Cleanroom Cleaning and Disinfection: Eight Steps for Success

Cleanrooms in healthcare and pharmaceutical facilities must be kept in a state of microbiological control. This article outlines eight key steps for keeping a cleanroom clean.

Dr. Tim Sandle

Cleanrooms in healthcare and pharmaceutical facilities must be kept in a state of microbiological control. This is achieved in a number of ways, including the physical operation of Heating, Ventilation, and Air Conditioning (HVAC) systems, control of materials, properly gowned and trained personnel, and through the use of defined cleaning techniques, together with the application of detergents and disinfectants.

The object of cleaning and disinfection is to achieve appropriate microbiological cleanliness levels for the class of cleanroom for an appropriate period of time. Thus the cleaning and disinfection of cleanrooms is an important part of contamination control.[1] This article examines the eight key steps to be followed, in relation to cleaning and disinfection, in helping to keep cleanrooms "clean."

EIGHT KEY STEPS FOR KEEPING A CLEANROOM CLEAN

Step 1: Understanding cleaning and disinfection

Cleaning and disinfection mean different things and they are sometimes confused. Most importantly cleaning, using a detergent, must come before disinfection. Detergents are cleaning agents and are deployed to remove 'soil' (such as dirt, dust, and grease) from a surface.[2] The removal of soil is an important step prior to the application of a disinfectant, for the greater the degree of soiling which remains on a surface then the less effective the disinfection step becomes.

Detergents generally work by penetrating soil and reducing the surface tension (which fixes the soil to the surface) to allow its removal (in crude terms, a detergent increases the 'wettability' of water).

A disinfectant is a type of chemical germicide which is capable of eliminating a population of vegetative microorganisms (in addition, some disinfectants are sporicidal).

Step 2: Selecting the most appropriate agents

Selecting the most appropriate cleaning and disinfectant agents is important. The cleanroom manager will need to be confident that the agents will work and are appropriate for the type of cleanroom. Care also needs to be taken as some agents are not compatible with each other.

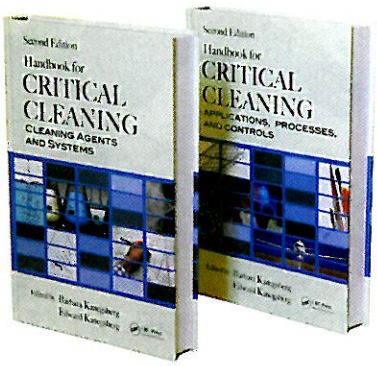
In selecting detergents, it is important that:

a) The detergent is neutral and a non-ionic solution.
b) The detergent should be non-foaming.
c) The detergent should be compatible with the disinfectant (that is the residues of the detergent will not inactivate the disinfectant).

BOOK REVIEW

Kanegsberg and Kanegsberg, *Handbook for Critical Cleaning:*

Book I: Cleaning Agents and Systems & Book II: Applications, Processes, and Controls



Darren Williams

Barbara and Ed Kanegsberg (a.k.a. "The Cleaning Lady and the Rocket Scientist") have produced an excellent resource for the manufacturer and for those researchers and consultants like myself who support the manufacturers.

My involvement in the cleaning community over the past decade has been focused mostly on solvent substitution, solvent blending, and cleaning verification. Although I could lecture for hours on the topics, I know there are many areas where I am in need of clear, concise, and accurate reference material. This two-volume encyclopedia of cleaning has filled this need almost completely.

