Cleaning and disinfection

15

15.1 Introduction

Cleaning and disinfection practices are an essential part of contamination control in the pharmaceutical industry, especially in relation to the microbiological control of cleanrooms. Disinfectants are also important for use in the microbiology laboratory.

An important step toward achieving microbial control within a cleanroom is the use of defined cleaning techniques, together with the application of detergents and disinfectants. The objective of cleaning and disinfection is to achieve appropriate microbiological cleanliness levels required and for an appropriate period of time [1].

This chapter examines both detergents (which "clean") and disinfectants (which remove or eliminate microorganisms). Detergents are cleaning agents and are deployed to remove "soil" from a surface. The removal of soil is an important step prior to the application of a disinfectant, for greater the degree of soiling remaining on a surface, then the lesser the effectiveness of disinfection. A disinfectant is a type of chemical germicide that is capable of eliminating a population of vegetative microorganisms (although some disinfectants are sporicidal, a chemical does not need to be sporicidal to be classified as a disinfectant). A disinfectant that can kill spores is sometimes described as a sterilant or chemosterilant [2]. Disinfectants, of varying formulations, have been used since the late nineteenth century [3].

Disinfectants vary in their effectiveness against different types of microorganisms, a variation relating to both the intrinsic resistance of different microorganisms and the range of different types and formulations of disinfectants. Furthermore, different disinfectants act in different ways depending upon their active ingredients.

15.2 Cleaning

Cleaning is the process of removing residues and "soil" (such as dirt, grease, and protein residues) from surfaces to the extent that they are visually clean. This involves defined methods of application and often the use of a detergent. Importantly, the act of cleaning is necessary prior to the application of a disinfectant for a surface needs to be properly cleaned before the application of a disinfectant in order for the disinfectant to work efficiently [4], as disinfectants can either be inactivated by organic residues or the soil can create a barrier which prevents the disinfectant from reaching all of the microbial cells.

While "cleaning" is not "disinfection", the cleaning process can remove or dilute microbial populations. Furthermore, many detergents have chemical additives that can "disinfect." However, a cleaning agent will not meet the criteria for disinfection required by the European and US standards for disinfectant validation in terms of reducing a microbial population of a defined range by the required log reduction.

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The act of cleaning normally requires the use of a detergent. A detergent is a chemical used to clean equipment or surfaces by removing unwanted matter (soil). Detergents generally work by penetrating soil and reducing the surface tension (which adhere soil to the surface) to allow its removal (in crude terms, a detergent increases the "wettability" of water). Many detergents are synthetic surfactants (an acronym for surface active agents).

Surfactants are schizophrenic molecules that have two sides to their nature. One part is solvent-loving or lyophilic (hydrophilic), and another is solvent-hating or lyophobic (hydrophobic). Surfactants remove particles from surfaces by either capillary effects or electrostatic forces (many detergents contain differently charged ions that can cause microorganisms to repel each other). This repulsion causes the microorganisms to disassociate from the surface and become suspended. Suspended microorganisms (planktonic state) are easier to remove from the surface by the rinsing effect of the detergent (or a subsequent water rinse) or to be destroyed by the application of a disinfectant [5].

There are two key considerations when selecting detergents.

1. The chemical composition of the detergent.

With the chemical nature of the detergent, it is typical that detergents are neutral and non-ionic solutions. Furthermore, it is preferred that the detergents used are low- or nonfoaming.

2. The compatibility of the detergent with the disinfectant.

In terms of compatibility, it is important that any detergent used should be compatible with the disinfectants used, for some detergents can leave residues that can neutralize the active ingredient in certain disinfectants thereby reducing the microcidal properties of the disinfectant [6].

15.3 Disinfection

A disinfectant is a chemical agent, one of a very diverse group of products, which reduces the number of microorganisms present either by removing or destroying them. In literature, various terms are applied in relation to this activity: disinfectant, antiseptic, asepsis and sanitizer.

