Particle Shedding Study of Perform Sterile Dry Wipes

Study undertaken during July 2013

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The results quoted in this report relate to the sample(s) supplied and should not be quoted in any other way.

Summary data has been recorded. The raw data will remain with Microbiology Solutions.

1. EXECUTIVE SUMMARY

This validation report examines the results from the examination of airborne particles generated from different types of cleanroom wipes. The study was undertaken during July 2013 at within a pharmaceutical grade isolator.

This validation report demonstrates wipes manufactured for use in ISO class 5 cleanrooms are suitable for use in such environments, whereas wipes manufactured for use in lower class cleanrooms are not suitable for use in 'cleaner' cleanrooms.

The study examined the following type of wipe:

- Perform sterile dry wipes manufactured by Schülke (30 x 30 cm)

Each of the types of wipes was examined under the following conditions:

- Opening a packet of wipes.
- Removing wipes from each packet (carried out for the 10 wipes inside each packet and repeated).
- Slow wiping technique (carried out for the 10 wipes inside each packet and repeated).
- Fast wiping technique (carried out for the 10 wipes inside each packet and repeated).

The study demonstrated that:

The level of particles generated increases through each condition examined, that is the counts increase from removing wipes compared with opening a packet, and then with slow wiping and then with fast wiping.

However, the study additionally showed the Perform dry wipes manufactured by Schülke are low particle generating and that they are suitable for ISO class 5 cleanroom use.

2. INTRODUCTION

Cleanroom wipes are provided in pouches and are either supplied dry or they are saturated with alcohol solutions, which acts as the disinfectant. The wipes examined in this study were dry wipes.

The wipes examined were Perform dry wipes (lot number 9644012), Schülke & Mayr GmbH Germany. The three types of wipes were manufactured from a polyester (low-particle cloths with laser-cut edges). The wipes are held in sachets (pouch) which permits them to be removed individually and allows the pack to resealed thereby preserving the remaining wipes within the pouch; within the pack the wipes are supplied double-folded. The number of wipes per pouch was 10 and the size of each wipe was 30 x 30 cm.

The highly absorbent wipes allow a rapid clean down of surfaces, equipment and production components.

There are alternative approaches for measuring the particles generated from wipes. Here the standard tests for cleanroom clothing are deployed, such as the Helmke drum test method (IEST RP CC004.3 "Evaluating Wiping Materials Used in Cleanroom and Other Controlled Environments", Institute of Environmental Science). This method is used to quantify particles dislodged through the application of mechanical energy under dry conditions as a means of simulating particle shedding from the surface of the garment during use. The items being tested are tumbled in a rotating drum to release particles from the fabric in a controlled manner, while a discrete-particle counter is used to sample the air within the drum.

Although such methods can be useful it is not measure in-use conditions or relate to the actual application of a wipe within a cleanroom. What is of more relevance is what happens when a wipe is removed from its packet and moved around through the act of wiping. The study presented here is orientated towards practical situations closer to the use of the wipes in "real life", where packets are opened in cleanrooms and under laminar airflows and then used.

To assess this, a study was conducted on dry wipes designed for ISO class 5 conditions. Cleanrooms are classified according to the number and size of particles permitted per volume of air. Within the healthcare and pharmaceutical sectors, ISO class 5 represents the cleanest class.

The wipes were assessed within an isolator under different conditions and the level of airborne particles measured using ISO class 5 particulate limits.

For the study, the wipes were assessed under the following conditions:

a) Opening the packet.
b) Removing each wipe from the packet.
c) Slowly wiping each wipe across a surface.
d) Fast wiping each wipe across a surface.

The activities were repeated for each wipe within the packet (10) and for two different packets.

The object of each stage was to show the number of particle counts produced and whether this had a significant impact upon the environment in relation to the class limit for the area (that is, did the use of the wipes taken the particle counts above the class limit?). This is an important concern because wipes can be a large contributor of large particles and fibres (in particular unsealed or poorly sealed edges are usually responsible for shedding large particles).

The first stage looked at the level of particles generated when a packet of wipes was opened. The second stage looked at the particle levels when a wipe was removed from the packet. The third and fourth stages considered the level of releasable particles when each wipe was used to wipe a surface. The surface examined was 3315 pharmaceutical grade stainless steel.

3. ACCEPTANCE CRITERIA

Results were assessed by measuring airborne particles against ISO 14644 class limits. The two cumulative particle sizes required by EU GMP were considered: 0.5 µm and 5.0 µm (for the FDA aseptic filling guide, the 0.5 µm size is required to be measured).

