random sample areas evaluated. Pictures were taken from different garments.

Kilograys: Minimum and Maximum? 22.5kGy to 40kGy?

## Pictorial Description of the Effect of Gamma Radiation on Polymer Molecule Chains



# Where's the risk in the use of cleanroom garments?



Bacterial Filtration Efficiency example

# FDA 483 Warning Letter Sterile Product site in India - 12/2016, continued

- *...**Provide an action plan** that describes how your firm will...*
  - *Select appropriate gown suppliers. Include the role of the **quality unit** in making supplier selection and ongoing qualification decisions.*
  - ***Reduce your maximum number of gown sterilizations** to ensure that gowns are discarded before they show signs of breakdown. Provide the **maximum number of re-sterilizations** you will allow, and describe how you will **document and validate** this procedure.*
  - *Correct your visual inspection procedures for sterile garments to improve detection and rejection of defective garments.*
  - *Ensure that the **quality unit** makes final decisions relating to release of raw materials and supplies (e.g., garments) you use in production.*
  - *Conduct a **risk assessment** of the effects of damaged garments on your drugs*





# Cleanroom – 1960-70 Designs

*Slide courtesy of Jim Agalloco, Agalloco & Associates 2020*

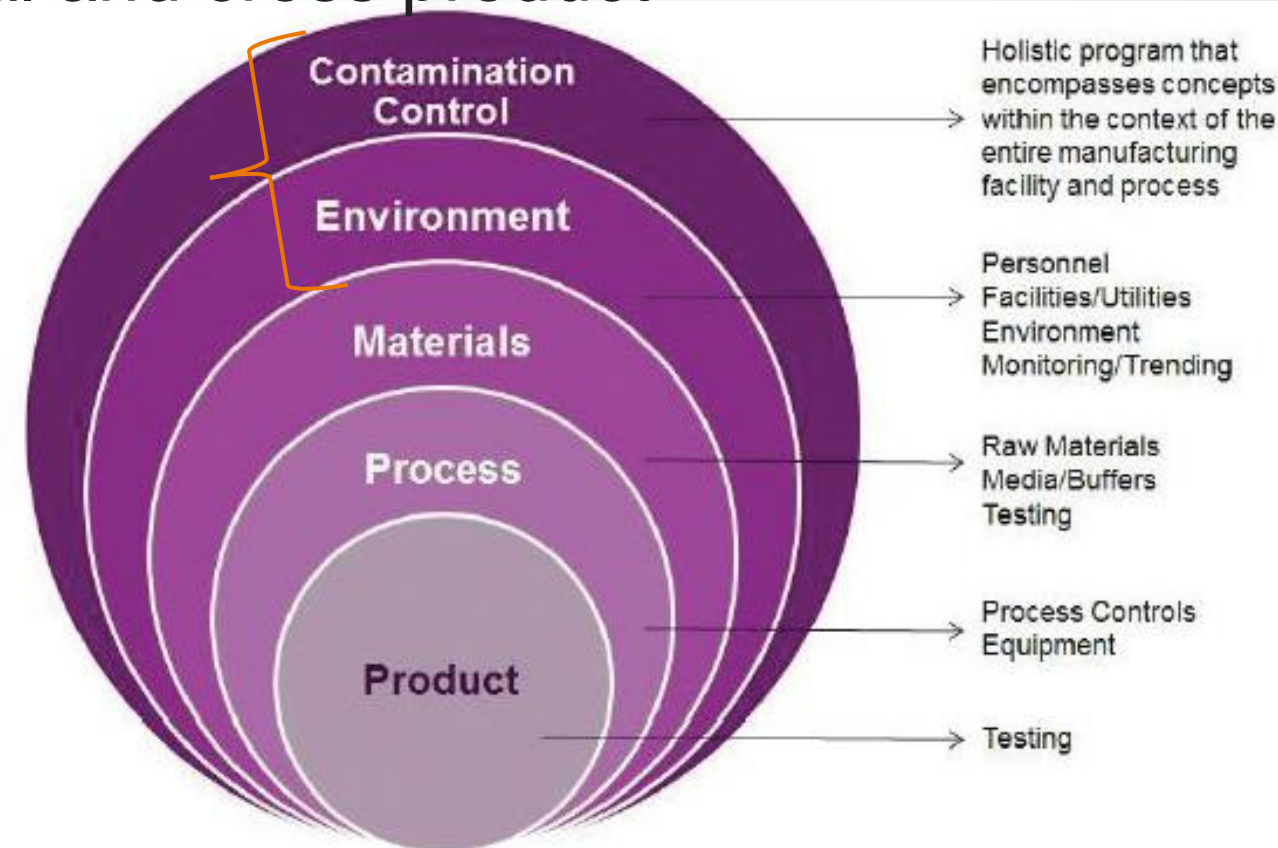




# Annex 1- Contamination Control Strategy

- Requires a **holistic approach** to identification, assessment, control and monitoring process for contamination risks that include microbiological, particulate, chemical and cross product contamination. Including:

- Facility Design
- Process Design
- Personnel Training and Gowning