The term disinfection is normally applied to an inanimate object (sometimes the term biocide is used, although this relates to a larger group of chemical agents). The term antiseptic is used to describe the reduction of a microbial population on living tissue [7]. Thus, an antiseptic is a disinfectant that can safely be applied to the surface of the skin (sometimes the terms "hand sanitizer" or "hand disinfectant" are used interchangeably) [8]. In turn, the term disinfectant is usually reserved for liquid chemical germicides, which cannot be applied to tissues because of their corrosive or toxic nature [9].

Asepsis can relate to the use of disinfectants to disinfect an area such as an operating theater (and the term is more commonly associated with healthcare) [10]. It is a

separate term to "aseptic technique," which, in the laboratory sense, relates to avoiding personnel contamination of devices intended to be sterile [11].

The term sanitizer is open to different interpretations. Within Europe, it is normally taken to be an agent that both cleans and disinfects (normally a disinfectant that contains a cleaning agent). Within North America (defined by the US Environmental Protection Agency), however, the term is normally applied to an antimicrobial agent for use on nonfood contact surfaces. Sanitization is a general description for reducing a microbial population. Disinfection is a more precise term, as it can be related to the requirements of international standards in relation to the requirement that the chemical agent must reduce a known number of microorganisms (a property demonstrated through validation).

15.3.1 Disinfectant efficacy

There are a number of important criteria that affect the performance and efficacy of disinfectants. These factors are:

(i) Concentration

Disinfectants are manufactured or validated to be most efficacious at a set concentration range (the proportion of the chemical to water). The setting of this concentration range involves ascertaining the minimum inhibitory concentration (MIC). The MIC is the lowest concentration of the disinfectant that is shown to be bacteriostatic or bactericidal under experimental conditions. Experimental conditions are normally based on the examination of a disinfectant solution in suspension in the absence of soil. The MIC is measured through kinetic studies of the dilution coefficient. Kinetic studies demonstrate the effect of a change in concentration against cell death rate over time. The higher a disinfectant's concentration exponent, the longer it takes to kill cells. For example, if a disinfectant with a set concentration exponent was diluted by a factor of 2, the time taken for it to kill cells comparatively would double [12]. The MIC is normally set by the manufacturer of the disinfectant.

(ii) Time

Time is an important factor in the application of disinfectants for two reasons: in relation to the contact time of the disinfectant and the expiry time of the disinfectant solution. Contact time (sometimes called the dwell time) is the time taken 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. Many disinfectants work best and meet product label claims when allowed to work for several minutes before wiping or rinsing.

Contact time relates to the concentration of the disinfectant (variation to the concentration of a disinfectant may alter the contact time required). In practical situations, there are many variables which can alter the contact time. These include the type, concentration, and volume of the disinfectant; the nature of the microorganisms; the amount and type of material present that is likely to interfere with the active ingredient; the temperature of the disinfectant; and the surface that the disinfectant is applied to.

Another aspect relating to time is the deterioration of a disinfectant solution over time. This is more important where a solution of disinfectant is prepared "in-house" from a concentrate than to ready-prepared solutions, which have been validated by the manufacturer and will come with an assigned expiration time. For ready-prepared solutions, an expiry time limit for the disinfectant solution should be established through chemical testing. As a rule, fresh solutions of a disinfectant should be used for each application and between cleanrooms.

(a) Number

An antimicrobial agent, like a disinfectant, is considerably more effective against a low number of microorganisms than a higher number or a population with a greater cell density. Similarly, a disinfectant is more effective against a pure population than mixed grouping of microorganisms. A routine disinfectant procedure will be unlikely to kill all microorganisms present, and a number will remain viable. Whether the surviving microorganisms multiply in sufficient number is dependent upon the conditions in which the surviving population remains, the available nutrients and the time between repeat applications of the disinfectant.

(b) Type of microorganism and resistance

Different types of microorganism have varying levels of resistance to broad spectrum disinfectants as Figure 15.1 shows. The increased resistance shown is primarily due to the cell membrane composition or type of protein coat.