These limits are:

ISO 14644	**0.5 µm (counts per cubic metre)**	**5.0 µm (counts per cubic metre)**
Class 5	3,500	29

It is noted that the equivalent limits for EU GMP are somewhat tighter, so that EU GMP Grade A is actually equal to ISO 14644 class 4.8. These limits are:

EU GMP	**0.5 µm (counts per cubic metre)**	**5.0 µm (counts per cubic metre)**
Grade A	3,520	20

For the study, ISO class 5 limits were used for direct comparison to provide an international baseline although reference is made in the results analysis to EU GMP.

Reference documents:

ISO 14644-1: Cleanrooms and associated controlled environments - Part 1: Classification of air cleanliness. International Organization for Standardization ISO, Geneva (May 1999)

Food and Drug Administration. Guideline on Sterile Drug Products Produced by Aseptic Processing, *Food and Drug Administration*, Rockville, MD: 2004

EU Guidelines to Good Manufacturing Practice Medicinal Product for Human and Veterinary Use, Annex 1 Manufacture of Sterile Medicinal Products. The Rules Governing Medicinal Products in the European Union. Brussels : Commission of the European Communities, 2008, Vol. 4.

4. MATERIALS AND METHODS

The work was undertaken within an EU GMP Grade A environment provided by a barrier isolator, as illustrated below:

(Photograph taken by Tim Sandle, July 2013)

Airborne particle counts were measured using an optical particle counter. This was a MetOne model 3315 counter (HachLange instrument). A particle counter is a discrete-particle-counting, light-scattering instrument that is used to determine the concentration of airborne particles, equal to and larger than the specified sizes, at designated sampling locations.

The counter was fitted with an isokinetic sampling probe. Isokinetic sampling collects particles in a moving stream which moves at the same velocity in the sampling nozzle as elsewhere in the stream. This increases the accuracy and reliability of results.

The particle counter was purged before each session for five minutes to verify that the counter was recording particles at satisfactory level.

An equivalent cubic metre of air was sampled for each step. Depending upon the sampling time the counts were extrapolated so that the results could be compared to the maximum level of permitted counts per cubic metre of air (as shown above).

a) Prior to each session starting, the background environment was assessed and the level of particles verified to ensure that an ISO class 5 level was achieved. This was in order to verify that any counts recorded were generated from the wipes or associated activity and not from the environment in which the activity took place.

b) For the first step, a packet of wipes was unwrapped and opened. The counts were measured. This typically took ten seconds.

c) One minute was allowed to elapse so that the counts returned to the norm.

d) For step 2, a wipe was removed. The counts were measured. This typically took ten seconds.

e) One minute was allowed to elapse so that the counts returned to the norm.

f) For step 3, the wipe was rubbed along a piece of sterile stainless steel slowly. This was to simulate a slow wiping activity. This took one minute.

g) One minute was allowed to elapse so that the counts returned to the norm.

h) For step 4, the wipe was rubbed along a piece of sterile stainless steel quickly. This was to simulate a fast wiping activity. This took one minute.

i) One minute was allowed to elapse so that the counts returned to the norm.

Steps 2 to 4 were then repeated until each wipe from a packet had been removed from its pouch and rubbed. For the Perform wipes there were 10 wipes per pouch.

Steps 1 to 4 were then repeated for a second pack of wipes used in the study.

The study took around 20 hours to complete and was undertaken between 23th and 26th July 2013.

5. RESULTS SUMMARY

The data summaries below are all for counts per cubic metre. The background environment for each test was within limits prior to undertaking each stage of the study.

a) Step 1 –opening a packet of wipes

	0.5 micron Count	5 micron Count
Mean (average)	0	0
Minimum count	0	0
Maximum count	2	0

The data indicates that for each individual wipe removed, and for the averages for each of the packets, the counts were all within the ISO class 5 limits.

b) Step 2– removing wipes from the packet

	0.5 micron Count	5 micron Count
Mean (average)	16	1
Minimum count	0	0
Maximum count	250	5

The data indicates that for each individual wipe removed, and for the averages for each of the packets, the counts were all within the ISO class 5 limits.

c) Step 3 –slow wiping technique

	0.5 micron Count	5 micron Count
Mean (average)	25	2
Minimum count	3	0
Maximum count	336	11

The data indicates that for each individual wipe removed the counts were all within the ISO class 5 limits.