This Handbook's strongest suit is the careful presentation of the Kanegsbergs' philosophy of process development and improvement. This is NOT an edited handbook that contains a collection of contributed chapters with a loosely-related, "sticky-note" introduction and conclusion. It is clear that this handbook was sincerely produced to benefit the manufacturing community and society in general through responsible process evaluation and improvement. For evidence, see the two-page discourse on "*How Not to Clean Critically with Household Products,*" which is appropriately followed by a summary of "*How to Choose a Cleaning Agent.*"

The Second Edition contains new material on non-chemical cleaning processes (i.e. CO_2, steam, and plasma). Two new chapters are included that address ultrasonic metrics, addressing the question, "*How do I select an ultrasonic process that maximizes cleaning and minimizes damage.*" Also, five chapters are provided that discuss cleanroom design, operation, monitoring, and behavior. These chapters contain detailed descriptions, highly illustrated examples, and a practical approach that is immediately useful.

Digging into the specifics, I was initially concerned by an emphasis on the one-dimensional Kauri-butanol (KB) value as a measure of solvency, since I am an avid user of the Hansen solubility parameters (HSP) as a basis for understanding solvency. But my concern was allayed by the quote: "Comparing the KB number with the Hansen system is somewhat analogous to comparing a black and white TV of the 1950s with a current full-color, high-definition color broadcast." This is a great example of the clear and humorous writing style of the authors.

In line with my interests in HSP, I was impressed with John Burke's chapter "*Solvents and Solubility.*" His chronology of the development of the Hansen system is very helpful. He presents a very nice example of the deficiencies in the one-dimensional Hildebrand solubility parameter.

In closing, I greatly appreciated the chapter "*Blunders, Disasters, Horror Stories, and Mistakes You Can Avoid.*" If Oscar Wilde was right that "Experience is simply the name we give our mistakes," then it behooves us to learn as much as we can from the "experience" of others! Some will see this chapter as a humorous interlude, but I think they miss the point. We often assume success in our endeavors. This chapter shows that assuming success can have extremely negative consequences to our businesses, our careers, and by extension our lives, and the lives of our families.

Likewise, we can learn a lot by the experience and success of Barbara and Ed Kanegsberg, as they have produced a very useful resource in these two handbooks.

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When selecting a disinfectant, points to consider are:[3]

a) To satisfy GMP regulations, two disinfectants should be used in rotation. While scientifically this may not be necessary, many regulatory agencies expect to see two different disinfectants in place. For this, the two agents selected should have different modes of activity.[4] It may be prudent for one of the disinfectants to be sporicidal.
b) The disinfectant should have a wide spectrum of activity. The spectrum of activity refers to the properties of a disinfectant being effective against a wide range of vegetative microorganisms including Gram-negative and Gram-positive bacteria.
c) Ideally the disinfectant should have a fairly rapid action. The speed of action depends upon the contact time required for the disinfectant to destroy a microbial population. The contact time is the period of contact when the surface to which the disinfectant is applied must remain wet.
d) Residues from organic materials or detergent residues should not interfere with the disinfectant.
e) Disinfectants used in higher grade cleanrooms (like ISO 14644 classes 5 and 7) must be supplied sterile or be sterile filtered by the cleanroom operators.
f) The disinfectant should be able to be used at the temperature at which the cleanroom operates. If a cleanroom is a cold store then it needs to be checked whether the disinfectant will work at that temperature.
g) The disinfectant should not damage the material to which it is applied or some other measures should be taken. Many sporicidal disinfectants are chlorine based and will damage material like stainless steel unless the residue is wiped away after use.
h) The disinfectant should be safe for operators to use and meet local health and safety laws.
i) The disinfectant should be cost effective and be available in the required formats like trigger spray bottles or ready-to-dilute concentrates.

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Step 3: Understanding types of disinfectants

There are a number of different types of disinfectant with different modes of activity and of varying effectiveness against microorganisms. Disinfectant action against the microbial cell include: acting on the cell wall, the cytoplasmic membrane (where the matrix of phospholipids and enzymes provide various targets), and the cytoplasm. Understanding the distinction between different disinfectants is important when selecting between non-sporicidal and sporcidial disinfectants (the division between non-oxidizing and oxidizing chemicals).[5]

Non-oxidizing disinfectants include alcohols, aldehydes, amphoterics, biguanide, phenolics, and quaternary ammonium compounds. Oxidizing disinfectants include halogens and oxidizing agents like peracetic acid and chlorine dioxide.

