Gloves on Isolator

- Gloves are subjected to same conditions as isolator working chamber
- Gloves should be capable to perform manual intervention

Picture : https://skan.com/de/produkt/isolatoren/skanfog-spectra/

Norm, Guidelines…etc.

- Gloves should be regularly disinfected during operations. Garments and gloves should be changed immediately if they become damaged and present any risk of product contamination.
- The materials used for glove systems (for both isolators and RABS), should be demonstrated to have appropriate mechanical and chemical resistance. The frequency of glove replacement should be defined within the CCS.
  - Leak testing of the glove system should be performed using a methodology demonstrated to be suitable for the task and criticality
  - Testing should be performed at defined intervals
  - Generally glove integrity testing should be performed at a minimum frequency of the beginning and end of each batch or campaign
  - Additional glove integrity testing may be necessary depending on the validated campaign length.
  - Glove integrity monitoring should include a visual inspection associated with each use and following any manipulation that may affect the integrity of the system.

Source: https://www.pda.org/docs/default-source/website-document-library/scientific-and-regulatory-affairs/annex1/2020_annex1ps_sterile_medicinal_products_en.pdf

Glove Types
Glove Selection
Glove Substitution

Types of Gloves

- One Piece or Two Piece
- Material:
  CSM (Hypalon)
  Neoprene
  EPDM

- Dimensions:
  - Length (750 mm – 850 mm)
  - Diameter
  - Hand size (7-11)
  - Thickness*
  - Handshape (Ambidextrous, Fully anatomical version)

Pictures : google image search

General overview of glove manufacturing

Ceramic / Aluminium

Washed and Dried

Chemical bath

Diped into liquid rubber

Dried

Quality Control

Marking

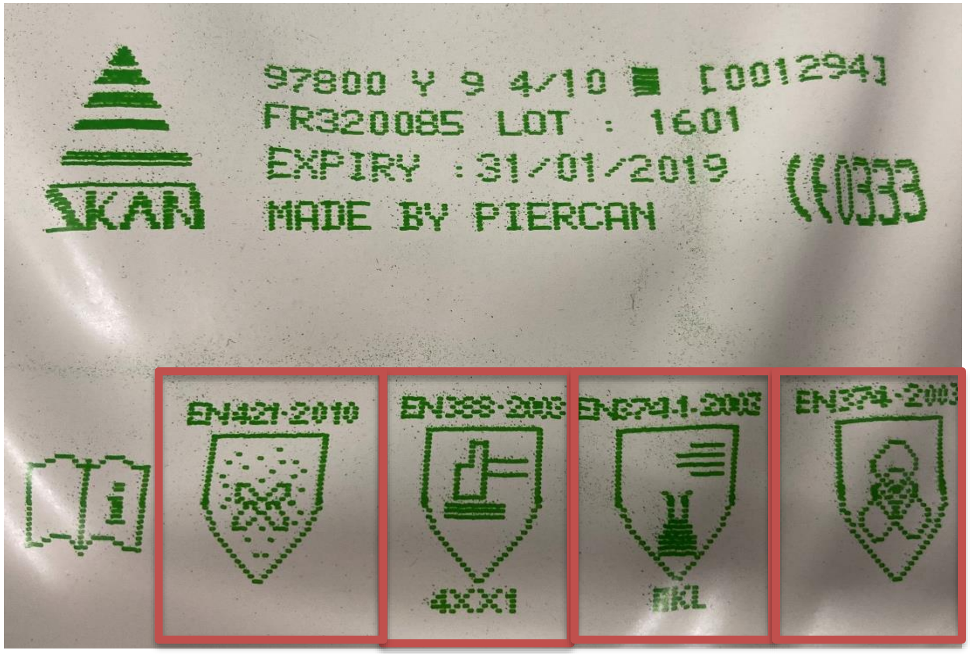
Packed

Pictures :Piercan website

Evaluation of a glove marking

- Type number: 97800 Y 9 4/10 (E5 5):

