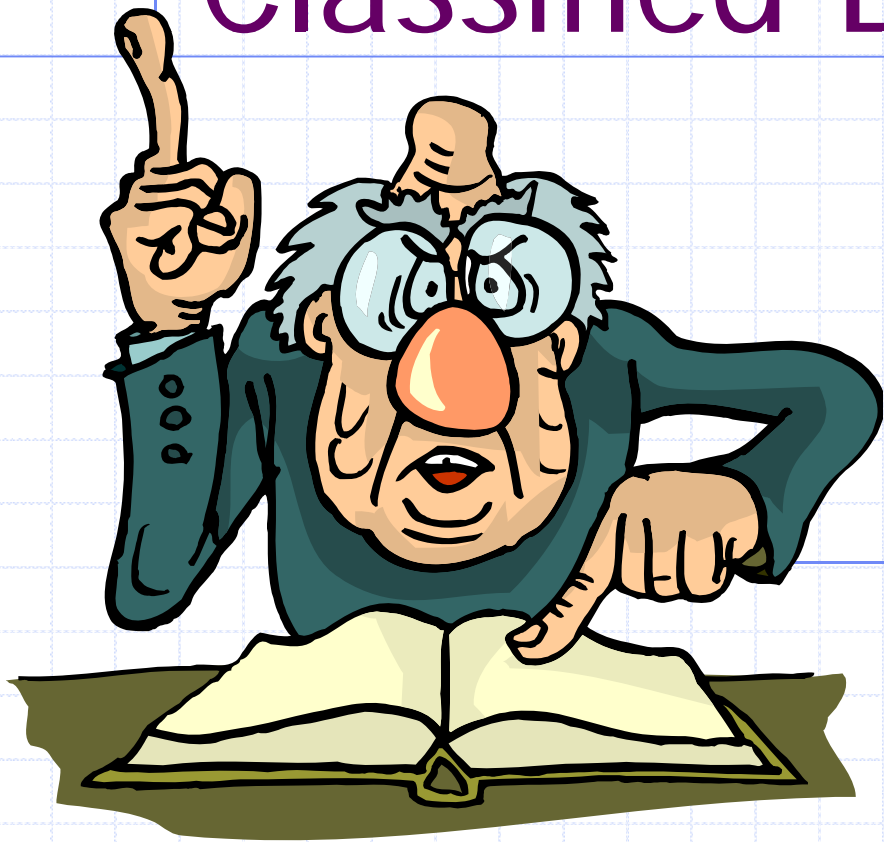


# Decontamination of Classified Environments



James Agalloco  
Agalloco & Associates

# Presentation Outline

- ◆ Opening Thoughts
  - ◆ Cleanroom Realities
  - ◆ The Processes
  - ◆ The Agents
  - ◆ The Execution
  - ◆ The Trouble Spots
- 
- ◆ Isolators are not in the scope of this presentation, nor are fogging or gassing

# Some Opening Thoughts

- ◆ The objective isn't constant.
  - ISO 5 (Class 100) -> ISO 8 (Class 100,000)
  - Aseptic -> Classified -> Controlled, unclassified
- ◆ The frequency, and extent of treatment should vary with the objective.
- ◆ The methods are pretty much constant.
- ◆ The objective is usually non-absolute.

# Some Cleanroom Realities

- ◆ A good facility design is essential. Poorly conceived and/or poorly maintained facilities are more difficult to maintain at the desired conditions.
- ◆ Within a single facility the differences between classifications may come down to single factor – differing amounts of clean air supplied to the environment.
- ◆ There are more air changes in the higher classified rooms.

# More Cleanroom Realities

- ◆ HEPA filters in different environments all have the same efficiency.
- ◆ Cleanroom construction differences in different classes great.
  - Walls and floors are often identical.
- ◆ There's one basic aspect that while universal is sometimes all too often forgotten - they are supposed to be clean.
- ◆ It's not just the room, you have to address every surface and item in it as well!

