EJPPS

EUROPEAN JOURNAL OF PARENTERAL AND PHARMACEUTICAL SCIENCES

EJPPS – European Journal of Parenteral and Pharmaceutical Sciences Volume 28 Issue 3

Glove disinfection and aseptic technique: Creating a schema for the cleanroom and laboratory

Corresponding Author: Tim Sandle

The weakest link? Assessing isolator glove integrity failures

Tim Sandle

Introduction

For several decades isolators, as separative devices, have been commonplace in pharmaceutical and healthcare products manufacturing. Although isolators presented a significant step forward on the contamination control continuum, isolators, if not appropriately operated, can be vulnerable to contamination ingress. The primary mechanism for ingress is through air leakage and with the different points across the overall structure that are potentially vulnerable it is gloves that are the most leak-prone aspect (1). The gloves (or sometimes gauntlets, when in the form of a one-piece sleeve and glove) of an isolator are a necessary function of most isolators given they are the primary way through which humans interact with the environment inside (EU GMP Grade A / ISO 14644 class 5). As the PIC/S guidance states, Grade A can only be maintained when accessed through glove stations: "A Grade A internal environment is created, and manipulations are carried out through glove ports". Given the availability of some gloveless isolators that rely upon robotics, this statement is a little out of date, however it makes the point that if personnel are present in an environment nominally called 'Grade A' then this environment ceases to be 'Grade A'.

One of the significant points of failure with any isolator or restrictive access barrier system (RABS) is the glove, should a loss of integrity occur (2). The main mechanism by which a loss of integrity can occur is a tear, seal weakness or some form of abbreviation (3). The central concern is with detecting damage and assessing the impact. While we can measure any pressure loss to the isolator and we can perform environmental monitoring, neither of these are sufficiently sensitive since the overall pressure drop is insufficient to reveal so-termed 'pinholes' in gloves (4) and we cannot often detect whether microorganisms have entered the isolator environment given the considerable limitations of the environmental monitoring methods. Sometimes monitoring detects contamination, especially in the event of a gross failure but zero growth on a finger dab (or from a swab of the glove and sleeve) taken some hours later is not a source of comfort should a glove integrity failure be detected. To use the aphorism attributed to Andrew Hopkins: "*Absence of evidence is not evidence of absence*." Hence, gloves need to be assessed for integrity using specialist integrity testing equipment.

Contamination control leads in healthcare and pharmaceutical facilities that use separative devices need to understand the weaknesses with isolator gloves and, should failures occur, be able to analyse the likelihood of failure and learn from these to put in place measures to reduce the likely rate of any future failures.

Risks

Although gloves and gauntlets will be subject to quality control assessments by the supplier, pre- and post-sterilisation, the accepted quality level (AQL) will be set at somewhere between 1.5 and 3.0, indicating that occasional flaw can occur in manufacturing. Furthermore, micro-perforations could be incurred during use. While visible tears are apparent to the operator, sub visible holes are not. With the loss of glove integrity, there are two types of risks that relate to the use of isolator gloves:

Glove failure: This is an unplanned opening in a glove caused by degradation of the mechanical properties of the material over time. This can be caused by exposure to chemicals.

Glove breach: This is an unplanned opening in a glove caused by mechanical damage during operations, such as penetration with a sharp object or pinch points.

The consequence of one of the above failures is contamination ingress into the isolator (an additional risk exists where the isolator is used for containment purposes in terms of operator exposure). There are other risks relating to the use of gloves, not least the disruption of 'first air' but this falls outside the scope of this article.

It is common to refer to non-visible damage to a glove as a 'pinhole'. While widespread in common parlance the term is not especially useful; a pinhole refers to a hole with a diameter between a few micrometres and a hundred micrometres. In some of the studies reviewed below, researchers have described the pinhole as a breach that is 'sub-millimetre'. While this provides an upper threshold it still lacks precision. Perhaps the best course is to simply consider damage that is not visible to the human eye under standard lighting conditions.

The need for analysis

The requirement to assess the causes and likelihood of glove integrity failure are outlined in a PIC/S guidance. The guidance describes that measures must be in place to prevent a loss of isolator glove integrity (5):

"*A program to minimize the risk of loss of integrity of gloves, sleeves and suits should be present. This should include operator practices, vigilance and the absence of sharp edges. There should also be an all-encompassing preventative maintenance program that includes specification of examination and pre-emptive replacements*."