The hierarchy of microorganisms in Figure 15.1 is placed in order of resistance. Resistance is either due to the natural genetic properties of the microorganisms (intrinsic), as shown in Figure 15.1, or it is acquired through phenotypic (organism's actual observed properties, such as colony pigment) or genotypic (genetic) variations (similar to antibiotic resistance, through the over-use of one type of disinfectant. However, This form of "acquired resistance" is contentious). Generally, innate sensitivity results in

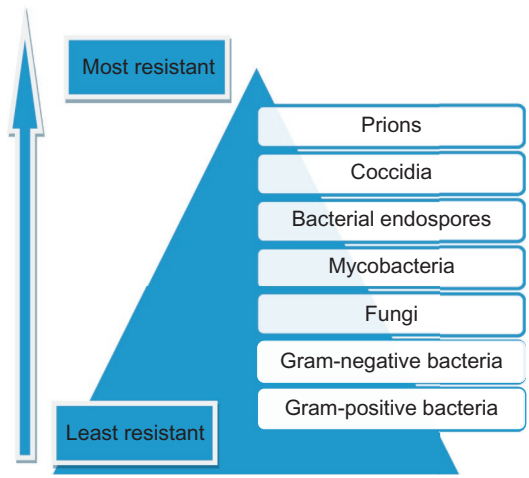

Figure 15.1 Sensitivity of different microorganisms to broad spectrum disinfectants.

Gram-negative bacteria being more resistant to disinfectant applications than Gram-positive bacteria, based on the composition of their cell wall. In turn, for bacteria, endospores are the most resistant because of the relative impermeability of the spore coat.

(c) Location of microorganisms

The location of microorganisms influences the effectiveness of disinfectant treatment. Microorganisms in suspension are easier to kill than those affixed to surfaces. This is due to the mechanisms of microorganism attachment, such as bacteria fixing themselves using fimbriae or when a biofilm community develops. A biofilm is a complex aggregation of microorganisms growing on a solid surface. Bacteria living in a biofilm can have significantly different properties from free-floating bacteria, as the dense and protected environment of the film means that they have increased resistance to detergents and antibiotics, as the dense extracellular matrix and the outer layer of cells protect the interior of the community.

Thus, such positioning can impact upon the contact time required for the disinfectant to bind to the microorganism, cross the cell wall and act at the required site. This is why, with disinfectant validation, the surface test is regarded as more meaningful and robust than the suspension test.

(iii) Temperature and pH

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

Temperature influences the rate of reaction. Most disinfectants are more effective and kill a population faster at higher temperatures although many disinfectants, due to practical considerations relating to cleanroom use, are manufactured to be used at ambient conditions. Disinfectants that are sensitive to temperatures other than at ambient are normally assessed using a temperature coefficient, or Q_{10} (which relates the increase in activity to a 10 °C rise in temperature) [13].

The effect of pH is important because it influences the ionic binding of a disinfectant to a bacterial cell wall thereby ensuring disinfectant molecules bound to a high number of microorganisms. Many disinfectants are more stable at a set pH range. The use of a disinfectant outside of its desired pH range results in reduced efficacy.

(iv) Interfering substances

The presence of different substances on the surface or in the equipment requiring disinfection can affect the efficacy of the disinfectant in various ways ranging from increasing the contact time to complete inactivation. In order for a disinfectant to be effective, it must come into contact with the microbial cell and be absorbed into it. If substances (or organic load), such as oil, dirt, blood serum, protein, food body waste paper or grease, act as a barrier between the microbial cell and the disinfectant, the efficacy of the disinfectant will be adversely affected. The presence of such substances (soil) halts disinfectant efficacy by either reacting with the disinfectant or creating a barrier for the disinfectant. This effect is increased if the surface itself has defects and crevices, which limit disinfectant penetration [14]. When purchasing disinfectants, it is important to note if the label claim indicates if the disinfectant remains effective in the presence of small amounts of organic matter.

