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CLEAN
FACTS
Cleanroom Hygiene

CLEANING & DISINFECTION OF
GMP-CLEANROOMS IN PHARMACIES

According to the pharmacy operating regulations the pharmacy managers are responsible for the hygiene within their cleanrooms. But they are often no experts in cleanroom technology. Often we get asked similar questions when it comes to the "correct" cleaning and disinfection of their different cleanroom areas. In this article, we aim to give a basic overview of cleaning and disinfection processes as well as state-of-the-art solutions for these.

That a routine and reliable cleaning (dislodging and removing impurities) and disinfection (killing of microorganisms) in cleanrooms is an essential part of the operational hygiene is a matter of fact. In this article, we will not be considering correct behavior, cleanroom garments or the training of cleaning staff.

REGULATORY REQUIREMENTS

In addition to ISO 14644-1 (2) and VDI 2083 (3) the GMP guidelines are relevant for qualification and auditing by authorities as well as for the requirements of the processes in the pharmacy. Other requirements include:

- Risk assessment and adoption of appropriate measures
- Validation of cleaning and disinfection processes, documentation (SOP's)
- Regular effectiveness checks (Monitoring) (4)
- State of science, standards, and guidelines
- Use of cleanroom suitable equipment including cleanroom suitable mops and wipes
- Suitable disinfectant concept

All products for cleaning and disinfection in GMP A/B areas must be sterile (mops, wipes disinfectant, etc.) (5). To avoid the necessity of autoclaving on-site, the procurement of sterile consumables makes sense. Cleaning equipment should be disinfected the first time it is brought into a cleanroom and then regularly, if necessary, with a sporicide. In addition, good ergonomics and work safety is required for the cleaning staff e.g. by telescopic handles and touch-free cleaning procedures.

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MOPS

Special, cleanroom-suitable mops which only emit a low level of particles and fibers should be used. (6). These are made of polyester, ideally microfiber. Proof of cleanroom suitability can be provided e.g. through certificates (Fraunhofer IPA).

Regarding the risk of contamination spreading, disposable mops provide higher safety, as they are always in a new condition and of consistent high quality. Especially in cytostatics manufacturing it cannot be guaranteed, that washable (reusable) mops are completely free of residues after washing or whether these residues have been inactivated. With respect to the cleaning performance and surface capacity, a professional cleanroom disposable mop can be as good as a reusable mop. Furthermore, the ongoing condition checking of reusable mops due to their abrasion and usage, can be omitted. After wiping a defined area the mop must be discarded, and a new unused mop (mop change method) has to be used for the next area.

ACCESSORIES / EQUIPMENT

Cleaning materials such as trolleys, handles and frames should be made of suitable materials. Preferred products are made of stainless steel, which has a higher resistance to disinfectants, autoclaving and general wear and tear. For wall/ceiling cleaning extendable handles and lightweight accessories are recommended.

Cleaning systems should be selected according to the required number of mops. Especially for pharmacies and small cleanroom areas there are small, space-saving solutions. Ready-to-use presaturated mops can be a good solution so that usage of a trolley can be avoided altogether.

WIPES

Special cleanroom wipes, which will not become a source of contamination (particulate or microbial) themselves, should be used in cleanrooms. Typically wipes are divided into the two categories:

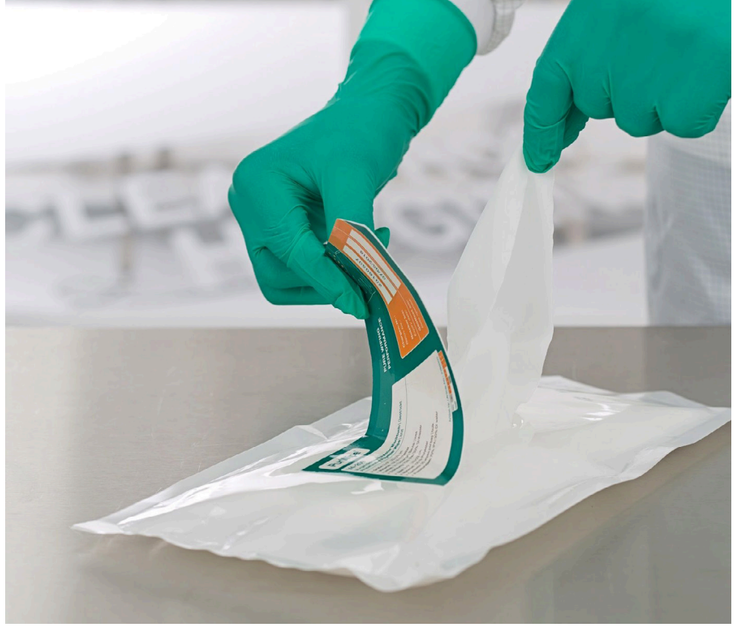
a) Nonwoven wipes (e.g. made of polyester/cellulose, polyester microfiber or polypropylene nonwoven)
These materials are not washed and consequently can show a significant level of contamination. Nonwoven wipes should not be used in the proximity of the product (workbenches / isolators).

b) Knitted wipes (e.g. 100 % polyester knit, polyester microfiber knit or other mixtures)
These offer a very high purity, as they are extensively washed, dried with ultrapure air, and packed in cleanrooms. During the washing process most of the residues are removed. Knitted wipes are designed for use on critical surfaces (GMP A/B).