# An Extreme Example

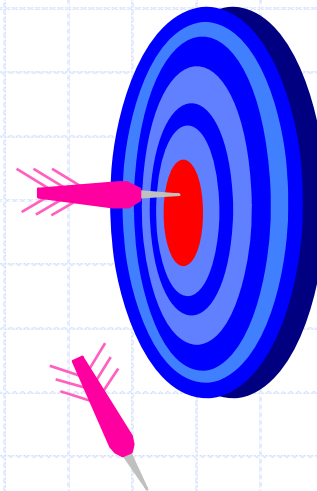
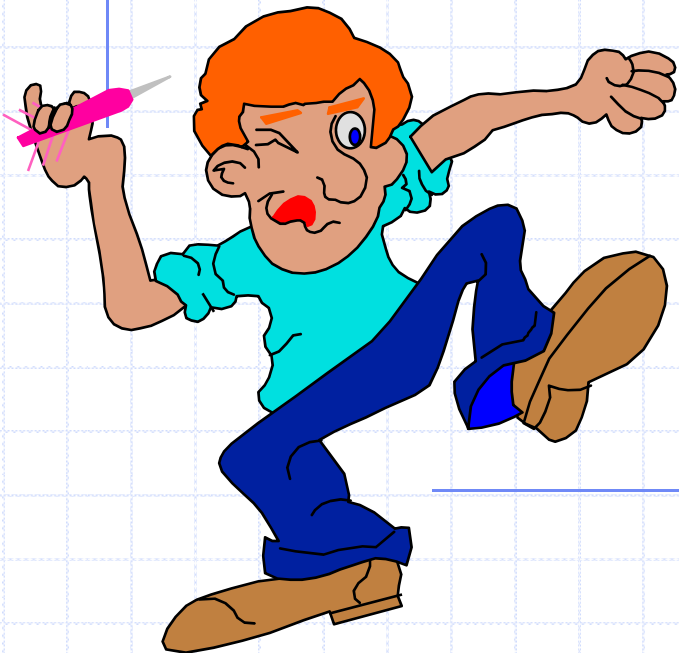


# What does your cleanroom look like?



# What should your cleanroom look like?

# The Processes





# Sanitization – Loosely Defined

- ◆ Practices utilized to control microbial populations on materials and surfaces.
- ◆ Cover a broad range of processes
  - Routine disinfection of cleanrooms.
  - In response to microbial excursions.
  - Processing of materials into cleanrooms..
  - Bioburden reduction prior to sterilization.
  - For equipment incompatible with sterilization.

# Disinfect or Sanitize or Sterilize?

- ◆ The distinction between these processes is not great.
- ◆ All of the agents will kill vegetative cells (disinfect /sanitize), and many of them will also destroy resistant spores under the appropriate conditions (sterilize).
- ◆ Limitations of use, application methods, process time, etc may reduce the effectiveness of the agent.
- ◆ Thus we use the term sanitize, rather than sterilize to describe the treatment process regardless of what agent is used.

# How Effective are Sanitizers?

- ◆ Many of these agents are lethal to all organisms including spores.
- ◆ Limitations in how they are applied reduces their effectiveness.
- ◆ The more manual the delivery process the less effective the treatment.
- ◆ In highly automated systems, these agents will sterilize!

# Sterilization - Sanitization

- ◆ The difference between these processes relates to:
  - Level of documentation provided by the process / treatment.
  - Ability to define, measure and control key operating parameters.
- ◆ A lethal agent used with inadequate controls cannot be confirmed as sterilization process.

# The Agents



# The Ideal Agent

- ◆ Broad spectrum: wide antimicrobial spectrum
- ◆ Fast acting: a rapid kill
- ◆ Not affected by environmental factors
- ◆ Nontoxic: should not be irritating to the operator
- ◆ Non-corrosive: should not corrode / erode materials
- ◆ Easy to use with clear label directions
- ◆ Odorless
- ◆ Economical
- ◆ Soluble
- ◆ Solubility: should be soluble in water
- ◆ Stability: should be stable in concentrate and use-dilution
- ◆ Cleaner: should have good cleaning properties
- ◆ Environmentally friendly:
- ◆ **Actually exists**