Step 4: Validating disinfectants

For pharmaceutical facilities, the disinfectants used must be validated. This involves laboratory testing and using either U.S. AOAC methods or European norms. Some of this testing can be carried out by the disinfectant manufacturer and some should be carried out in-house.

Disinfectant testing involves challenging the disinfectant solution (as a suspension test) and challenging different surface materials with disinfectant and a range of different microorganisms including isolates from the facility.[6]

Step 5: Factors which affect disinfectant efficacy

There are a number of factors which affect how well disinfectants work in practical situations, and it is important to understand these in order for the cleaning program to be effective. Factors affecting disinfectant efficacy include:

a) Concentration: this is the optimal dilution of the disinfectant to give the greatest microbial kill.[7] It is a fallacy that by making the concentration of a disinfectant greater it will kill more bacteria when it is the validated concentrations which work.
b) Time: The time that the disinfectant is used for is important. Sufficient time is needed for the disinfectant to bind to the microorganism, traverse the cell wall, and to reach the specific target site for the disinfectant's particular mode of action.
c) The numbers and types of microorganisms, in terms of some disinfectants being less effective against certain species which are more resistant. If high numbers of bacterial spores are isolated, a non-sporicidal disinfectant will be ineffective.

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d) Temperature and pH: each disinfectant has an optimal pH and temperature at which it is most effective. If the temperature or pH are outside this optimal range, then the rate of reaction (log kill over time) is affected.

Step 6: Cleaning materials

The cleaning materials used to apply disinfectants and detergents must be appropriate. The materials must be able to apply an even layer of each agent. For disinfectants and detergents used for floors, surfaces, and walls in sterile manufacturing areas, these must be applied using materials which are cleanroom certified and non-particle shedding (non-woven and lint-free).

Step 7: Cleaning techniques

The cleaning and disinfection techniques are important. If detergents and disinfectants are not used in the correct way, areas will not be cleaned effectively and unduly high levels of microbial contamination will remain as the disinfectant will not penetrate layers of dirt.

Defined cleaning and disinfection steps must be in place, such as:[8]

- Sweeping away dust and debris (if applicable).
- Applying a detergent solution through wiping or mopping.
- Ensuring that the detergent has dried.
- Applying a disinfectant solution through wiping or mopping.
- Keeping the surface wet until the contact time has elapsed.
- Removing disinfectant residue through wiping or mopping with water for injections or 70% IPA.

Detergents and disinfectants for use on surfaces (walls, floors) must be applied using the double or triple-bucket system to avoid cross contamination. Both of these techniques involve using a bucket of disinfectant and a bucket of water. In the "two-bucket" technique there is a "wringer" (for the mop) over the bucket of water. In the "three-bucket" technique there is a third bucket, empty except for having a wringer mounted over it.

Step 8: Monitoring cleaning and disinfection efficiency

The main test of how well a cleaning and disinfection program is working is through the results from the environmental monitoring of cleanrooms. This is assessed by viable microbiological sampling of surfaces using techniques like contact plates and swabs. If the results obtained are not within recommended action levels or company in-house limits, this suggests a problem with either: the cleaning and disinfectant agents, the frequency of cleaning, or the techniques used. Conversely, if the results are satisfactory, the cleanroom manager can have confidence that the cleanroom is indeed "clean."

SUMMARY

This article has presented an eight step approach to keeping cleanrooms clean. The best practice advice presented in this article should be captured into a Standard Operating Procedure and the staff members that need to be aware of it should be properly trained. Once a facility is under control, the most important thing is to continue to clean and disinfect using the correct techniques and the correct agents at defined frequencies. That way, cleanrooms will stay clean.