(v) Water

Many disinfectants do not work well in hard water. For use in the pharmaceutical and healthcare sectors, disinfectants are normally prepared using deionized or demineralized water (or water for injections in the higher grade cleanrooms).

15.3.2 Types of disinfectants

There are various types of disinfectants available. Different types of disinfectants have different spectra of activity, modes of action and differing efficacies. Some disinfectants are classed as bacteriostatic, where the ability of the bacterial population to grow is halted. Here the disinfectant can cause selective and reversible changes to cells by interacting with nucleic acids, inhibiting enzymes, or permeating into the cell wall. Once the disinfectant is removed from contact with bacteria cells, the surviving bacterial population could potentially grow.

Other disinfectants are bactericidal in that they destroy bacterial cells through different mechanisms. These include causing structural damage to the cell, autolysis, cell lysis, or by the leakage or coagulation of the cytoplasm. Within these groups, the spectrum of activity varies, with some disinfectants being effective against vegetative Gram-positive and Gram-negative microorganisms only, while other disinfectants are effective against fungi. Other disinfectants have a broader spectrum and are sporicidal in that they can cause the destruction of endospore-forming bacteria. However, a chemical agent does not have to be sporicidal in order to be classed as a "disinfectant" [15]. The bacteriostatic, bactericidal, and sporicidal properties of a disinfectant are influenced by many variables.

There are a number of disinfectants available in the market with different modes of activity and of varying effectiveness against microorganisms. There are various approaches to the categorization and sub-division of disinfectants including grouping by chemical nature, mode of activity or by microstatic and microcidal effects on microorganisms. The two principal categories are the division into oxidizing and nonoxidizing chemicals.

The majority of nonoxidizing disinfectants have specific modes of action against microorganisms, but generally they have a lower spectrum of activity compared to oxidizing disinfectants [16]. The most common types of nonoxidizing disinfectants are alcohols, quaternary ammonium compounds, and phenolics. With oxidizing disinfectants, these chemicals generally have nonspecific modes of action against microorganisms. They have a wider spectrum of activity than nonoxidizing disinfectants, with most types able to damage endospores, but they pose greater risks to human health. Examples include halogens, peracetic acid, and hydrogen peroxide.

15.3.3 Selecting disinfectants

Deciding the types of disinfectants to be used represents an important decision. Key criteria include [17]:

(a) A disinfectant must 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. For in cleanrooms, disinfectants should be bactericidal (that

is rather than simply inhibiting microbial growth, it should be capable of killing bacteria). A separate decision to be made is whether the disinfectant is required to be sporicidal. Furthermore, in some facilities the disinfectants should also be virucidal.

(b) A 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. Thus, the "minimum" contact time is the time required for the disinfectant to be effective after its application. The contact time is sometimes referred to as the "action time" or "dwell time." Given the requirements of most pharmaceutical manufacturers and healthcare facilities, a disinfectant should ideally have a contact time of 10 min or less, although certain sporicidal disinfectants can require longer contact times.

(c) Disinfectants should not be neutralized by residual matter

Although detergents and effective cleaning practices can remove the majority of soil, including organic matter, some traces will remain. It is important that these organic residues do not interfere with the active ingredient of the disinfectant and reduce its efficacy.

(d) Environmental conditions

Some disinfectants require certain temperature and pH ranges in order to function properly. One type of disinfectant, for example, may not be effective in a cold room due to the lower temperature. The reason for this is the validation standards for disinfectants measure the bactericidal activity at 20 °C; therefore, the disinfectant may not be as effective at higher or lower temperatures.

(e) Non-corrosive

Disinfectants should be noncorrosive. If the disinfectant causes extensive abrasion of a surface, it will either degrade the material or cause cracks and recesses that can harbor microorganisms. It is recognized, however, that the most efficacious disinfectants, especially those that are sporicidal, through repeated applications over time will cause some corrosion. A postdisinfection step to remove disinfectant residues, such as a sterile water rinse or wiping with a milder disinfectant such as 70% isopropyl alcohol (IPA), can minimize material surface damage.