Adapted from Molinari, 1987

# Agent Comparison Table

**TABLE 8-3 Activity of disinfectants in addition to being bactericidal, pseudomonacidal and fungicidal\***

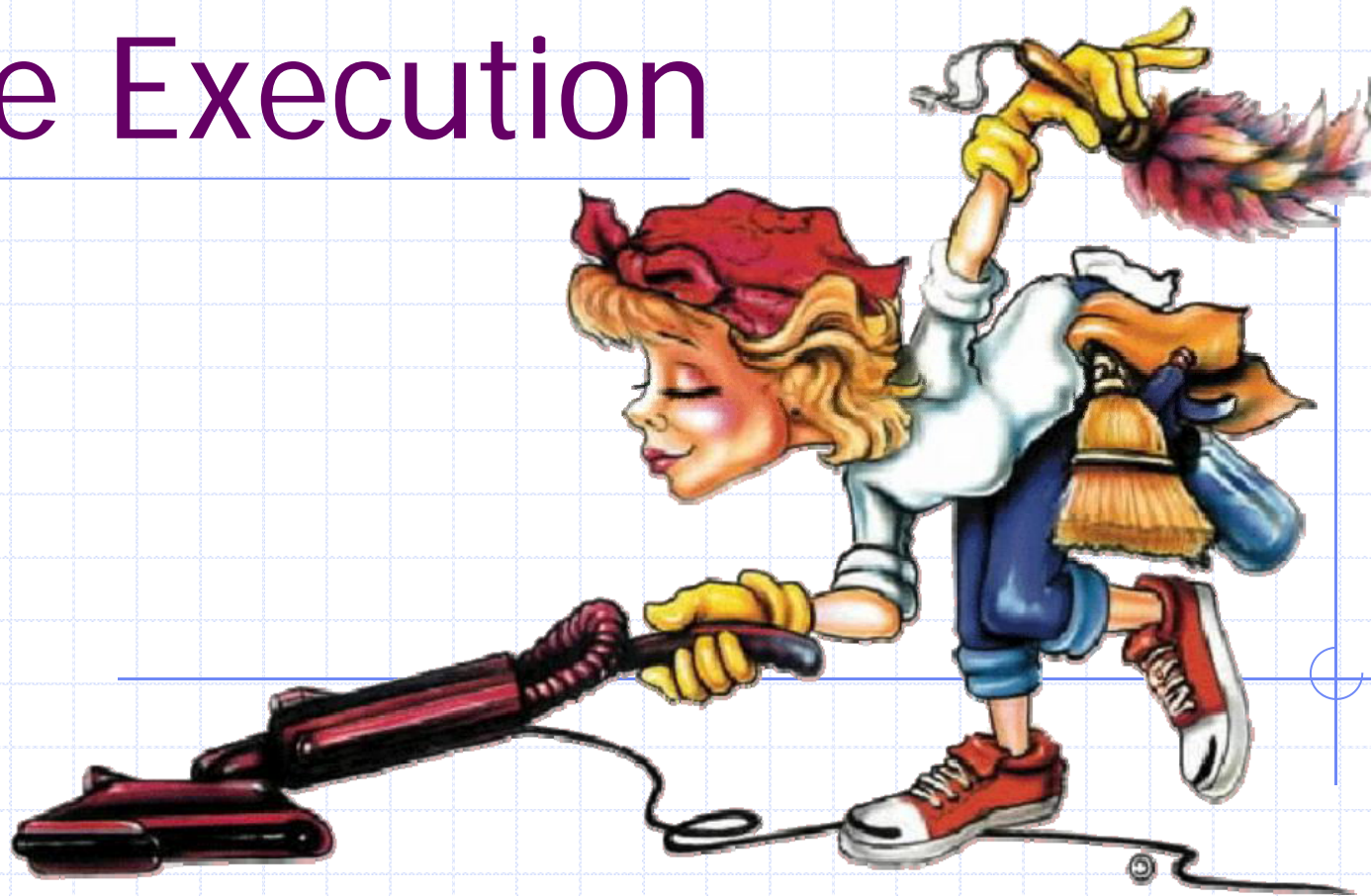
Disinfectant	Microbial activity				Immersion time				Hazard
	Activity level	HIV	Hepatitis B+	Tubercle bacillus	Tuber-culocide	Sporicide	House-keeping		
<b>Chemicals</b>									
Alcohol, 70%-95% ethyl	Intermediate	Yes	Yes	Yes	15 min	N/A	Yes	Flammable	
Alcohol, 70% -95% Isopropyl	Intermediate	Yes	Yes	Yes	15 min	N/A	Yes	Flammable	
Chloride compounds	Low	Yes	Yes	Yes	N/A	N/A	Yes		
Formaldehyde, 37% Aqueous	High	Yes	Yes	Yes	15 min	12 hr	No	Toxic fumes	
Formaldehyde, 8% in Alcohol	High	Yes	Yes	Yes	10 min	12 hr	No	Toxic fumes	
Glutaraldehyde, 2%	High	Yes	Yes	Yes	45-90 min	10 hr	No	Irritating fumes	
Iodophors, 450 ppm	Intermediate	Yes	Yes	Yes	20 min	N/A	Yes		
Iodophors, 100 ppm	Low	No	No	No	N/A	N/A	Yes		
Mercurial compounds	None	No	No	No	N/A	N/A	No	Bacteriostatic only	
Phenolic compounds	Low	Yes	No	Yes	20 min	N/A	Yes	Skin irritant	
Quaternary ammonium	Low	Yes	No	No	N/A	N/A	No		
<b>Physical</b>									
Boiling water	Low	Yes	No	No	N/A	N/A	No		
Ultraviolet irradiation	Low	Yes	No	No	N/A	N/A	Air and water	Skin and eye irritant	

