Effective reduction in the microbial count in cleanrooms with the use of polymeric mats

Preparation unit of Meander MC sees significant results

Two years of use of polymeric mats in the Meander Medical Centre in Amersfoort have led to an effective reduction in the microbial count in the cleanroom. It is therefore possible that these mats also offer a solution for other pharmaceutical preparation units. 'But good personal hygiene and proper practices within cleanrooms remain vitally important'.

In order to be allowed to prepare medicines, Dutch hospital pharmacies must meet GMP-z standards (the Dutch Good Manufacturing Practice standards for a Hospital Pharmacy), for which the Good Manufacturing Practice (GMP) standards were used as a starting model [1, 2]. The hospital pharmacy in the Meander Medical Centre prepares medicines for their own patients, delivers to other pharmacies, and prepares for clinical research into medicine. Therefore, the pharmacy must meet standards for both the GMP-z and the GMP. For the production of sterile medicines, there are specific standards that apply to pharmaceutical microbiology.

When monitoring the new cleanroom, high counts of microorganisms were recorded in the staff airlocks. This is why special mats were installed as an extra barrier to microorganisms. In March 2015, the first mat was used as a test, and a year later, these mats were placed in all staff airlocks and other airlocks as well. Two years later, in February 2017, we checked to see whether this new measure had led to an effective reduction of microorganisms.

Particles in the air

The most important source of contamination is humans [3-5]. Ongoing regenerative processes in our bodies mean that our flakes of skin and hair moult. Furthermore, humans also cause contamination by movement, sneezing/coughing, and through production operations in cleanrooms [4, 5]. In this way, a cleanroom can become contaminated with particles, but also microorganisms. These travel through the air by latching onto particles in the air, or by direct physical contact.

The prevention of the contamination of pharmaceutical preparations is essential in reducing the risk of infections. There are multiple strategies to achieve this (see box) [6]. One of these strategies is preventing contamination from entering the cleanroom. To achieve this, the Meander MC placed special mats in the staff airlocks in the preparatory unit. These are polymeric mats (manufactured by Dycem), which are made from a non-toxic, plasticised material, and are developed to trap contamination that comes into contact with the floor [6].

The mat generates electrostatic forces that operate over the optically flat, flexible surface, and traps particles of varying sizes. Particles are then enclosed in the cellular structure of the polymers, which also contain silver ions. These mats have been found to be effective in reducing microbiological contamination with bacteria, fungi, and yeasts [3, 5, 7]. In addition, the material used stays effective for a minimum of three years, and therefore does not need to be regularly replaced.

The mat does need to be regularly cleaned with a mop and dried (third strategy, see box). After washing, the mat's original effectiveness is entirely recovered [6]. This is in contrast to so-called 'peel-off/adhesive' mats, which must be regularly replaced, are less effective in trapping particles, and are less user-friendly [3, 5].

Retrospective analysis

After the commissioning of the new-build of the Meander MC, the number of colony-forming units of bacteria did not appear to comply with GMP standards, particularly in the women's airlocks of the hospital pharmacy preparatory unit. This is why measures were taken to reduce the number of colony-forming units, including the introduction of polymeric mats in March 2015 (in the women's airlocks) and in June 2016 (in the men's airlocks and other airlocks).

In order to determine whether the introduction of these mats contributed to a reduction in the microbial count, we performed a retrospective analysis with the data collected as a part of the microbiological monitoring. It included several measurements regarding microorganisms, however these are also indirectly a measurement for particle contamination. We acquired data from January 2014 (the inauguration of the cleanroom) and were able to differentiate air measurements (calculated every four hours; sedimentation plates were used, samples were collected from behind the benches in the airlocks) and contact measurements (Rodac plates were used; samples were collected from airlock benches and on the wall and floor behind the benches). By comparing the number of colony-forming units in the periods before and after the placement of the polymeric mats, we were able to see whether the mats had effectively reduced the microbial count.

As a result of the air measurements, we observed a significant reduction ($p<0.05$) of 91 colony-forming units to just 35 respectively before and after the polymeric mats were installed in the women's airlocks. In the men's airlocks, a significant reduction of colony-forming units ($p<0.05$) was also observed: from 37 to just 14. For contact measurements, we did not find a significant reduction in the number of colony-forming units.

On the basis of our retrospective analysis, we concluded that by installing polymeric mats, the average number of colony-forming units on the sedimentation plates was reduced. The mats appeared, however, to have no influence on the average number of colony-forming units on contact plates. The electrostatic forces of the mat in general seemed to lead to the attracting and capturing of particles in the air, so that the presence of these in the air was reduced, but were less effective in terms of particles that (via direct contact) were already attached to a surface. The polymeric mats thus seem to be particularly successful for the results found when using sedimentation plates.

Other measures

In order to be able to comply with GMP standards, simply installing a few polymeric mats will not be sufficient on its own, and other precautions will have to be taken. This is why it has been decided to store shoes in the staff airlocks, and to clean the mats in the women's airlocks four times a day, so that the surface does not become saturated. This means that there are confounding factors that we were not able to correct. Aside from that, maintaining good, personal hygiene and utilising proper methods of practice within cleanrooms is of vital importance when trying to minimise the contamination of preparatory areas.

Sjanne van Roijen is a Masters student of Pharmacology, University of Utrecht (from 1st August: pharmacist, Wijchense Pharmacy), and Rogier Lange is a hospital pharmacist, Meander Medical Centre.

Minimising contamination

Preventing the contamination of products is an important goal of the GMP/GMP-z. Strategies to help minimise contamination are:

- Prevent microorganisms from entering the cleanroom by maintaining a difference in air pressure in the airlocks and with the help of such a mat;
- Hygiene and clothing: wearing cleanroom clothing and shoes, and washing and disinfecting hands;
- Physical removal of contamination by regular cleaning;
- Reducing the vitality of microorganisms, for example by leaving areas dry after cleaning;
- Killing microorganisms with disinfectant.

Bibliography

1. GMP-Ziekenhuisfarmacie. KNMP/NVZA. Available via: http://nvza.nl/voorprofessionals/gmp/.
2. Eudralex - Volume 4 - Good Manufacturing Practice (GMP) Guidelines. Available via: https://ec.europa.eu/health/documents/eudralex/vol-4_en.
3. Sandle T., 'Examination of air and surface particulate levels from cleanroom mats and polymeric flooring.' *European Journal of Parenteral & Pharmaceutical Sciences*, 2012;17 (3):110-19.
4. Prout G., 'The nature and environmental impact of control of floor level contamination.' *European Journal of Parenteral & Pharmaceutical Sciences*, 2009;14(1):13-18.
5. Clibbon C. 'An evaluation of the effectiveness of polymeric flooring compared with "peel-off" mats to reduce wheel- and foot-borne contamination within cleanroom areas.' *European Journal of Parenteral Sciences*, 2002;7(1):13-15.
6. Sandle T. 'A final floor show for bugs.' *Cleanroom Technology* 2006;12(4):19-21.
7. Ranta LS. 'An evaluation of polymeric flooring and its effectiveness in controlling airborne particles and microbes.' *European Journal of Parenteral Sciences*, 2002;7(3):79–80.