- Cleaning and Disinfection
- Environmental Monitoring
- Process Simulation



# Contamination Risk Mitigation is key

- Excerpts from Annex 1 Draft
  - 4.10: Prior to use, Sterile Garments and eye coverings should be checked for Sterility and Packaging Integrity... Reusable garments should be **replaced based at a set frequency** determined by qualification or if damage is identified.
  - 4.11: The clothing and its quality should be appropriate for the process and the working area. It should be worn in such a way as to **protect the product from contamination**.

# Contamination Risk Mitigation is key, *continued*

- Excerpts from Annex 1 Draft

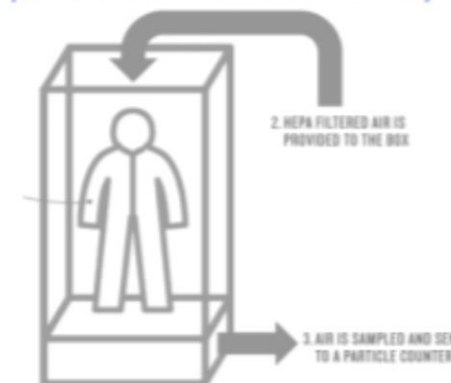
- 4.12.C: Garments should be folded and packed to minimize contact with the outer surface when gowning. The protective clothing should shed virtually no fibres or particulate matter and **retain particles shed by the body**.
- 4.15: After washing and before sterilization, garments should be **checked for integrity**

## Drop-Down Gowning

### BODY BOX TESTS

#### IEST-RP-CC003.4

- simulates particle release under real wear conditions. A test person performs a series of defined movements in a cabin.
- Concentration of particles are counted by a particle counter



# FDA 483 Warning Letter Sterile Product Manufacturing site in North Carolina - 03/2013

<https://www.fda.gov/media/85847/download>

*Senior Purchasing Agent confirmed that there is **no standard procedure that defines and establishes the minimum and maximum life of a garment** In addition, there exists **no record to document the life cycle** of the gowning attire, which would assure that the garments and personnel attire are fit for use.*

