Selecting gloves

Choosing which type of disposable glove is best for a particular process is complex. **Nick Gardner**, Shield Scientific, reviews the range of choices, limiting factors and documents required to ensure they meet cleanroom criteria

Validation of any glove used in a cleanroom is typically a long and demanding process. In the face of an increasingly regulated industrial environment, the needs for disposable gloves have changed dramatically.

Two decades ago it was common practice to accept standard gloves in PE packaging for use in the cleanroom. Likewise vinyl gloves were widespread, particularly in the microelectronic industry, but a better understanding of the contamination and barrier issues posed by these types of glove have contributed to their disappearance. Meanwhile, in the pharmaceutical industry, the practice of using standard surgical gloves (i.e. those where the wallets and outer packing are both made of paper) continued even in aseptic environments.

The adoption of ISO 14644-1 at the beginning of the decade introduced a single standard for cleanroom classification and made it much easier to understand airborne particulate cleanliness. A similar convergence was taking place in Europe for the pharmaceutical industry, with the publication of the Guide to Good Manufacturing Practice for Medicinal Products and its Annexes (EC GMP).

Specific areas, such as the manufacture of sterile medicinal products, are covered in the annexes. While none of these developments focuses specifically on disposables for use in the cleanroom, the trend towards the adoption of cleaner practices in an increasingly regulated environment is clear.

Possibly as a way of trying to fill potential gaps, the VDI-Society Civil Engineering & Building Services in Germany began publishing a series of guidelines known as the VDI manual of Cleanroom Technology. With reference to consumables to be used in the cleanroom, this is covered in Annex H of VDI 2083 Part 5.1 "Cleanroom technology - Cleanroom operation".

Throughout the electronic, aerospace and solar industries, evaluation procedures have undergone a significant transformation. The same pace of change does not appear to have been mirrored in the pharmaceutical industry, where in some sectors surgical and medical examination gloves continue to be used in sterile and non-sterile areas, respectively. Some hospital pharmacies, where cytotoxic drugs and parenteral products are prepared, may view personal safety as the main priority followed by cleanliness of the product. However, under the influence of ISO 14644 and especially the EC GMP, these areas are undergoing change.

Why do cleanroom applications need a specific glove? In many cases, the primary purpose for wearing gloves is to avoid contamination of the product. Apart from the costs associated with high batch failure rates, contamination by biological agents of parenteral drugs can have serious consequences for patients. A similar concern is the need to maintain the cleanliness of the surrounding cleanroom environment, as this can contribute to product contamination.

The first step in the evaluation is the choice of glove material (see Table 1).

Where electrostatic discharge (ESD) is a concern, the following points should be borne in mind:

- Natural Rubber Latex gloves are static insulative – static insulative materials are considered as having a surface resistance of higher than 1 x 10^{12} ohms/sq. The danger here is that the charge is held to a certain point then released in an uncontrolled fashion. Even with high surface residues, such as ionic contaminants, the gloves appear to remain static insulative.
- Nitrile gloves are, in terms of surface resistance, considered to be on the border between the insulative and static dissipative ranges. Extensive cleaning, especially in deionised water, may reduce the glove's dissipative properties. Static dissipative means that the electric charge bleeds out in a controlled manner and does not affect the properties of an item. A glove that is static dissipative has a surface resistance of more than 1 x 10^{5} but less than 1 x 10^{11} ohms/sq.
- Vinyl gloves (often referred to in the past as ESD gloves) offer the best dissipative qualities, by virtue of the high level of surface contaminants.
- Neoprene may exhibit similar ESD behaviour to nitrile. Furthermore, as many neoprene gloves have an inner coating (often polyurethane or silicone) to facilitate donning, it is unlikely that they will have undergone rinsing in deionised water to enhance cleanliness. Therefore any favourable static dissipative properties are likely to be derived from high levels of surface contaminants.

