Sampling Programme for GMP Grade Controlled Environments, Section 10 Unlicensed Units. Active air samples, Settle Plates, Surface Samples, Locations and Number of Samples.

1st Edition

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Introduction.

To demonstrate compliance with the microbiological standards required in GMP environments it is necessary to monitor the number of microbes in the air and on the surfaces. The microbiological standard of air may be monitored by active or passive sampling. The microbiological standard of surfaces may be monitored by the use of contact plates or swab samples.
The limits for active and passive air samples and for contact plates are prescribed in 'Rules and Guidance for Pharmaceutical Manufacturers and Distributors'[1](Annex 1), and 'Quality Assurance of Aseptic Preparation Services [2.]
These publications do not describe the number or location of samples to be taken.
This document provides guidance on the minimum number of samples to be taken and their locations in GMP environments.
Gas sterilised isolators are not covered in this document.

Terminology.

Active air sampling [3]
This is a sampling method in which microbes are actively collected from air samples, usually by impingement or centrifugation on to an agar growth medium.
The growth medium may be contained in a Petri dish or a flexible plastic strip.
The sampling device is capable of accurately measuring the volume of air sampled, normally 1 cubic metre.
Active air sampling is the preferred sampling method because it gives results, which are more reliable and more quantifiable than passive sampling methods.

Passive air sampling [4]
These are sampling methods that utilise the tendency of microbes to settle out of the air under the influence of gravity. The microbes are captured on an agar growth medium, usually contained in a petri dish 90mm diameter, which when used for this purpose is referred to as a 'settle plate'.

Surface Samples [5]
This is an agar growth medium contained in a dish that gives a slightly curved agar surface raised above the rim of the dish so that impression samples can be collected, (often referred to as a 'Rodac', or contact plate.)
Surface sampling may also be undertaken using swab samples however there are no GMP limits for swab test results.

Sampling.

Sampling should be performed in the 'at rest' condition for commissioning studies and in the operational condition for routine monitoring. Sampling methods used in operation should not interfere with the environmental standard required, and hence not compromise the environment.

Routine Sampling Programme.

Workstations, Controlled Environments and Rooms.

Numbers of Samples			
Device / Room	Active Air Sample	Settle Plate	Surface Sample*
LAFCs < 1.5 m	1	2	2
LAFCs > 1.5 m	2	2	2
Isolators < 1.5 m	1	2	2
Isolators > 1.5 m	2	2	2
Isolator Hatches	1	1	1
Process and preparation areas, GMP grades 'B','C'&'D'	1 sample per 25 m^2 of floor area, above 25m^2 pro rata. Minimum 1 per room.	Sample no. = 1 per 10m^2 floor area, and pro rata for areas above 10m^2. Minimum 2 per room.	Sample no. = 1 per 10m^2 floor area, and pro rata for areas above 10m^2. Minimum 2 per room.
Change rooms, final Stage.	1	1 'clean side', 1 'dirty' side. Consideration should be given to monitoring the step over bench.	1 'clean side', 1 'dirty' side. Consideration should be given to monitoring the step over bench.
Passive transfer hatches to rooms	0	1	1
Actively ventilated transfer hatches to rooms	1	1	1

* After monitoring with contact plates the area should be thoroughly cleaned using a validated cleaning procedure.

During commissioning and re commissioning studies, additional samples, (for example corners of rooms and other areas that may cause airflow problems) should be included in the sampling programme. This should be repeated on at least three occasions, until satisfactory results have been obtained. These samples may be removed from the programme when satisfactory performance has been established.
If results indicate a failure to comply with required standards the frequency of monitoring should be increased, product shelf life restricted and the cause of failure investigated. The investigation should be documented.

References.

1. MHRA Rules and Guidance for Pharmaceutical Manufacturers and Distributors 2007, Annex 1.
2. Quality Assurance of Aseptic Preparation Services 4th Edition 2006. NHS Pharmaceutical QA Committee. Chapter 11.
3. Quality Assurance of Aseptic Preparation Services 4th Edition 2006. Pharmaceutical QA Committee. Appendix 1, A1.3
4. Quality Assurance of Aseptic Preparation Services 4th Edition 2006. Pharmaceutical QA Committee. Appendix 1, A1.4.1
5. Quality Assurance of Aseptic Preparation Services 4th Edition 2006. Pharmaceutical QA Committee. Appendix 1, A1.4.2

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