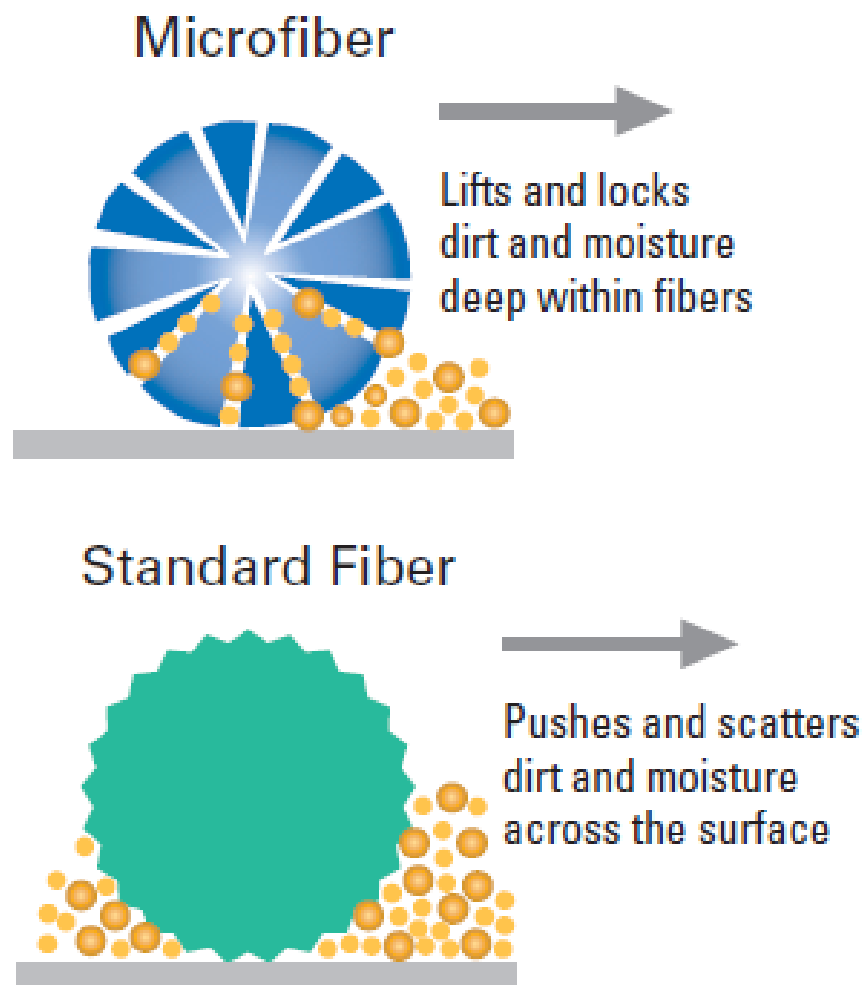


# Contamination Risk Mitigation is key, *continued*

- Excerpts from Annex 1 Draft
  - 6.5: The **cleaning process should be validated** so that it can be demonstrated that it:
    - a) Can remove any residues that would otherwise create a barrier between the sterilizing agent and the equipment surfaces.
    - b) Prevents chemical and particulate contamination of the product during the process and prior to disinfection.