# Controlling the Agents

- ◆ Control like a raw material,
  - Specifications, release, labeling, storage, etc.
  - FIFO
- ◆ Filter to sterilize if not purchased sterile.
- ◆ Follow manufacturers directions on storage, and application (if available).
- ◆ Label all containers with date of preparation when making dilutions.
- ◆ Store properly to preserve shelf life, protect workers as required.
- ◆ Be aware of safety concerns at all times



# The Execution



# Process Essentials

- ◆ Every antimicrobial process relies on similar concepts
  - The concentration of the agent
  - Its ability to penetrate to the target
  - The duration of exposure / contact time
  - The presence of humidity (usually easy)
- ◆ The operator plays a major role in ensuring that these are fulfilled in order to accomplish the desired effect.

# An Oft Forgotten Aspect

- ◆ To properly decontaminate a cleanroom, it is always preferable to start with a clean room!
  - Remove soil, and product residues
  - This process should reduce particles as well.
- ◆ Remove anything that doesn't have to be there. Storage should be in lower classified environments.
- ◆ Clean before you decontaminate, not all agents can penetrate soil or product residues.

# Operator Impact

- ◆ The operator performing the process might slough off enough organisms on previously treated surfaces that the efficacy of the agent performance can be questioned. Thus organisms are found on the surface after the process.
- ◆ This can happen regardless of the agent's effectiveness against the microbial population.
- ◆ The more diligent the worker, the more likely this may be!

# The Solution or The Problem?



# How to Disinfect the Surface

- ◆ Always start with clean surfaces.
- ◆ Remove any items that cannot be treated.
- ◆ Apply from top down.
  - Ceiling, walls, equipment, then floor.
- ◆ Overlap strokes or passes minimally.
- ◆ Use 2- or 3- bucket system to prevent recontamination.
- ◆ Allow sufficient residence time.
- ◆ Removal of agent may be required.

# How to Disinfect the Room

- ◆ Start with the ceiling (if it's scheduled).
- ◆ The critical environment within the room starting at the top as well. Curtains & barriers on the inside.
- ◆ The walls, doors, windows, curtain & barrier externals and all permanently installed items in the room. Remove all items from surfaces , cabinets & shelves. Treat the shelves empty, and then the items as they are replaced.
- ◆ Last the floors.