Additionally wipes need to be selected, according to the purpose of use: cleaning (microfiber), liquid release (presaturated wipes) or absorption (dry, absorbent wipes). Presaturated cleanroom wipes offer benefits in handling (time and effort savings, avoidance of spraying, higher efficiency). Simultaneously it is guaranteed that the wipes are properly soaked, as often wipes are too dry (low disinfection effect) or too wet (unnecessary costs). Presaturated wipes are available in combination with various biocides and even sporicides.

DISINFECTANT

In principle, the GMP stipulates that several disinfectants (i.e. at least two) with different spectrum of efficacy must be used. A disinfectant that works against the formulation of spores, should be regularly used as well. (7) The definition of “regular” is not specified.



Because effective sporicidal disinfectants (oxidizing agents) are often aggressive and harmful to health and/or can cause material damage, they should be used as often as necessary, but as little as possible. A common cycle for sporicidal disinfection in pharmacies is 1 x / week for A/B areas (floor) and 1 x / month in C/D areas – of course varying routines are possible.

It therefore makes sense to qualify one disinfectant in each category after an internal risk analysis and followed by validation. Depending on the cleanroom requirement and product application (e.g. type of surface) as well as the risk assessment, suitable products must be selected along with corresponding application frequencies (daily / weekly / monthly...) and defined in the hygiene plan.

Typical for disinfection of surfaces of any kind (workbenches, tables etc.) are alcohol based, residue-free disinfectants such as isopropanol 70 / 30. Mostly other types of disinfectants are used for floors. If these are not residue-free, an additional cleaning step needs to be planned (see below).

Ready-mixed disinfectants (Ready-2-Use) are the preferred choice, as compared to manual dosing, especially in small rooms such as in pharmacies where the mixed fluid often cannot be completely used up in one cleaning session and has to be disposed of unused. When using concentrates, the risk of dosing errors is not to be underestimated. Furthermore, pharmacies often do not have access to purified water (e.g. WFI quality). To achieve the best possible result, disinfection by wiping is preferred over spray disinfection. Presaturated mops and wipes offer significant advantages in handling.

OVERVIEW OF POSSIBLE DISINFECTANTS (SELECTION)

GENERAL DISINFECTION (bactericidal, fungicidal, depending on the agent [limited] virucidal)	SPORICIDAL DISINFECTANTS
Alcohol-based products (isopropanol 70 / 30 or ethanol)	Chlorine-based products (Hypochlorous acid or sodium hypochloride or chlorine dioxide)
Aldehyde	Peracetic acid
Quaternary ammonium compounds	Hydrogen peroxide (H_2O_2)
Amine / Diamine	
Biguanid	

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WORKBENCHES / ISOLATORS (GMP A AREAS))

Workbenches / isolators are disinfected at least before and after the manufacturing process, but usually also in between. The ideal choice here is sterile isopropanol 70 % / WFI quality water 30 %. Regular additional sporicidal disinfection is also important. In addition, an alkaline cleaning step for inactivation of proteins and cytostatics can be useful.

For the side and rear panels, the use of a special cleaning tool (ICT tool) is helpful, so that the cleaning staff are not required to lean inside of the workbench. Sterile ICT mop pads are also available in presaturated version with different disinfectants.

TRANSFER INTO THE CLEANROOM

Contamination by materials transferred into the cleanroom must be avoided. Therefore an appropriate transfer disinfection, especially for non-sterile materials entering the cleanroom, is essential. In special material airlocks, this can be done by means of VHP (Vaporized Hydrogen Peroxide, H2O2). Alternatively material can enter through pass-through autoclaves or by manual wipe disinfection of the products – either with isopropanol 70 / 30, or with a sporicidal agent.

CLEANING

In many cases, a separate cleaning step will not be performed, as long as the routine disinfection is effective at removing regular soiling. The new GMP Annex 1 (draft) however, explicitly refers to this process. BEFORE each disinfection step it must be ensured that the area is free of contamination (even non-visible) to guarantee an effective disinfection. At the same time, cleaning can prevent residue build up on surfaces which quickly lead to corrosion, especially with sporicidal agents. Cleaning is carried out with a high-performance mop / wipe (microfiber material). Suitable cleaning agents are low residue or pH neutral detergents, isopropanol 70 % / WFI quality water 30 % or 100 % purified water.

AFTER disinfection (biocide hold times) and depending on the biocide used, it is recommended to implement a rinsing step with purified water, to remove the disinfectant residues and to prevent material corrosion.

SUMMARY

To achieve the best possible success in cleaning and disinfection in GMP areas several aspects must be considered. Competent and experienced suppliers of cleanroom cleaning solutions play an important role in selecting the ideal solution for the cleanroom user's specific environment and to make cleanroom hygiene as cost effective and safe as possible.

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(1) ApoBetrO, Section 4a. https://www.gesetze-im-internet.de/apobetro_1987/__4a.html
(2) DIN EN ISO 14644-1:2016-06
(3) VDI 2083 Sheet 9.2 Consumables in the cleanroom
(4) GMP Annex 1 [8-20]. https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-4/2008_11_25_gmp-an1_en.pdf
(5) GMP Annex 1 [62]. https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-4/2008_11_25_gmp-an1_en.pdf
(6) VDI 2083 Sheet 9.2 [14]
(7) GMP Annex 1 [61]. https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-4/2008_11_25_gmp-an1_en.pdf
(8) Annex 1 to the EU-GMP Draft Guide 2017 [5.31]. https://ec.europa.eu/health/sites/health/files/files/gmp/2017_12_pc_annex1_consultation_document.pdf

Pure Passion
for Cleanroom Hygiene

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