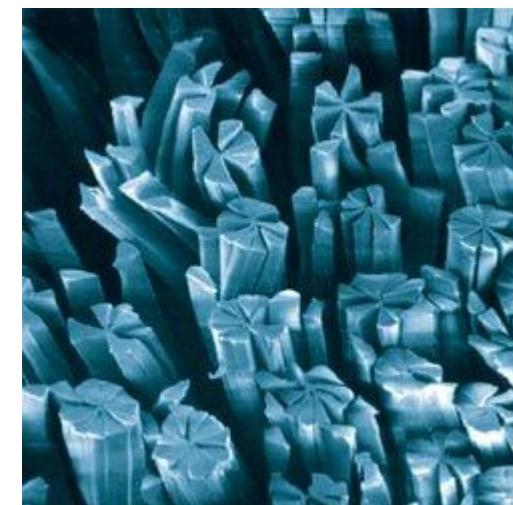


# Removing contamination – mops and wipers



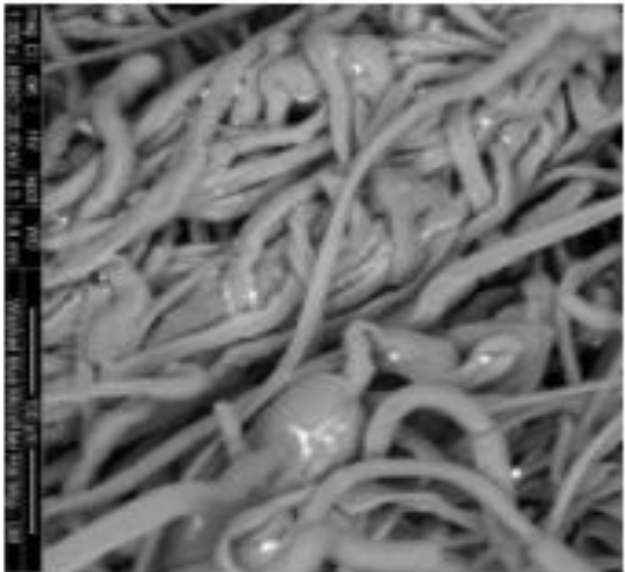
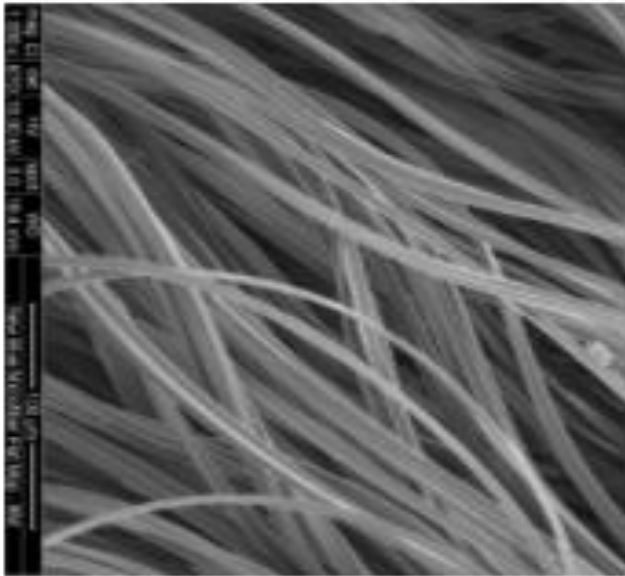
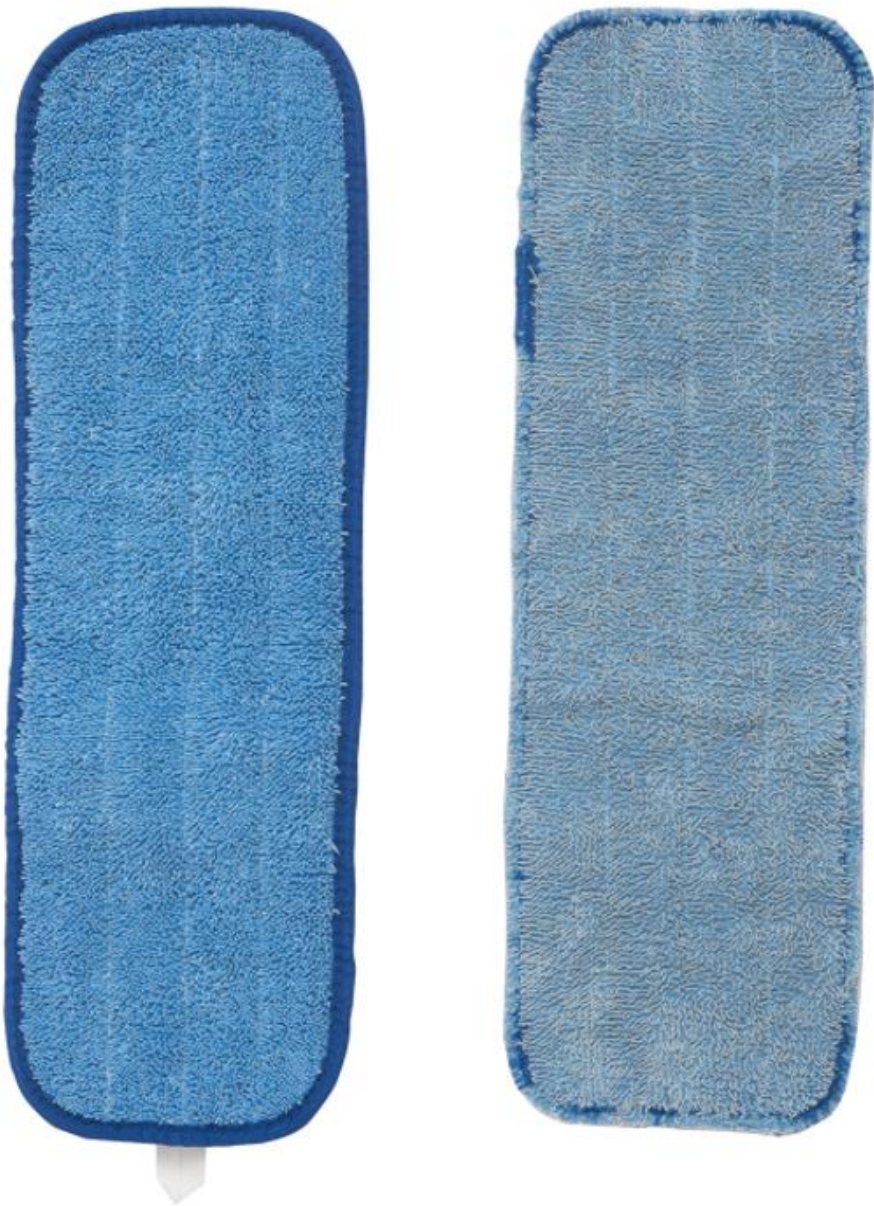
Source: Contec Inc. published:  
<http://www.pharmtech.com/hidden-problems-relaunders-microfiber-mops>