- 97 code for the diameter of the glove ring
- 300 mm
- 800 length of glove with 800 mm
- Y material code for CSM
- Hypalon
- 9 glove size
- 4/10 thickness 0,4 mm
- 5 thickness of the cuff beading



Radioactive contamination & ionizing radiation

Mechanical resistance

Chemicals

Microorganism

Future aspects:

- Individual identification for each single glove

Task: Glove data collection

Describe different control measures which reduces the contmination risks

Glove Selection

- Operational Requirement
  - Use of glove port
  - Materials / products in contact with
- Glove Mounting
  - Complexity of glove mounting
  - Impact of glove stretchers
- Operator Comfort
  - Rigidity, Softness.

Pictures: https://www.youtube.com/watch?v=UD8KZ5WUcJg

Glove Selection

- Persistence of gloves
  - Visual difference
  - Surface Roughness
- Adsorption
- Decontamination factor

Glove	C_3H_7OH	C_2H_5OH	H_2O_2 35%	H_2O_2 50%	HCl	H_2SO_4
PIERCAN CSM	1	1	1	1	1	1
Honeywell CSM	1	1	1	1	1	1
Jugitec B	1	1	1	1	1	1
Jugitec PharmaPlus	1	1	1	1	1	1
Jugitec ISOFlex	1	1	1	1	1	1
PIERCAN Neopren	1	N/A	1	5	N/A	N/A

Glove	The decontamination of the material…
PIERCAN CSM	Requires expert knowledge
Jugitec B	Is easy to achieve
Jugitec PharmaPlus	Is very easy to achieve
Jugitec ISOFlex	Is easy to achieve

	Amount of damage	Size of damage
1	No damage; no visible damage	Not visible at 170x magnification
2	Very few number of damages	Only visible with min. 10x magnification
3	Few, i.e. small but significant number of damages	Just visible with the bare eye (up to 0.2mm)
4	Moderate number of damages	Visible with the bare eye (0.2mm-0.5mm)
5	Damages with significant number	0.5mm-5mm in size

Tables: SKAN analytix *(Glove Tests Persist)*

Glove Substitution

- Scenario 1: New gloves of the same part number is installed

Change according to SOP defined by company

Recommendation:
-Not in production mode.
-Wearing surgical gloves
-Avoid using sharp objects

- **Repetition of Leak test**

Pictures : SKAN

Glove Substitution

JUGITEC® Safety Gloves

PIERCAN

Honeywell

- Scenario 2 : existing glove is exchanged with a glove
  - 1. having different material
  - 2. different dimensions
  - 3. from different manufacturer
  - 4. having two piece/ one piece

- Repetition of the leak test
- Performance of the material persistence tests according to SKAN standard operating procedure
- Test for isolator suitability with regard to dimensions and design of the glove
- Determination of suitable SOP for physical glove test (SKAN – Parameter for WGT)
- Aeration cycle test
- Life time evaluation /analysis