This leads into consideration of the risk assessment. For any isolator system, a risk assessment should be in place (such as one based on Failure Modes and Effects Analysis) (6). When a risk assessment is undertaken on an isolator, whichever method is used, gloves invariably are identified as the highest risk area. This is because:

Gloves are used during each batch.

Simply having gloves provides a contamination control concern since the leak checking of gloves and, when needed, their reinstallation can introduce a point of contamination transfer.

Gloves are more prone to damage, based on the material and design (there needs to be a trade-off between the robustness of the material and the level of dexterity required by the human operator who needs to manipulate the glove) (7).

It cannot easily be quantified what level of damage constitutes a risk. While it is possible that the risk stemming from 'pinholes' (non-visible damage) has been overstated (8), factors of glove material, glove use, pressure fluctuations and so on represent additional variables for microbial transfer risk.

Some gloves will be located in the most critical areas, close to product or sterilised surfaces or components.

When gloves are used, there is often a rise in positive pressure. For example, Maier and Drinkwater describe how gloves can develop momentary rises in pressurisations as an operator's hand passes through the wrist section and then on entry into finger pockets (9).

Gloves are not necessarily fully protected by the maintenance of positive pressure. This can arise due to weak localised sealing effects (quality by design approaches should have eliminated this as the glove port should be hermetically sealed to the isolator wall, but not all isolators are as well-made as others). There is also the 'piston effect', which is created when an operator inserts their arm into a sleeve (the forced-air flow inside the sleeve that is caused by the moving of the arm, much like a train entering a tunnel) (10). It is good practice only to access gloves when an active aseptic process is not happening and when a line clearance has been performed (acknowledging the instance that need to use a glove might be in order to perform a line clearance when this cannot happen automatically).

If a leak occurs, microbial contamination can be transferred from the operator into the isolator environment.

Where holes occur, these tend to be most often the locations between the fingers; fingertips; and glove edges.

Eliminating the risk?

There is only one way to completely remove the risk of glove integrity failure and this is through the elimination of gloves. This is something that can be achieved with the use of automation and automation can, currently, only be applied to certain aseptic operations. Therefore, for most isolator users the risk remains ever present; what is incumbent upon pharmaceutical personnel is with reducing the risk, as per the intent of the PIC/S guidance.

Understanding the likelihood of failure

Understanding the risk of glove failure is a combination of knowing what can cause glove damage, and then minimising these factors, and understanding how likely risks are to occur under a state of normal running by drawing on data. This sequence of understanding risk factors and putting in place technical control measures is a fundamental activity, as Drinkwater and Van Laere have documented (11).

To understand the likelihood of failure, data needs to be analysed. This is easier for a system that has been running for a year or more. One approach is to assess time-to-failure data by running a time series plot (which requires 50 or more data points). The plotted data should be assessed for trend, cycle, seasonal variations and irregular fluctuations. A trend is defined as a non-constant mean (signalling the yet-to-be-identified causes). One of the causes that can be accepted or eliminated is a seasonal fluctuation. Other information that can be extracted includes:

How long are gloves fitted for before failure occurs?

How many decontamination cycles are gloves subjected to prior to failure?

How often is a glove used:

For setting-up?

During an aseptic process?

For any post-aseptic work cleaning?

Does a glove come into contact with anything that can be construed as a sharp object?

Do glass breakages occur within the vicinity of the glove?

Is the glove used for handling needles?

How often is a glove tested for integrity?

How is a glove prepared and positioned for the decontamination of the isolator?

What is used to support the glove?

How consistently is the support tool fitted?

Does the support tool have sharp edges?

Any association with environmental monitoring data? (Such as finger dabs / glove swabs or adjacent settle plates).

Further clarification of potential factors can be obtained using other tools, such as Pareto charts. Understanding the frequency of failure and the specific locations where failures can occur provides valuable information for assessing the cause(s) of failure.

Identifying causes of failure

There are different causative factors for glove failure. Among the potential causes are:

Inappropriate glove material.