Why is it important to consider the cleanroom classification? Based on ISO 14644-1, the lower the ISO Class, the lower the permitted concentration of airborne particles. While the electronic industry will tend to focus on particles and extractables, the pharmaceutical sector will give particular attention to bacterial contamination. For ▶

Table 1: Summary of main features of glove materials

Material	Material properties	Cleanroom (CR) suitability
Vinyl/PVC	Low strength and elongation. Poor flexibility and ergonomics. High non-volatile residues and wet particle counts.	For use in CR with low sensitivity to particle contamination and where there is minimal need for protection from microbiological hazards.
Natural Rubber Latex	High tensile strength, with good elastic properties. Prone to shedding particles in use. Responds well to extra rinse cycles to produce gloves low in particles and ionic extractables.	For CR applications where there is a need to avoid particulates and ionic contaminants. Excellent barrier properties to biohazards. Compatible with gamma-irradiation for sterile gloves.
Synthetic Latex: Nitrile, Neoprene (Polychloroprene), Polyisoprene and Polyurethane	Good to acceptable elongation and tear resistance. Good abrasion resistance. Following additional laundering, possible to produce glove with very low ionic and particle residues	Ideal for CR seeking highest cleanliness levels in terms of low particulate and ionic contaminants. Excellent barrier protection to biohazards. Suitable for gamma-irradiation in sterile gloves.

◀ those operating under sterile conditions, the potential for endotoxin contamination will be of special interest. However, for both non-sterile and sterile applications, the potential of a glove to cause particle contamination should be a source of interest as these particles could support microbial life.

Glove manufacturers can ensure that the lowest contamination levels are maintained, by laundering gloves in deionised water, drying under HEPA filter driers and adopting cleanroom protocol for packing and sorting the gloves. The latter stage is often done in an ISO 5 or even ISO 4 cleanroom.

Other criteria for selection of cleanroom gloves: While operators' comfort when wearing gloves along with their personal safety are clearly significant factors, any validation process will also want to consider the supporting documentation.

Feeling and comfort: Feeling and comfort are important since an operator who experiences discomfort and is unable to perform correctly various tasks may cause errors. However, just because a glove is comfortable does not automatically mean that it is the right choice. Natural rubber latex is probably the most comfortable glove material, but brings with it the risk of natural rubber latex allergy and poor abrasion resistance leading to potential shedding of particles in-use.

Gloves with an inner-coating may be viewed as desirable by users, as they offer effortless donning. However, these gloves are unlikely to have been subjected to the extensive laundering (particularly in deionised water) needed for cleanroom gloves to render them low in particles and extractable contaminants.

Nitrile gloves may not provide the same level of comfort and dexterity, but multiple rinses in deionised water can produce a glove with the lowest levels of particle and extractable contamination. Additionally, compared with natural rubber latex, nitrile offers superior abrasion resistance coupled with more favourable ESD properties.

Nitrile gloves offer excellent barrier protection to biohazards

Availability of documented performance: A glove manufacturer's ability to provide comprehensive and insightful documentation will not only facilitate the validation process, but could ultimately lead to the reduction or even elimination of incoming inspection. In this respect, lot-specific data is often preferred to periodic tests, such as those done annually or every quarter. For many years, the electronic industry has been using such data as part of its Standard Operating Procedures (SOPs). Increasingly, the pharmaceutical sector has been requesting information of this nature to support at least the evaluation process.

Specific data that could be requested includes:

- Particle residues by lot for sterile and non-sterile gloves, tested in accordance with IEST – RP – CC005.3
- Endotoxin testing by lot for sterile gloves to confirm low endotoxin content claim. Testing to be based on the Limulus Amoebocyte Lysate kinetic tubidimetric technique (LAL)
- Sterilisation by lot confirming that gloves have been sterilised to a Sterility Assurance Level (SAL) of 10^{-6} in accordance with ANSI/AAMI/ EN ISO 11137:2006

Product data sheets that are frequently found on manufacturers' websites will often give a snapshot of the quality of the data available. To assess the potential of the manufacturer to deliver documented consistency, requesting copies of certificates of analysis or conformance for three or more recent lots could be helpful.

Under "Physical Test Data", the total number of samples of final product is shown

Using longer gloves, such as those with a length of 300mm, provides complete coverage of bare skin

for various physical tests. The column referred to as "barrier defects" gives important information in terms of the incidence of pinholes. Lots are accepted on the basis of whether or not the number of defects exceeds the number of statistically permitted defects (as determined by AQL). Thus "Pass" will be shown when the number of permitted defects was not surpassed. It will be noted that particle contamination analysis is defined both by concentration (average particles/cm^2) and distribution (particle size range expressed in µm).

Those operating in sterile environments will seek reassurances as to sterility of the gloves. A certificate of irradiation will show the minimum and maximum doses of irradiation to which the gloves have been subjected. Often as part of the initial evaluation process, additional information will be sought covering sterilisation validation procedures. The latter is most likely to include dose-mapping, GMP audits of contract sterilisation facilities, etc.