# How to Disinfect the Facility

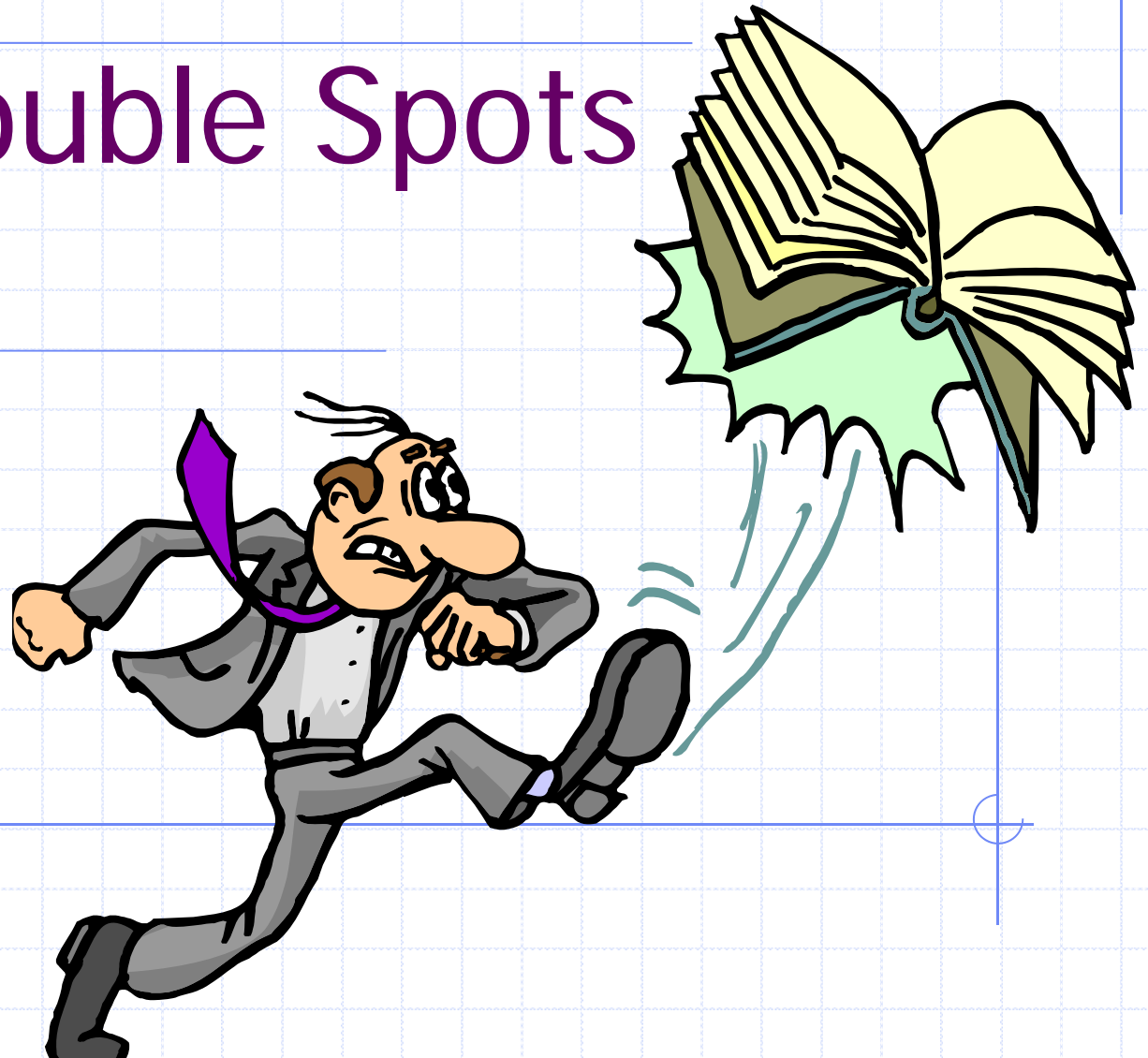
- ◆ Work from the cleanest environments out towards those of lower classification.
- ◆ The frequency of decontamination can vary with the criticality of the environmental use.
- ◆ Even if a room hasn't been used for production it still needs to be decontaminated.
- ◆ Start with fresh materials in each room to avoid spreading contamination.



# The Acceptance Criteria?

- ◆ Surfaces should consistently meet the expected environmental limits of FDA & EMA.
- ◆ Decontamination in airlocks & pass-throughs has been validated, but the criteria vary widely.
- ◆ To expect these processes to sterilize is likely excessive, the process controls are robust enough to assure that.

# The Trouble Spots



# It's Largely a Manual Process

- ◆ The effectiveness of the process is largely dependent upon the diligence of the personnel executing it.
- ◆ Delegating this critical activity to the most recent hire or outsourcing may be counterproductive.
- ◆ The task should not be rushed, performed haphazardly or considered unimportant.

# Rotation of Disinfectants

- ◆ **There is no reason to rotate among 2 or more non-sporicidal agents.**
- ◆ Microorganisms cannot develop resistance to disinfectants the way they can to antibiotics. It's recontamination during decontamination or sampling.
- ◆ Use a sporicide as needed and sparingly due to:
  - Corrosive action on surfaces & materials
  - Concerns for worker safety

# Validation of Disinfection

- ◆ Room & equipment surface treatments – demonstrated by environmental results.
- ◆ Component entry
  - By sampling post treatment against environmental limits.
  - By spiking pre-treatment & sampling post-process.
    - ◆ Spike of USP microbial panel
    - ◆ Spike of environmental isolates (bioburden?)
    - ◆ Using a resistant sporeformer is over the top