(f) Operator safety

Many disinfectants are toxic or irritant and unpleasant for staff to use. Consideration must be given to safety requirements, material safety data sheets, label information, the toxicity upon human health, and to the protective measures required for staff to use them (such as avoiding contact with exposed skin or the need to use a disinfectant in a well-ventilated area).

(g) Compatibility with the surface to be disinfected

Certain disinfectants may be less effective with certain materials or may cause excessive damage to certain materials, such as the reaction of chlorine dioxide against stainless steel.

(h) Compatibility with detergents used

As discussed above, it is important that the disinfectant and detergent are compatible and that detergent residues do not inactivate the active ingredients in the disinfectant solution.

(i) Residual activity of the disinfectant

Residual activity of the disinfectant may lead to resistant strains or cause problems when an alternative disinfectant is applied. It is a good practice to remove disinfectant residues with a water rinse.

(j) Sporicidal properties

If isolates from the environmental-monitoring program include the recovery of endospore-forming bacteria on a frequent basis or in high numbers, then the use of a sporicidal disinfectant is essential, with the frequency determined by a review of the environmental monitoring program.

(k) Range of formats available

The cleanroom facility will require a disinfectant to be available in several formats. For example, a type and formulation of disinfectant may be required in a ready-to-use format, as a concentrate, or an impregnated wipe, and so on.

(l) Cost

The calculation of cost needs to include not just the price of the disinfectant but also other cost factors such as the time taken to prepare or apply the disinfectant, protective clothing requirements, wastage, and the steps needed for the removal of residues.

(m) Health and safety

The safety aspects of a disinfectant are an important consideration and standard operating procedures should contain appropriate health and safety requirements for using detergents and disinfectants. This should include reference to appropriate personal protective equipment. In particular, contact to eyes, skin and mouth is to be avoided. Safety data sheets must be examined for all disinfectants and detergents and appropriate measures taken to ensure that they are applied properly, in well-ventilated areas.

15.4 Good manufacturing practice requirements

An effective cleaning and disinfection program in pharmaceutical grade areas of a good manufacturing practice (GMP) facility is critical to assure the quality of the products. The use of detergents and disinfectants, and the need to keep cleanrooms clean, is a regulatory requirement within the pharmaceutical sector. The main regulatory documents relating to the use of disinfectants in pharmaceutical manufacturing are:

- FDA Code of Federal Regulations: 21 CFR 211.56b and 21 CFR 211.56c (which refer to sanitation); CFR 211.67 (which refer to equipment and maintenance); CFR 211.182 (which describes the need for a cleaning program); and CFR 211.113b;
- FDA Aseptic Processing Guide, revised 2004;
- USP (General Chapter <1072> Disinfectants and Antiseptics);
- Annex 1 to the EU Guide to Good Manufacturing Practice.

For example, the 21 CFR 211.67 states:

That surfaces and equipment must be "....cleaned, maintained, and sanitized at appropriate intervals to prevent malfunctions or contamination that would alter the

safety, identity, strength, quality, or purity of the drug product beyond the official or other established requirements."

To meet regulatory expectations in the pharmaceutical industry, a cleaning and disinfection program is required. The program should consist of a policy, outlining the objectives and the criteria for the selection of materials and cleaning agents; and a procedure, detailing how cleaning is undertaken, along with the techniques and cleaning frequencies. There is an expectation that such programs are regularly reviewed and reflect any changes to cleanroom design and respond to changes to environmental monitoring data.

