Cleaning and Disinfection Regimes for Clean Rooms

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Scope

The purpose of this document is to provide advice on the principles of cleaning and disinfection regimes used in clean rooms and aseptic suites provided within hospital pharmacy departments operating under the Section 10 exemption for pharmacists. The standard for these units is provided in the Quality Assurance for Aseptic Preparation Services 4th edition 2006[1].
It is not intended to provide detailed guidance, which will depend on individual circumstances.

Introduction

The microbial integrity of a clean room should be maintained according to its classification. The recommended limits for microbial contamination are specified in the current edition of the Rules and Guidance for Pharmaceutical Manufacturers[2]. It is not possible to rely on the airflow to sweep a room clean. Microorganisms are usually attached to larger particles, which may fall onto surfaces. They sometimes attach to surfaces by electrostatic forces. The frequency and type of cleaning will depend on the classification and extent of use.

Commissioning

This section applies to a new clean room or following substantial building work. Cleaning should commence from the room of the highest grade towards the unclassified environment. Particles of masonry or plaster can scratch floor surfaces and therefore floors should be protected after laying down. Once floor covering is removed a vacuum cleaner is a good way to remove any particles and general dirt from the room. A cylinder vacuum cleaner is preferred since the hose and variety of attachments allow corners to be more readily cleaned. It is not essential to use a HEPA filtered vacuum cleaner for a unit that will subsequently have every surface disinfected. A wet wash should follow preferably using a sterile neutral detergent and disposable mop head (R Baird 1981[3]). Neutral detergents are non-ionic surfactants and therefore will foam less during use. During the cleaning process care should be taken not to damage any HEPA filters, especially by wetting them with cleaning agents. Cleaning should commence with the ceiling followed by the walls and then floors. Benches, hatches, doors, cabinets and other clean room equipment should be cleaned by hand using low linting wipes (see general caution below). The detergent clean should be repeated until the bucket at the end of the process is free from solid particles and the mop head does not look dirty. A sterile sporicidal disinfectant should be used finally to remove any spores (see general caution).

General caution

Disinfectants such as chlorine dioxide, hypochlorite or dichloroisocyanurate may corrode stainless steel surfaces or painted metal. After application it is recommended that they are removed using sterile water or sterile 70% IMS, a disinfectant contact time of up to 15 minutes, which includes time to allow the surface to dry, is usually sufficient but refer to the manufacturers guidance. A low lint wipe should be used of the removal process. The use of aggressive chemical disinfectants should be kept to a minimum.

Surface microbial monitoring during commissioning

It is advisable to monitor clean rooms before, during and after the cleaning and disinfection stages. Contact plates with appropriate inactivators and swabs wetted with appropriate inactivator solution should be used. Monitoring the microbial content of the bucket after cleaning and disinfection is useful in validating the cleaning process. All microorganisms should be identified to at least Genus level to allow comparison with future monitoring isolates. The monitoring results should indicate that the room has been cleaned to a level well below the maximum given in the guidelines[1, 2]. If the results do not achieve this level then the suitability of the cleaning programme should be reviewed. It is often possible to achieve microbial levels corresponding to the GMP Grade above the designed Grade.

Routine Cleaning Regimes for Clean Rooms

Microbial contamination in a clean room can often be traced back to either an operator or inadequate cleaning and disinfection of items transferred into the clean room. The correct use of protective clean room apparel and rigorous transfer procedures is essential.

Agents for use in GMP Grade A and B environments must be sterile. Agents for use in GMP Grade C and D environments, if not sterile, should be monitored for microbiological contamination and in use dilutions discarded after use. Cleaning materials used in GMP environments must be subject to the same level of control. If items such as mops are to be re-used they should be subject to a validated cleaning and sterilization process.

The regular cleaning regime for clean rooms should be divided into three categories dependant on the monitoring results for the room;

1. **Routine Cleaning**

   This uses a sterile detergent to achieve the removal of general dirt and particles. Cleaning should be regular to prevent the build up of dirt and particles on all surfaces and is the method of choice where clean rooms consistently are well within their recommended limits. Monitoring with contact plates or swabs will indicate the effectiveness of this procedure.

   The use of household disinfectants is discouraged (Whyte 2001, [4]) as they may be abrasive and leave residues. Whyte also advocates the use of non-ionic surfactants as they are non-aggressive and low foaming.

   Work surfaces, benches, isolators and LFC's are additionally cleaned and disinfected with sterile 70% alcohol wipes and sprays. This should occur before, during (if required) and following work sessions.

2. **Disinfection**

   The use of sterile disinfectants as part of the regime should be on a less regular basis, either as an added assurance (e.g. weekly or monthly depending on the classification of the room) or if monitoring indicates a

higher than normal result. If monitoring indicates a build up of spores the next stage of using a sporicidal agent may be required.

The range of suitable disinfectants generally comprises biguanides, quaternary ammonium compounds and amphoteric agents. Occasionally a combination of two or more types are incorporated into one product to improve effectiveness. Consideration should be given to changing the disinfectant if microbial resistance is a concern.

3. Sporicidal Cleaning

These agents are aggressive and should be used carefully to prevent damage to surfaces and equipment. They should be used on a minimum number of occasions until the source of the spores can be determined and eliminated.

The range of suitable sporicides includes chlorine agents, peroxygens, including hydrogen peroxide and peracetic acid.

Routine surface microbial monitoring

It is advisable to monitor surfaces within clean rooms and devices using contact plates or swabs as detailed in Beaney 2006 [(1)].

References

(1) Beaney A M ed. Quality Assurance of Aseptic Preparation Services 4th edition Pharmaceutical Press 2006.
(2) Medicines and Healthcare products Regulatory Agency. Rules and Guidance for Pharmaceutical Manufacturers and Distributors 2007 Pharmaceutical Press.
(3) Baird R Cleaning and Disinfection in the hospital pharmacy in Collins et al Disinfectants, their use and evaluation of effectiveness. Society Applied Bacteriology TS16 p154 1981.
(4) W.Whyte Clean Room Technology 2001 p287 Wiley

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