As the Dust Settles

Roy Cannon at Teknek discusses how to combat viable contamination in the medical and pharmaceutical packaging environment

Modern medical and pharmaceutical packaging operations take place in the strictly controlled conditions of a cleanroom. One would assume, therefore, that all contamination risks are eliminated. However, particulate contamination is a particular problem for effective cleanroom operation. Air quality in the room can be measured using a tyndleometer, which gives a qualitative measure of the number of particles in the air. The sampling process is very quick and enables real-time analysis of air quality at various locations in a room. Settling plates should also be placed in the room to determine efficiency. Unfortunately, the results from this testing method may not reflect the true picture depending on where the plates and the sampling tubes are positioned within the room.

There are wide variations in the comparative size of particles. Human hairs, for example, are typically between 50 and 150 microns. The naked eye can register down to 50 microns in normal light, and 10 microns if the particle is on a reflective surface (bacteria are typically 0.5 to 50 microns).

Air filtration systems within cleanrooms require unrestricted airflow to allow the particles to be extracted. The introduction of machines, transport devices (trolleys), materials and people all contribute to creating dead areas or alternative vortices of airflow, which in turn allow particles to be randomly distributed around the room. The primary function of a cleanroom is to remove airborne contamination. If a particle is above a certain size then it has a natural settling rate that will make the filtration system ineffective (see Table 1). This table indicates that any particle over 60 microns in size could settle on a surface in a cleanroom.

Table 1: Settling rates (airborne particles)

Diameter of particles Microns	Velocity of settling Feet per minute
1	0.007
5	0.2
10	0.59
60	21.3

QUALITY CONTROL

Quality control is paramount within the pharmaceutical packaging environment; the principles embodied in the Good Manufacturing Practice (GMP) and the Hazard Analysis and Critical Control Points (HACCP) regulations dictate that manufacturers take all steps possible to control and eliminate the presence of non-viable contamination. Particle contamination on a medial device is categorised as 'filth' by the FDA and its guidelines warn that products cannot be adulterated by filth. It should be noted, though, that reducing particulate contamination is not a sterilisation issue.

To meet these standards, medical and pharmaceutical manufacturers need to ensure that such risks are contained and removed, and most importantly, that the systems put in place to do this can be validated and verified to the satisfaction of the regulatory authorities.

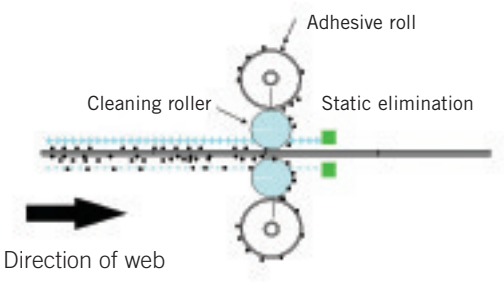
Non-viable particulates can cause an issue for a finished product; for example, dust or human hair may appear on secondary packaging, which is unacceptable to the end user. As we have demonstrated, no matter how controlled the environment, there is still scope for particles such as fibres, epidermal tissue and hair to enter the production process. In addition, the raw materials themselves, for example metal slitting particles from foil used in blister packs, along with the packaging machinery can be a potential source of non-viable contamination.

To ensure that the final step, the packaging process, does not cause an issue, it is necessary for these raw materials to be decontaminated before coming into contact with the product.

THE USE OF CONTACT CLEANING EQUIPMENT IN A CLEANROOM

Typical packaging materials used, such as PET, PP and non-woven aluminium foil are normally processed in a cleanroom of the same standard as the final production facility.

Figure 1: Double-sided cleaning



Sterilisation processes take care of viable contamination, but non-viable particulate still needs to be removed. These small particles will only be removed by contact cleaning equipment. This system should be installed at a critical point in the operation, such as before coating, lamination, forming or closure of the product. This equipment uses a unique elastomer roller which runs directly in contact with the substrate being cleaned. It removes dry unattached particles (down to 2 microns) from the substrate it is rolling over. The polymer is engineered to attract the particulate from the substrate as it rolls over it. A reverse wound adhesive roll then runs in contact with the polymer roller. The particles are transferred from the polymer roller onto the adhesive roll where they are then permanently trapped. Once a revolution of the adhesive becomes saturated, it is peeled off revealing a fresh layer below. The saturated layer can then be removed from the cleanroom, taking the trapped particulates with it. In some cases, detailed analysis of the quantity and type of particles captured in the adhesive can help with root cause analysis and should offer some guidance on where operational practices can be improved to minimise the risks of non-viable contamination getting into the cleanroom in the first place. Figure 1 shows the contact cleaning principle.