Although there are some differences between the regulations, a number of similar areas are covered. In summary, the regulations require [18]:

- the need to have written procedures (CFR/EU GMP);
- responsibilities for cleaning should be assigned (CFR). Often this is interpreted as the need to have independent cleaning staff separate from those involved in product manufacture;
- staff must be trained in cleaning techniques and have a training record (CFR/EU GMP);
- details of cleaning frequencies, methods, equipment, and materials must be recorded in written procedures (CFR). This may relate to an approved supplier specification;
- the cleaning of equipment and materials must take place at regular intervals (CFR);
- in designing a disinfectant protocol for the sanitization of floors, walls and surfaces, a pharmaceutical organization will normally select two or three disinfectants for the same application. This is a requirement of regulatory bodies and the strongest pressure for it has come from Europe with the EU GMP guideline stating that "where disinfectants are used, more than one type should be employed" (Annex 1, paragraph 3714). This is normally interpreted as the need for disinfectant rotation (which is discussed below).
- Disinfectants should be rotated (EU GMP/FDA warning letters).
- Inspection of equipment for cleanliness before use should be part of routine operations (CFR).
- A cleaning log should be kept. The purpose is to keep a record of the areas cleaned, agents used and the identity of the operator (CFR).
- The microorganisms isolated (the "microflora") from environmental monitoring programs should be examined for resistant strains (EU GMP). The inference here is that such isolates are incorporated into disinfectant efficacy studies (see Chapter 10).
- The monitoring for microbial contamination in disinfectant and detergent solutions should be periodically undertaken (EU GMP).
- The storing of disinfectant and detergent solutions should be for defined (and short) periods (EU GMP).
- Disinfectants and detergents used in Grades A and B cleanrooms should be sterile before use (EU GMP).
- Room use should be recorded after each operation (CFR/EU GMP).
- Disinfectants should be "qualified" (validated) (CFR).
- There should be a technical agreement with the company who supplies the disinfectant. Ideally the disinfectants purchased should be lot tracked (EU GMP).

The most important GMP consideration in relation to Europe is, arguably, rotation. To conform with GMP expectations, pharmaceutical manufacturer is expected to use at least two disinfectants with different modes of activity [19]. With other territories, the requirement for rotation is not so exact.

While the phenomenon of microbial resistance is an issue of major concern for antibiotics, there are few studies that support development of resistance to disinfectants. The unlikelihood of resistance developing is particular when disinfectants are applied to dry environments, such as cleanrooms, for microbial replication, as the primary process for gaining resistance, is minimal. However, rotation is generally necessary in order to pass a European GMP inspection.

Policies for determining the frequency of rotation vary widely. Some facilities have adopted an even rotation (such as alternating between disinfectants daily or weekly) while others rotate at different frequencies, sometimes to an extreme of 3 months for one disinfectant against 1 week for the alternate disinfectant. Other companies build up a case for only using one disinfectant on a day-to-day basis with a second used very infrequently. In this latter example, it is argued that two disinfectants only need to be employed if the environmental-monitoring data indicate excursions from set limits, and therefore, the inference is that the primary disinfectant is not controlling surfaces [20].

The frequency of rotation needs to be defined by the user, and supporting data can be supplied through field trials. When established it is necessary to continue the detergent application between the changes of disinfectant types in order to remove residues. Once set, there may be a requirement to vary the frequencies of use, such as in response to an increase to microbial counts and as part of a formal investigation into a microbiological data deviation.

15.5 Measuring disinfection effectiveness: Environmental monitoring

To ensure the effectiveness of a cleaning and disinfection program, microbiological environmental monitoring of surfaces and equipment is necessary. The primary methods for conducting these tests involve the use of cotton swabs (with a recovery diluent and later plating onto agar or dissolving prior to membrane filtration) and contact plates or other surface agar techniques. The recovery efficiency of contact plates is generally superior to that of swab. The agars used should contain appropriate neutralizing agents in order to eliminate any disinfectant residues and, thus, allow any recovered microorganisms to grow (this is discussed further in Chapter 10). An appropriate general agar, such as soya-bean casein digest medium, is normally recommended. This agar, onto which swabs are sub-cultured or used in the contact plates, should have a dual incubation step designed to pick up a range of environmental microorganisms. A typical regimen would be 20–25 °C for 48 h followed by 30–35 °C for 72 h.