Gloves should be selected on the basis of being manufactured from robust materials and materials resistant to the chemical used for decontamination. Examples of common materials are: Latex (rubber); Ethylene propylene diene terpolymer (EPDM) rubber; chlorosulfonated polyethylene (trade name Hypalon); Nitrile (butadiene acrylonitrile); butyl (carboxylated acrylonitrile butadiene rubber); Viton; and neoprene (polychloroprene). Of the different materials, forms of chlorosulfonated polyethylene rubber appear to be the most common. EPDM is resistant against the greatest range of disinfectants in liquid form, including hydrogen peroxide. The glove material must be detailed within a specification, along with the thickness (which is generally between 15 and 30 mil).

The number of decontamination cycles

The enclosed space within the isolator needs to be periodically decontaminated. A common means to do this is using hydrogen peroxide vapour. If decontamination cycles are run too frequently or they are too harsh in their overall design, this can weaken the glove material (albeit that some materials are more compatible with VHP than others). Moreover, the frequency of cycles relative to the length of time a glove is used for can incrementally weaken the glove material but introduce fatigue (12).

Inappropriate operator use

Operators can damage gloves by coming into contact with sharp objects or where pressure is inadvertently applied (so-termed ‘pinch points’). The former is addressed through the elimination of sharp objectives and the use of tools to avoid direct touching of components; the latter relates to glove design and operator training.

Use of disinfectants

To address spillages and for other purposes, disinfectants are often held inside the isolator. If these are applied to gloves, repeated applications can affect the glove material and weaken it. The disinfectant deployed is often a sporicide and some types of materials are more resistant than others to chemicals like liquid hydrogen peroxide. Different materials will have maximum times that

the glove should be exposed to a chemical (either directly as a liquid or through gas or vapour) (13). When gloves are exposed a record should be kept and when this limit has been reached, the glove should be changed at the next opportunity (such as prior to the next campaign).

Glove movement and the frequency of use are additional factors that can affect chemical stability, in that excessive movement of the glove can decrease the durability to a chemical (14).

Use of expired materials

The shelf-life together with "in-house" stock rotational procedures are necessary control factors to ensure old and possibly degraded gloves are not used.

Effect of time

All materials will degrade over time, although some are more stable than others under static conditions when exposed to oxygen and ultraviolet light (the standard environmental conditions inside an isolator). A related factor is the frequency of use. The tensile properties (elasticity modulus and maximum elongation) of materials are set initially based on passing a force-at-break test (where a given force, expressed in Newtons is applied – typically 6 Newtons) and then further demonstrated through assessing any softening of the material with time (15). As well as the tactile response, this is also sometimes indicated by a colour change to the material. The length of time that gloves are fitted for should be evaluated, irrespective of whether the glove has been used for a batch operation. That is, the replacement frequency is both a dependent and independent factor of use. The glove manufacturer should have undertaken accelerated thermal aging studies.

Given that time permeates through the above examples it is good practice that when gloves are installed, they are labelled with their install and expiration dates.

Improving detection

Sometimes glove damage can be detected, as in the case of a large tear or when an operator, on using a glove, considers that damage may have occurred. However, more often holes cannot be seen, given the limits of human acuity (especially as the scale of damage moves down to the level of 'pinholes'). A similar issue arises for general pre-use checks. Gloves can be examined for visible signs of damage, but only visible failures can be detected. When undertaking a visual inspection, the glove should be stretched, and the likelihood of detection can be enhanced through the use of appropriate lighting. Risk assessments that place an over-reliance upon operator detection are flawed. As an alternative, post-use, gloves can be filled with water (a water intrusion test). While seeing water leaking through the glove can indicate a certain level of failure, the intrusion test is not as sensitive as automated forms of glove testing. A study suggests that the water intrusion test, for a glove that has been appropriately stretched and using 1 litre of water, can detect a 0.15 ± 0.05 mm hole, equivalent to what a 21-guage needle might cause in terms of a hole (16). As well as inspecting the glove for leakage, a variant of the water intrusion test is where air is sealed by pressure and an expanded rubber glove is submerged in a container filled with water to visually inspect the generation of air bubbles.