- The properties that make a microfiber product a good cleaning tool also make it nearly impossible to be cleaned
- Using laundered/reusable mops brings up some concerns for validating cleaning methods and disinfectant interactions/inactivation.
- Quat inactivation (Quaternary Ammonia disinfectants)
- Where storing? Dock? Mold?
- Washing/Drying Process:
  - Destruction of microfibers
  - Overloading washers don't allow for proper agitation/rinse
  - High heat used to speed up drying
  - Validating/managing cycles
  - When is too many?



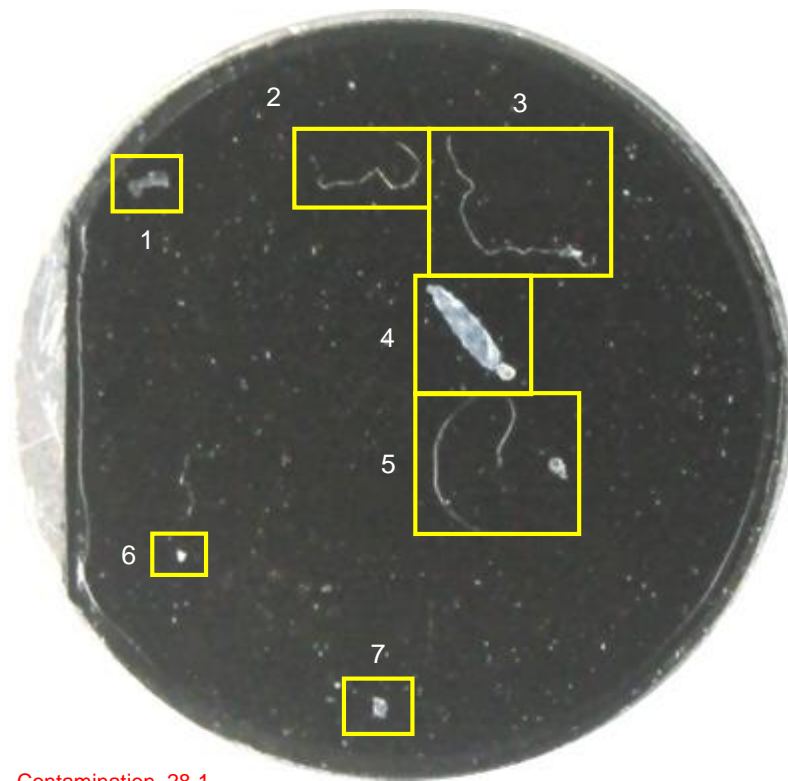
Stock SEM photo of Microfiber

# Visual and Microscopic Analysis

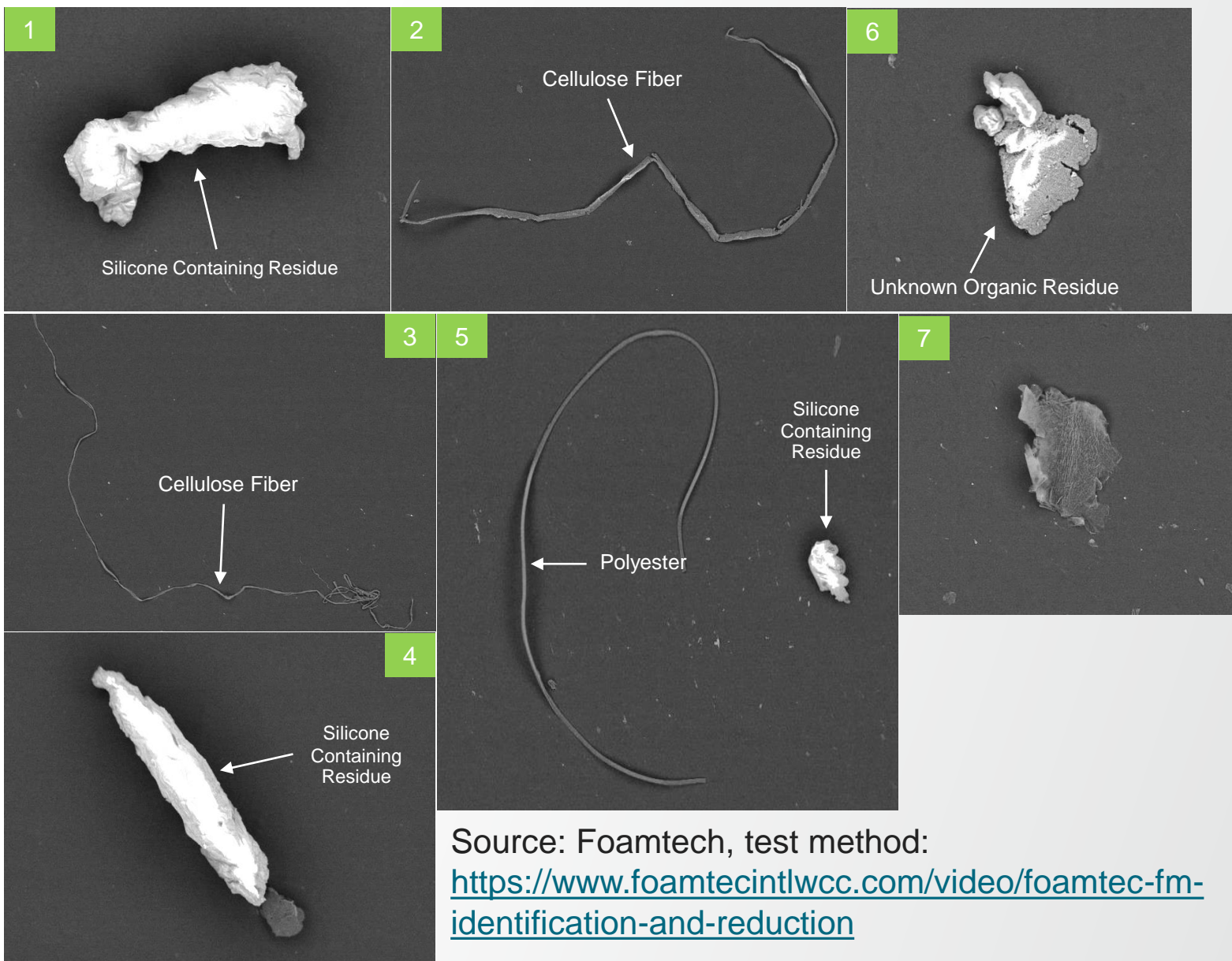
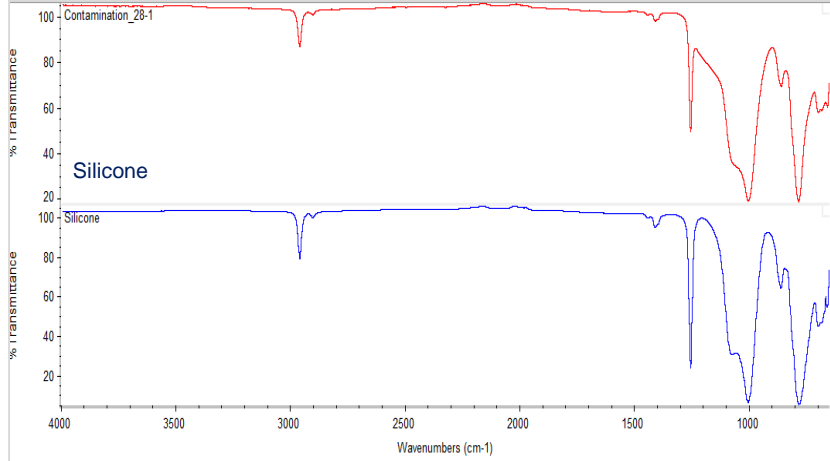




# What's recovered in "clean" mops



Contamination\_28-1



Source: Foamtech, test method:  
<https://www.foamtecintlwcc.com/video/foamtec-fm-identification-and-reduction>



# Comparison of Risk: Single-Use v. Reusable

- Risk is easy to identify but it would be speculation to assess the severity and frequency for your site.