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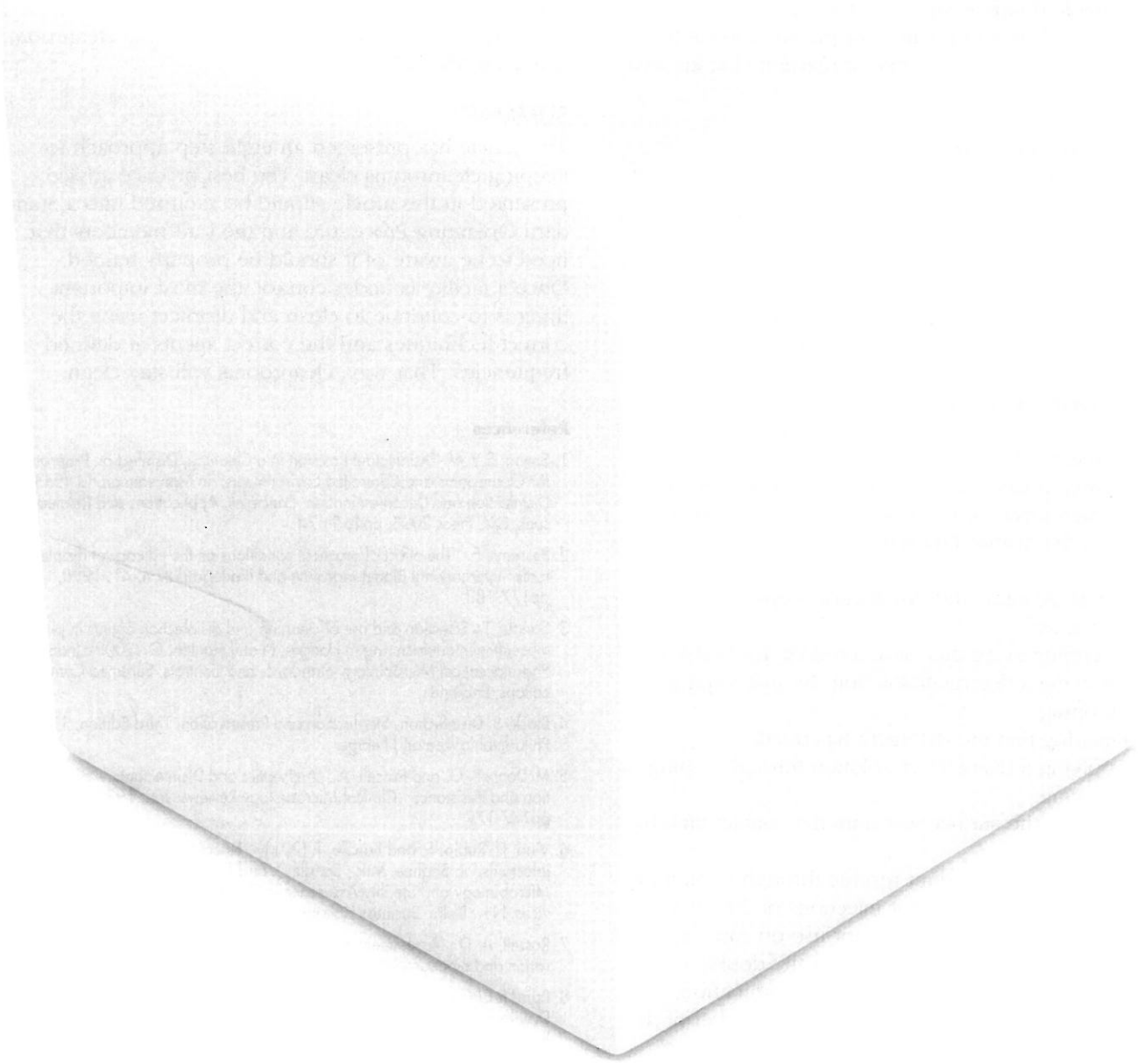

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