The use of glove integrity testing devices provides evidence of a leak. Devices that can be used without breaking the isolator barrier potentially enable 'real time' assessments to be made. Effective devices will assess both the inner and peripheral sections of each glove. Often these are *in situ* trace gas detectors to permit the pressure decay method to be deployed; although electrical conductivity tests using electrolyte as a conducting medium can also be used. However, most devices require the isolator to be inactive and these can only provide pre- and post-use data. Both approaches to

detection provide a means to safeguard a batch or a campaign of batches; nevertheless, the real usefulness is when a leak is paired with a cause and trending the data is undertaken in order to formulate preventative actions.

Glove testing methods include pressure hold and pressure decay methods (17, 18) (following the principles outlined ISO 10648) (19). Of these, the pressure decay method is more common. Prior to conducting the test, the glove should be stretched out. The run time for the test is partly dependent upon the material thickness and material type. The method requires the glove system is subjected to a predefined test pressure. Care needs to be taken, since applying too much or too little pressure can result in damage present not being detected in certain areas of the glove. ISO 14644-7 Annex E.5 outlines the basic requirements for leak testing (20). In implementing a glove leak testing device, the range that the user is intending to inflate each glove must be determined (the ISO standard requires this to be between 500 and 1000 Pa, with upwards to 1000 Pa being optimal). In addition, acceptance criteria for the pressure decay need to be set. The ISO standard places a suitable range as falling between 2 and 10 Pa, which enables pinholes of around 100 micrometres to be detected (below the level of human visual acuity). This will be partly dependent as per the sensitivity of the instrument. The test stabilisation and hold time also needs to be set for the assessment of the pressure differential (such as 10 seconds hold time). As part of qualification, some users elect to deliberately damage gloves (such as creating a pinhole) and then attempt to replicate pass and fail in relation to this deliberate damage.

Lowering the risk of failure

The process of avoiding glove failures or lessening the impact of a glove failure can be achieved through good operator behaviours. This foremost rests with operators recognising the vulnerability of gloves and using gloves only when necessary and under circumstances when product exposure is minimised (21). In addition, operators need to be mindful of the applications and objects that could cause glove damage. It is also important that, when gloves are used they do not directly touch any objects within the isolator; an important design approach is for sterile tools to be used. Hence, the principles of aseptic technique should be maintained at all times. This can substantially lower the risk of contamination transfer since microorganisms must be transferred from operator to isolator glove, to the tool, and then to the sterile item (the work of Whyte and Eaton is useful here for assessing contamination transfer coefficients) (22).

As mentioned earlier, when the arm of an operator enters an isolator glove, as described above, there can be a rise in pressure. If there is a hole in the glove the resultant air will seek to escape through the hole, and this can direct any particles outwards. To compensate this jetting effect, in the event of a pinhole, ideally line clearance will have taken place and gloves should be entered by positioning the glove away from a critical area. The accessed glove should not be used for a period of time (such as ten seconds) to enable the area to clear and to drive any particulates away from the working zone.

Evaluating risks in the event of a failure

Based on the previous discussion, occasional glove integrity test failure results are recorded. When a failure is detected the impact of the failure upon the batch processed needs to be assessed. This produces two actions:

An investigation to establish the root cause and to develop a preventative action (23).

An assessment of the risk.

In addressing the second point and developing a risk framework, not every scenario can be covered, but the framework enables a general assessment of low risk (blue) or high risk (red) or where further assessment is needed (green).

This framework is based on the risk of a non-integral glove being dependent upon:

- The location of the glove
- The use of the glove
- The size of the breach
- Location of the breach

With each of these:

With location, gloves are either:

- In a critical zone (over direct product contact parts or sterile product)
- In a non-critical zone
- Gloves in either zone should be defined and reviewed according to separate risk assessment trees

With the use of a glove, the risk is lowered when:

The operator wears a sterile glove before accessing. While this undoubtedly lowers the level of any contamination, it will never eliminate it given that the operator's cleanroom glove is not sterile (although sterile gloves are put on, and hand disinfection practiced, no declaration of sterility can be made).

- One accessing the sleeve is pulled towards the isolator wall and elevated
- Upon entering the glove, the glove is not used any further for ten seconds[1]
- A sterile tool is used with the glove[2]

With the size of the breach:

If the breach is visible to the human eye (which is theoretically >100 microns, although for most people >500 microns is more realistic) the risk is elevated.