Single Use Risk	Reusable Risk
Source raw materials and incoming bioburden	Contamination burden on the used garments, mops, or wipers can vary widely and can lead to inconsistent quality levels in the relaundered materials
Qualified Supplier	Are materials segregated? Cross contamination?
Control of the process	How do you verify the contamination has been cleaned from the washer itself?
Chain of custody	How to know when reached life expectancy (loss/ruin)
Inventory management challenges (COVID-19)	Consistency in product?
-	Weave gets relaxed - garment sizing
-	Slips hazard – boots sag, mops won't remove residues
-	Inventory management challenges (\$)

**QRM**

# Summary/ Call to Action

- Assess your contamination risk
- Be prepared to answer regulator questions related to a holistic approach to contamination control
- Be prepared to know the risk of reusables if you're using them in your cleanroom
- You can avert most of the risk by using a one-time-use product



# Reference & Supporting Materials

## Garment Testing Standards:

- <https://www.iest.org/Standards-RPs/Recommended-Practices/IEST-RP-CC003>
- [https://ips-group.dk/wp-content/uploads/2014/04/Tema-Renrum-presentation-DuPont-De-Nemours-2018\\_.pdf](https://ips-group.dk/wp-content/uploads/2014/04/Tema-Renrum-presentation-DuPont-De-Nemours-2018_.pdf)

## Garment Information

- [https://www.cleanroomtechnology.com/news/article\\_page/A\\_life\\_cycle\\_assessment\\_of\\_reusable\\_garment\\_properties/130358](https://www.cleanroomtechnology.com/news/article_page/A_life_cycle_assessment_of_reusable_garment_properties/130358)
- <https://www.kcprofessional.com/en-us/workplacesolutions/are-you-dressed-for-success/see-the-risks>
- [https://www.cleanroomtechnology.com/news/article\\_page/A\\_to\\_Z\\_guide\\_to\\_protective\\_garments/148566](https://www.cleanroomtechnology.com/news/article_page/A_to_Z_guide_to_protective_garments/148566)
- [Advantages of DuPont™ Tyvek® IsoClean® Single-Use Controlled Environments Garments](#)

## Wipers and Mop Information

- <https://www.berkshire.com/learning-center/relaunders-cleaning-cleanroom-wipes/>
- <http://www.pharmtech.com/hidden-problems-relaunders-microfiber-mops>
- <https://contecinc.wistia.com/medias/hnlge8aoz9>
- <https://www.foamtecintl.com/video/foamtec-fm-identification-and-reduction>
- [https://www.contecclean.com/resources/articles/PREMIRA\\_Microfiber\\_White\\_Paper\\_II\\_112017.pdf](https://www.contecclean.com/resources/articles/PREMIRA_Microfiber_White_Paper_II_112017.pdf)
- Quat binding: <https://www.youtube.com/watch?v=SYjCefnJAak>

## Appendix: IEST Garment Considerations (Testing for Garments & Materials) per RP-CC003.4

- **The tests that garments/ material can be subjected to are as follows:**
  - **Particle Penetration** – The ability of the fabric to filter particles generated by wearer.
  - **Equivalent Pore Diameter** – The air pressure to determine the relative pore size of the garment.
  - **Helmke Drum** – Measures particles 0.1-10 micrometer on material/garment usually to simulate particle shedding.
  - **Releasable Large Particles** – Air is filtered through a membrane filter for particle analysis of particles > 5.0 micrometer and fibers.
  - **Particle Dispersion (Body Box)** – Useful in determining relative differences between various sets of apparel.
  - **Microbial Penetration** – Assesses Microbial penetration of the garment.



# Thank you