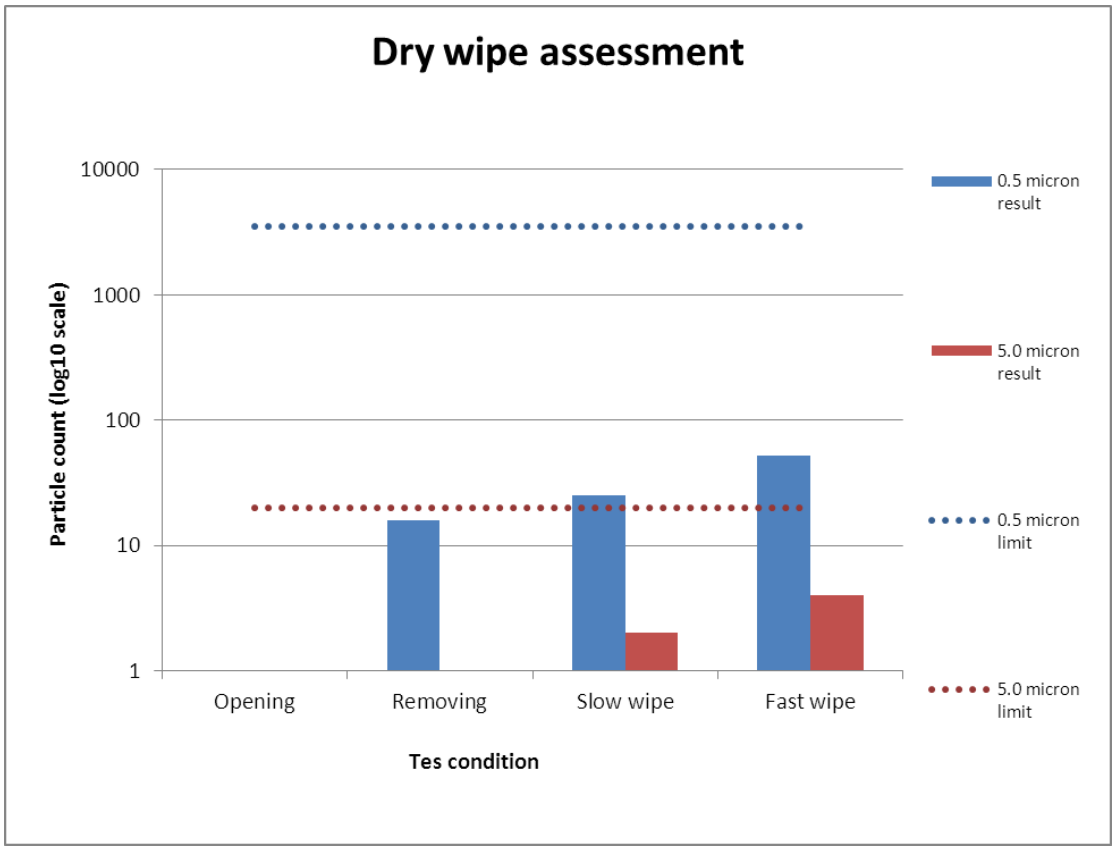
d) Step 4 – fast wiping technique

	0.5 micron Count	5 micron Count
Mean (average)	52	4
Minimum count	12	1
Maximum count	525	15

The data indicates that for each individual wipe removed, the counts were all within the ISO class 5 limits.

Graphical summary

The charts below compare the 0.5 µm and 5.0 µm size particles for the wipes and for each of the conditions examined:



The chart shows that the counts increased for each condition (that more particles are produced as wipes are removed, compared with a packet being opened; and that the counts increase further when the wipe is used to wipe a surface. Faster wiping creates the highest number of particles).

The counts produced are considerably below the ISO class 5 requirements for both 0.5 micron size particles and for 5.0 micron size particles.

The charts, and the earlier data summary tables and charts, indicate that the Perform wipes were suitable for use in ISO class 5 cleanrooms.

6. DISCUSSION

A cleanroom is an environment, typically used in pharmaceutical manufacturing and healthcare that has a low level of environmental pollutants such as dust, airborne microbes, aerosol particles and chemical vapours. More accurately, a cleanroom has a controlled level of contamination that is specified by the number of particles per cubic meter at a specified particle size.

One of the key aspects of cleanroom use is the control of airborne contaminants. These can be generated from several sources. One of the potential sources is cleanroom wipes. This study has established the Perform dry wipes are suitable for use in cleanroom environments.

The study was carried out on Perform dry wipes lot: 9644012.

The results of this study have shown that:

a) The Perform dry wipes, which are prepared and sterilised for use in ISO class 5 cleanrooms, are suitable for use in these areas. This was based on an examination of airborne particle counts.

b) When used to simulate wiping the Perform dry wipes produced a low level of particles and are suitable to be used in ISO class 5 cleanrooms.

c) The study also showed that different activities using wipes produced different levels of particle counts, in that:

- Opening a packet of wipes produced the lowest number of particles.
- Slow wiping produced fewer particles than fast wiping.

7. CONCLUSIONS

This validation report demonstrates that the Perform dry wipes manufactured by Schülke, designed for use in ISO class 5 areas, are suitable for cleanroom applications. This suitability includes the pharmaceutical industry.