If the breach is smaller than what can be discerned by human vision, the risk is considerably lowered[3].

---

[1] Why does this matter? The study by Maier and Drinkwater showed that when a hand enters an isolator glove, this creates a one-time jet stream effect, increasing the positive pressure to 500pa. This will push through any particles. In a short space of time, these particles will be removed by the downward unidirectional flow of the isolator and expunged from the isolator environment.

[2] Contamination on the glove is required to be transferred to a tool, and then from the tool to the critical zone. This additional step makes the transfer improbable unless there is any direct touching from one surface to another.

[3] Two studies have shown that the bioburden on the hand of the operator would need to be considerable for even the smallest of bacteria to cross over through a pinhole. Such a bioburden is improbable if sterile gloves have been worn.

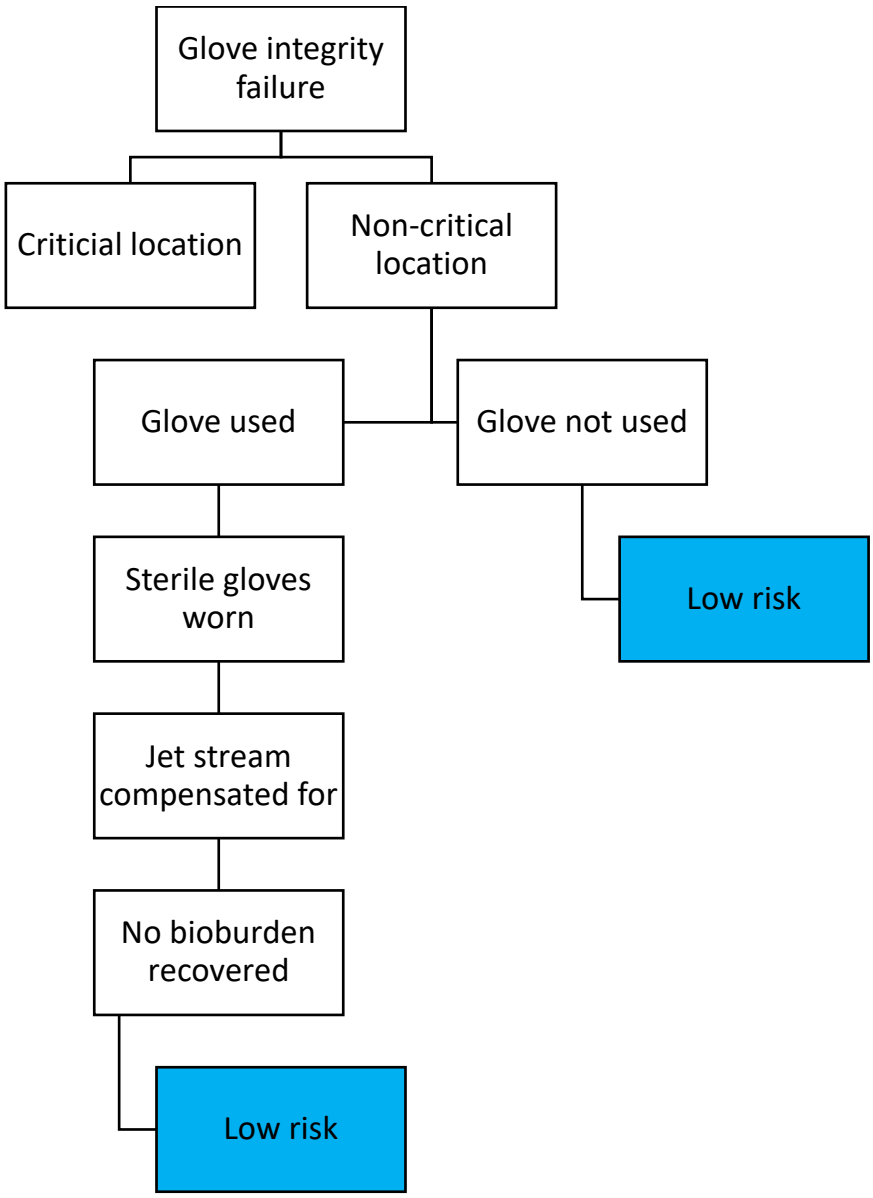
A visual examination of the glove during use or a visual examination of the glove following a glove integrity test failure may detect a visible tear or hole. Following a glove leak tester failure, the glove should be carefully examined by stretching out the glove and with the aid of a torch.