Contact cleaning technology is applied in a wide variety of medical and pharmaceutical manufacturing scenarios including:

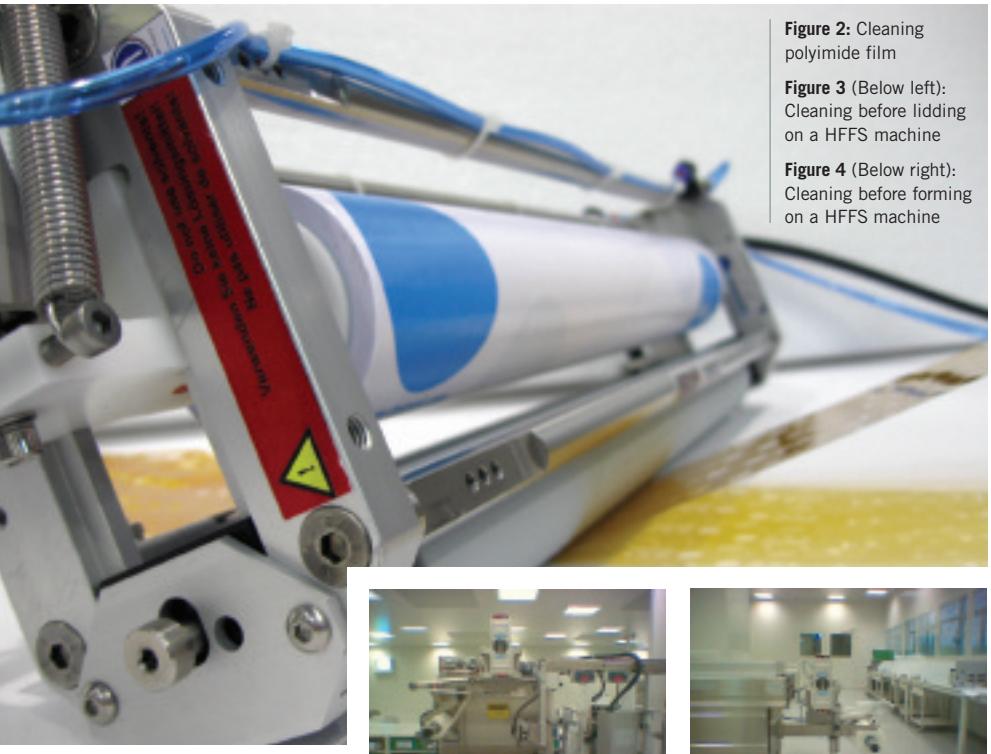


Figure 2: Cleaning polyimide film

Figure 3 (Below left): Cleaning before lidding on a HFFS machine

Figure 4 (Below right): Cleaning before forming on a HFFS machine

- Cleaning of foils and films for lidding operations
- Horizontal form fill and sealing operations
- Cleaning of film used in making medical pouches and bags
- Cleaning of specialist medical materials

Some processes currently in use include cleaning foil lids for contact lens packaging to avoid damage to the lenses, cleaning the surfaces of IV bags, and cleaning the interior surface of Tyvek after printing and before lidding to avoid ink migration into the medical package. Figures 2, 3 and 4 show contact cleaning equipment for a variety of such requirements.

ROOT CAUSE ANALYSIS

Failure to control contamination in the production environment can lead to a waste of expensive materials, and even product recalls. Therefore, it can be beneficial to carry out a contamination audit to discover the root of the problem. To complement existing cleanroom testing procedures, a special technique has been developed which uses a hand-held contact cleaner. A simple elastomer roller is used to pick up contaminants from a defined surface or substrate within the production environment. The contamination is then transferred onto a special adhesive pad, where it is recorded and then removed from the cleanroom for examination and analysis. This analysis is used to create a simple map to plot the type and concentration of the particles within the process. It can also allow you to produce a matrix where all the samples taken from each area are logged, along with their analysis results. This can immediately identify where manufacturing or housekeeping protocols need to be improved or changed. If this process is continued through the facility, it is then possible to create a secondary matrix for the whole production facility, with all departments listed and their total contamination levels logged. This should reveal how the contamination, if any, is flowing through the plant. Careful analysis of these matrices should identify areas of high risk and appropriate action can be taken to counteract the contamination.

Figure 5: Contact cleaning in action

CONCLUSION

The application of contact cleaning technology should be a fundamental part of any medical or pharmaceutical manufacturer's battle against contamination or 'filth'. It is a proven technology that is able to remove dry unattached particulate down to 2 microns. It allows a simple validation process to be implemented, as it shows the results of cleaning as the contamination is trapped in the adhesive layer. It permits permanent removal of the contamination at the critical point in the process. It allows diagnostics to take place and consequently permits suitable corrective action. Finally, it allows manufacturers to evaluate the process, which in turn will highlight the effects of any process changes that have been made.

Even in a controlled cleanroom environment, there are risks of non-viable contamination entering the production chain. The cleaning of packaging materials using contact cleaning equipment is one of the most effective methods of combating these risks and can be easily incorporated as part of the standard manufacturing procedures.

About the author

Roy Cannon is Teknek's global product specialist for medical, pharmaceutical, coating, converting and printing, with a responsibility for the development of these key strategic market sectors. A former teacher, Roy has been with Teknek for 25 years in various design, engineering, product development and marketing roles, and was instrumental in developing the company's original range of equipment. During his career, he has travelled extensively around Asia, Europe and the US advising clients on the effective implementation of yield improvement measures in modern hi-tech manufacturing operations. He has developed his engineering and problem-solving skills in electronics, and now works mainly in the converting sector.
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