Regulations and Norms: If, as part of a risk assessment, disposable gloves are being used for personal protection, then only those gloves that are registered according to the Personal Protective Equipment (PPE) Directive (89/686/EEC) should be used. Additionally, if the gloves are being used for personal protection against chemical splashes, then selection of gloves that are registered as Complex Design (Category III) according to the PPE Directive would be appropriate.

Gloves that are Category III and designed for micro-organism resistance must achieve at least an AQL of 1.5 (Level 2), based usually on the water penetration test. Gloves of this type may also exceed this minimum perform-ance requirement for micro-organism resistance by having an AQL of less than 0.65 (Level 3). AQL is a crucial parameter for assessing the barrier performance of a glove and specifically with regard to pinholes.

Through a process of random sampling, an AQL of less than 0.65 assumes a statistical probability that no more than 0.65% in any given batch can have pinholes. It is therefore significantly more stringent than an AQL of less than 1.5, which would permit up to 1.5% having pinholes. AQL also has implications for protecting the product as pinholes provide a path for human-borne contaminants.

Accordingly, in those areas where protection from microbial contam-ination is a key priority (e.g. aseptic areas), seeking gloves with an AQL of <0.65 may be prudent.

For applications where there is exposure to potentially harmful viruses, it should be noted that the above claim of micro-organism resistance does not extend to viruses. This may be a particular concern to vaccine manufacturers that routinely use live viruses. If there is a specific need for viral protection , then gloves that have additionally been tested for viral penetration may be the solution, such as the bacteriophage test defined in ASTMF1671. ▶

Table 2: Summary of key test data for cleanroom gloves

Test overview					
Personal and product safety		**people**	**production**		**lot-specific**
Regulation/Norm:			**sterile**	**non-sterile**	
89/686/EEC	Declaration of Conformity – PPE Cat III	x			
EN374-2:2003	AQL – resistance to penetration from micro-organisms & chemicals	x	x	x	x
ASTM F1671-97b	Viral Penetration Test		x	x	
EN374-3:2003	Chemical Permeation Tests	x			
EN455-3:2006	Latex protein test – cannot claim below 50µg/g, but note requirement from Institute for Occupational Safety and Health in Germany (BGIA) for <30 µg/g	x			
EN455-3:2006	LAL Test to substantiate low endotoxin content claim	x	x		x
ISO11137:2006	Sterilisation Guidelines		x		x
EN455-2:2009	Elongation and Tensile strength	x	x	x	
ISO10993-10:2010	Biocompatibility of material, specifically with reference to irritation and Delayed Type Hypersensitivity	x			
ASTM D257-07	Surface resistance	x	sometimes	x	
EN1149-1:1996	Surface resistance	x	sometimes	x	
IEST RP CC 005.3	Particle release and extractable matter		x	x	x

◀ **Need for special packaging:** Standard gloves packed in cardboard boxes are not compatible with most cleanroom environments. Gloves packed in this way will be prone to shedding cardboard particles, while it will be noted that the action of taking the gloves out of the boxes will often exacerbate the risk.

For the above reasons removing the gloves from the cardboard box and depositing them in plastic dispensers will not eliminate the risk of particle shedding in use. Consequently it is standard practice to accept only gloves in PE packaging for use in cleanrooms. Often these are double-bagged to facilitate safe transfer to the cleanroom. The use of ink on the packaging that is resistant to isopropanol (IPA) helps to reduce an additional contamination risk.

For sterile areas the continuing use of surgical gloves with PE outer-packing but inside a paper wallet may provide a further source of contamination. Often these gloves are registered according to Medical Device Directive (93/42/EEC) and may not be suitable where a risk assessment has identified personal protection as the principal intended purpose for wearing the gloves.

To minimise contamination of the environment and product, it may be desirable to select only those gloves that have been washed in deionised water, dried under HEPA filter driers and packed in a cleanroom (preferably ISO class 5 or 4). It will have been noted that not all glove materials are compatible with the rigorous washing process involved with multiple rinses in deionised water. Consequently if a high level of cleanliness is sought avoiding vinyl gloves may be necessary.

In the less critical environments (e.g. ISO class 8 or D, based on the EC GMP classifications), it may be common practice to use shorter-length gloves such as those of 240mm. However, the potential shedding of human-borne contaminants, especially from the exposed wrist area, should not be under-estimated. Accordingly it may be preferable to use longer gloves, such as those with a length of 300mm to provide complete coverage of bare skin.

The discussion on selection criteria for cleanroom gloves has highlighted the value for personal and product safety of documented performance. In this respect Table 2 may provide a useful summary of the key test data that could be requested. **CT**

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