With the location of the breach:

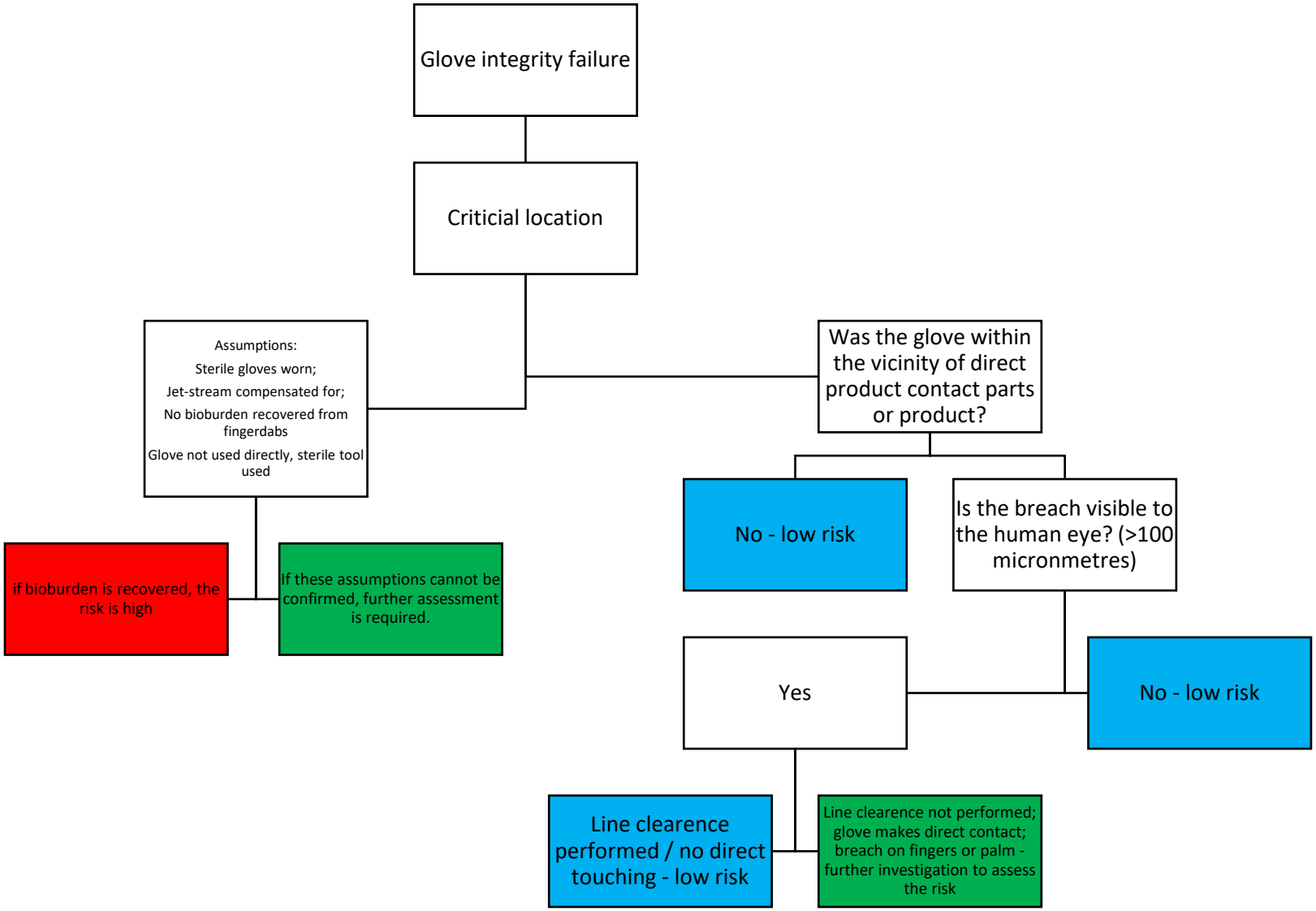
- The risk of the breach, in terms of contamination transfer is higher when the breach is at the fingers or on the palm
- The risk of transfer is lower on the sleeve
- Upon a glove integrity test failure, if the hole cannot be seen visually, it should be filled with water and the locations where the leak is situated observed

The following decision trees can aid the assessment (Tree A and Tree B):

Tree A: Non-critical glove location



Tree B: Critical glove location



The approaches laid out in the decision trees can provide the basis for an evaluation of risk to support a deviation investigation.