One way of assessing the effectiveness of a disinfectant is through a field trial [20]. The purpose of field trials is to test a disinfectant's efficacy in practical in-use conditions: the working environment. Most researchers consider that a field trial is the only accurate test of a disinfectant, given the problems with repeatability and reproducibility associated with laboratory-based tests. It is also because the trials examine a selected concentration on surfaces and equipment after the cleaning step has been

applied. Field trials have an advantage because they test the disinfectant against a wide range of surfaces and with all the different types of interfering substances that may be present, as well as different physico-chemical conditions, such as temperature and pH.

15.6 Disinfectant efficacy

Disinfectants need to be assessed through disinfectant efficacy studies. Unfortunately, there is no clear-cut approach for this, with differing international standards. The following organizations publish disinfectant validation standards.

- ASTM (American Society for Testing Materials) (ASTM E2614-08 Standard Guide for Evaluation of Cleanroom Disinfectants).
- AOAC (Association of Official Analytical Chemists International) (referenced below).
- CEN (European Standards) (referenced below).
- TGA (Australian Therapeutic Goods Administration).
- USP (US Pharmacopeia) (chapter <1072>).

The most widely used methods are the European CEN standards and the US AOAC standards. The European approach consists of suspension tests, surface tests, and field trials; whereas the emphasis in North America is strongly on surface testing (the hard surface carrier method). Here the carrier test differs slightly in methodology to the European surface test. It is generally regarded that the surface tests are more rigorous than the suspension tests [21].

With suspension tests, a test suspension of bacteria or fungi is added to a prepared sample of the disinfectant under test in simulated "clean" and "dirty" conditions. After a specified contact time, an aliquot is taken, and the bactericidal/fungicidal action is immediately neutralized by the addition of a proven neutralizer (as identified in the basic suspension test). Following this, the number of surviving microorganisms in each sample is determined, and the reduction in viable counts is calculated (expressed in logarithms to base 10).

With surface tests (or "carrier tests"), representative manufacturing surface samples are inoculated with a selection of microbial challenge organisms. A disinfectant is applied to the inoculated surfaces and exposed for a predetermined contact time after which the surviving organisms are recovered using a qualified disinfectant-neutralizing broth and test method (surface rinse, contact plate, or swab). The number of challenge organisms recovered from the test samples (exposed to a disinfectant) is compared with the number of challenge organisms recovered from the corresponding control sample (not exposed to a disinfectant) to determine the ability of the disinfectant to reduce the microbial bioburden. Successful completion of the validation qualifies the disinfectant evaluated for use [22].

Prior to initiating disinfectant efficacy validation, a comprehensive survey of the materials comprising the room surfaces (floors, walls, windows) and equipment (stainless steel, acrylic, vinyl) present in the facility that could potentially be exposed to the disinfectant should be conducted. The use of different surfaces is important because the rates of inactivation on microorganisms on different surfaces can vary

considerably. One study demonstrated that bactericidal activity reduced on polyvinyl chloride (PVC) compared with stainless steel. This was a factor both of the material type and the surface conditions, such as the number of pores or ridges. Surfaces of the material can also differ depending upon the degree of finishing with smoother surfaces, like stainless steel or Formica, giving greater repeatability and reproducibility.

15.7 Conclusion

Microbial control in cleanrooms and laboratories is of great importance, and to achieve this use of defined cleaning techniques, together with the application of detergents and disinfectants, is of great importance.

This chapter has examined the basics of cleaning and disinfection and has outlined the key requirements for the selection and use of such agents. In doing so, the chapter has introduced some of the key GMP concepts. The chapter has also outlined the important aspects for the qualification of disinfectants through disinfectant efficacy studies. Of these, the surface studies are the most important. That said, the ultimate assessment of the suitability of a disinfectant is established through a field trial where environmental monitoring data can be evaluated in order to set disinfectant frequencies and the order of disinfectant rotation.

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