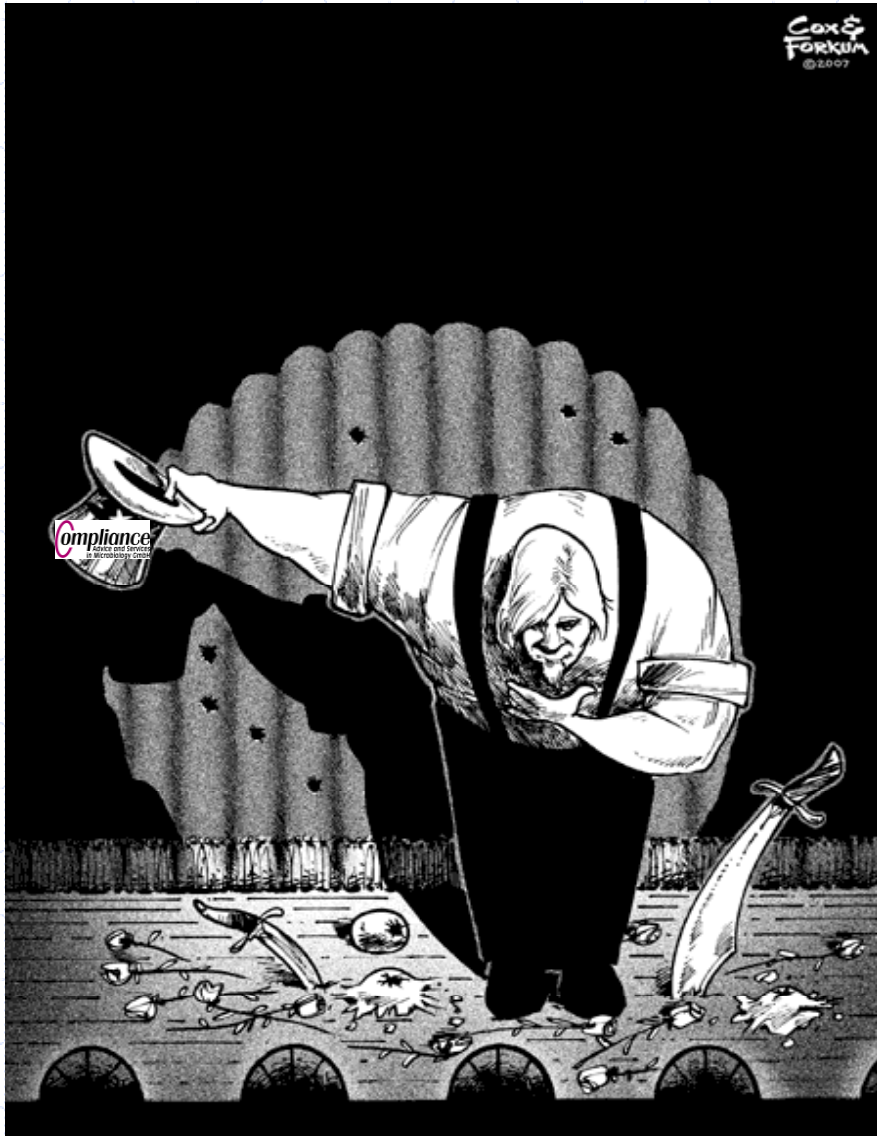
# Some Quick Tips

- ◆ Detection of mold means there's excess water somewhere even if it is not visible.
- ◆ Frequent detection of spores means you need to increase the frequency of sporicide use.
- ◆ You may need to decontaminate gown rooms, air locks and pass-throughs more frequently than the rest of the facility.
- ◆ The ceilings may need cleaning only infrequently, except where they might become dusty (i.e., compounding, weighing areas.) in which case they should be cleaned and decontaminated after each use.

# References / Reading

- ◆ CDC, Guideline for Disinfection and Sterilization in Healthcare Facilities, 2008.
- ◆ USP, <1072> Disinfectants and Antiseptics.
- ◆ Block, S.S., *Disinfection, Sterilization, and Preservation*, 5<sup>th</sup> ed.; Lippincott Williams & Wilkins Publishers: Philadelphia, 2000.
- ◆ AOAC, International Official Methods of Analysis, 17<sup>th</sup> ed, Arlington, VA.

# Thank You for Your Attention!



Questions?

Contact

James Agalloco

[Jagalloco@aol.com](mailto:Jagalloco@aol.com)

(908) 874-7558