Preventative actions

When particular vulnerabilities are noted, additional activities can be undertaken to ensure that gloves are replaced at an appropriate frequency by performing reliability analysis to predict when likely failures might happen and building this into a planned preventative maintenance programme. Studying the causes of failure and the frequency of failure aids the formulation of a pre-emptive glove replacement procedure. Replacement frequencies will be influenced by the frequency of exposure to the decontamination process; the frequency of integrity testing; the degree of use; and the risk of contact with objects that might cause damage to the glove. It is prudent to have six to 12 months of inventory since many types of gloves suitable for isolators have long lead times.

In addition, the likelihood of an integrity failure can be reduced by selecting more robust materials (as indicated above). It is also possible to use double-skin sleeves, which provides an additional layer of protection should an integrity failure happen away from the glove.

Conclusion

This article has examined the factors that can make the integrity of isolator gloves weaker and the process for assessing and then investigating glove related issues. The safest option moving forwards is eliminating gloves entirely by using robotics and other forms of automation, together with best design practices. However, the majority of isolators remain reliant on the use of gloves. It is incumbent upon each user to put in place a risk assessment and to follow-up on each failure, using the root cause to design a suitable preventative action.

In terms of assessing risk, the following mitigations should be considered:

The gloves selected should be of a suitable and durable material, such as being resistant to hydrogen peroxide and cleaning chemicals and being of sufficient thickness to avoid common damage. This will help to reduce the risk of integrity failures, but it does not provide a detection method.

Operators should wear sterile gloves prior to using isolator gloves. This helps to reduce the potential for microbial migration through microscopic holes in the gloves. Special attention should be paid to where holes are most likely to occur - these include locations such as between the fingers; fingertips; and glove edges. However, this activity in itself may not be a sufficient mitigation should an isolator glove fail integrity testing.

Operator practices and vigilance must be part of training, in relation to avoiding glove damage. In addition, in the isolator there is an absence of sharp edges.

Operators must practice aseptic technique and gloves must not be used to directly touch sterile objects inside of the isolator.

Finger plates will be taken at the end of a campaign. However, finger plates will only pick up gross contamination and do not have sufficient sensitivity to detect a small leak.

Gloves will be inspected visually - for macroscopic defects -before and after each batch. This will allow for tears and holes to be detected. The ability of an operator to detect a problem can be boosted through the use of a defect library (as with other forms of visual inspection). However, this will not be sufficient to detect ‘pin prick’ sized holes.

All gloves will be tested at the end of a batch and a campaign (where more than one batch is processed between isolator decontamination cycles). If all gloves pass the leak test, this will provide sufficient assurance that all batches filled will have been filled under satisfactory conditions (i.e. no Grade A breaches) in relation to the isolator gloves.

To summarise, the primary means of minimizing glove failures are through a robust glove inspection programme, by ensuring that operators use gloves in a way that avoids contact with sharp objects and by controlling glove service life.

If any glove fails, the only outcome can be to put all batches on hold and to undertake a risk assessment as to the sterility assurance of the batches. Such an exercise could lead to each of the batches deemed as not being suitable for release.

References

1. ISO 13408-6, Aseptic processing of health care products — Part 6: 2021, Isolator Systems, International Standards Organisation, Geneva
2. Coles, T. (2012) Leak rate measurement for pharmaceutical isolators: Practical guidance for operators and test engineers, *Clean Air and Containment Review*, Issue 11, pp8-12
3. Cournoyer ME, Casey JW, Taylor DJ. Minimizing glovebox glove breaches. *Enclosure,* 2004; 17(2): 6–21
4. Anon. Clarity in GMP Guidance Pharmaceutical Isolator Leak Integrity Classes and Leak Rates, *Pharmaceutical and Healthcare Sciences Society*, 2020, UK
5. PIC/S. Isolators used for aseptic processing and sterility testing, PI 014-3, Pharmaceutical Inspection Convention / Pharmaceutical Inspection Convention Cooperation Scheme, 2007
6. Sandle, T. (2003): The use of a risk assessment in the pharmaceutical industry – the application of FMEA to a sterility testing isolator: a case study, *European Journal of Parenteral and Pharmaceutical Sciences*, 8(2): 43-49
7. Sawyer J, Bennett A. Comparing the level of dexterity offered by latex and nitrile SafeSkingloves. *Ann Occup Hyg* 2006;50:289-96.
8. Gessler A, Stärk A, Sigwarth V, Moirandet C (2011) How risky are pinholes in gloves? A rational appeal for the integrity of gloves for isolators. *PDA J. Pharm. Sci. Technol*. 65 (3): 227-41
9. Maier C, Drinkwater JL (2016). Managing contamination risks in glove holes in barrier separation technology. *European Pharmaceutical Review*: https://www.europeanpharmaceuticalreview.com/article/45014/managing-contamination-risks-glove-holes-barrier-separation-technology/
10. Auvity, B.; Bellenoue, M.; Kageyama, T. Experimental study of the unsteady aerodynamic field outside a tunnel during a train entry. *Experiments in Fluids*. 2001; 30 (2): 221–228
11. Drinkwater, J. and Van Laere, M. Risk-based environmental control and process monitoring in aseptic processing, *European Journal of Parenteral & Pharmaceutical Sciences*, 2015, 20 (4): 133-142
12. Park, Y.H. and Tang, J. An efficient methodology for fatigue reliability analysis for mechanical components. *ASME Journal of Pressure Vessel Technology* 2006; 128(3):293-297
13. Elnaz EsmizadehBoon Peng ChangBoon Peng ChangDylan Fernand Jubinville Dylan Fernand Jubinville. Stability of nitrile and vinyl latex gloves under repeated disinfection cycles, *Materials Today Sustainability* 2021; 11-12(2):100067 DOI: 10.1016/j.mtsust.2021.100067
14. Phalen RN, Wong WK. Chemical resistance of disposable nitrile gloves exposed to simulated movement. *J Occup Environ* Hyg. 2012; 9(11):630–639
15. Perkins JL, Rainey KC. The effect of glove flexure on permeation parameters. *Appl Occup Environ Hyg*. 1997; 12(3):206–210
16. Phalen, R. Kee, W., Wong, W. Integrity of Disposable Nitrile Exam Gloves Exposed to Simulated Movement, 2011, *Journal of Occupational and Environmental Hygiene* 8(5):289-99
17. Haske, K J., Smith, J E., Sakowski, MR., and Preuss, D E. In-situ gloveport glove leak tester. United States: N. p., 2020: https://www.osti.gov/biblio/1651057
18. Castro, Julio M, Macdonald, John M, and Steckle, Jr., Warren P. In-Situ Leak Testing And Replacement Of Glovebox Isolator, Or Containment Unit Gloves. United States: N. p., 2004: https://www.osti.gov/biblio/879930
19. ISO 10648-2:1994 Containment enclosures — Part 2: Classification according to leak tightness and associated checking methods, International Standards Organisation, Geneva

20. ISO 14644-7, Cleanrooms and associated controlled environments — Part 7: Separate devices (clean air hoods, gloveboxes, isolators and mini-environments), International Standards Organisation, Geneva, (2004)
21. Schwope AD, Costas PP, Mond CR, Nolen RL, Conoley M, Garcia DB, Walters DB, Prokopetz AT. Gloves for protection from aqueous formaldehyde: Permeation resistance and human factors analysis. *Appl Occup Environ* Hyg. 1988; 3(6):167–176
22. Whyte W and Eaton T. Microbial transfer by surface contact in cleanrooms. European *Journal of Parenteral and Pharmaceutical Sciences* 2015;20(4):127-31
23. Park, Y. and Cournoyer, M. Root Cause Analysis of Glovebox Glove Failure, Conference: ASME 2007 Pressure Vessels and Piping Conference At: San Antonio, Texas, USA Volume 2: Computer Applications/Technology and Bolted Joints, July 2007, DOI: 10.1115/PVP2007-26121