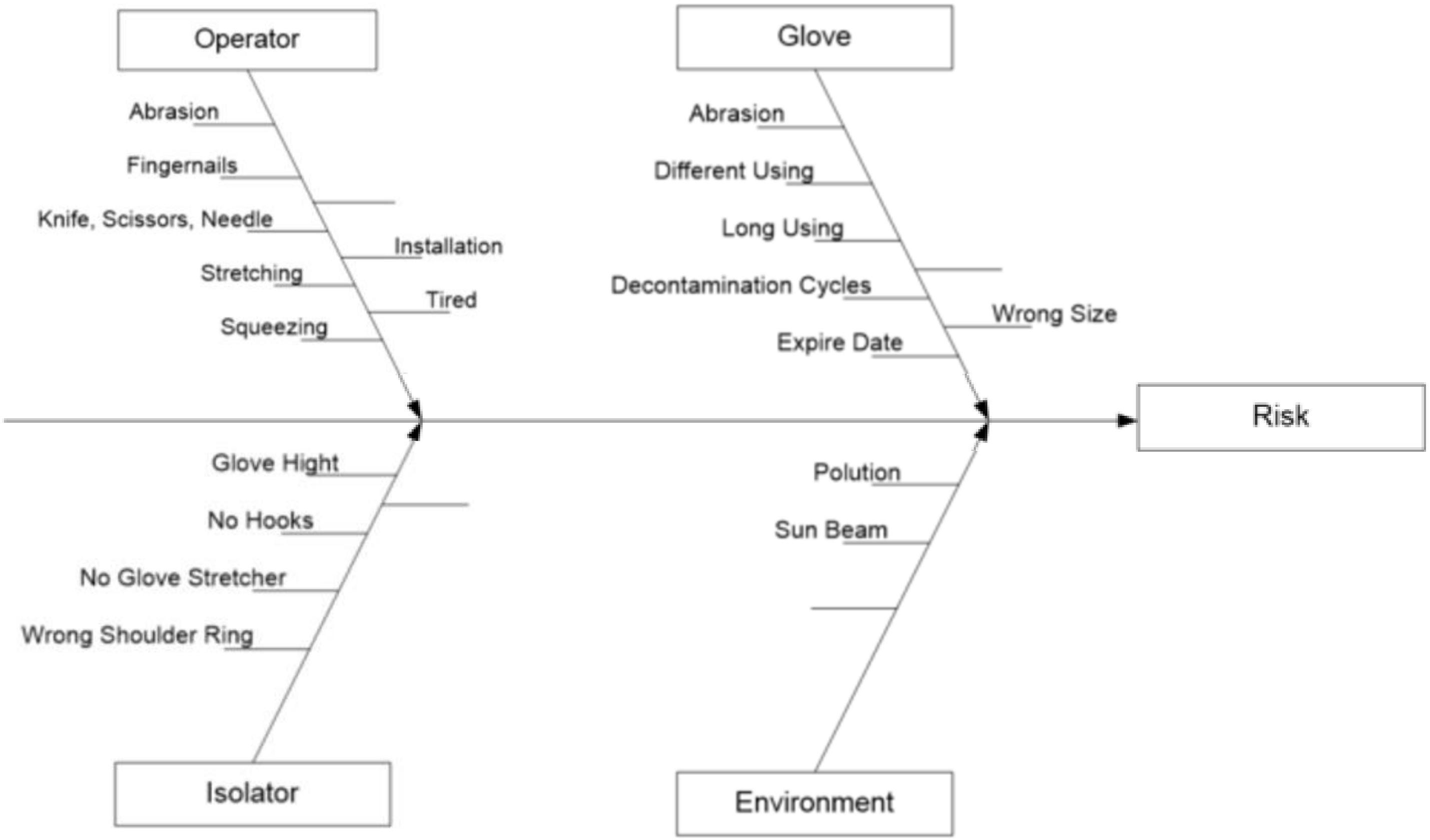
Pictures : https://www.google.com/search?q=Piercan+gloves+picture&rlz=1C1GCEA_enCH887CH887&source=lnms&tbm=isch&sa=X&ved=2ahUKEwjj1f75q8_2AhWTg_0HHeCUBRwQ_AUoAXoECAEQAw&biw=2276&bih=1122&dpr=1.13

Glove Contamination risk

Task: Sources

Describe different control measures which reduces the contmination risks

Risks


Operator
Abrasion
Fingernails
Knife, Scissors, Needle
Installation
Stretching
Tired
Squeezing
Glove
Abrasion
Different Using
Long Using
Decontamination Cycles
Wrong Size
Expire Date
Risk
Glove Hight
No Hooks
No Glove Stretcher
Wrong Shoulder Ring
Isolator
Polution
Sun Beam
Environment

Gloves & Holes

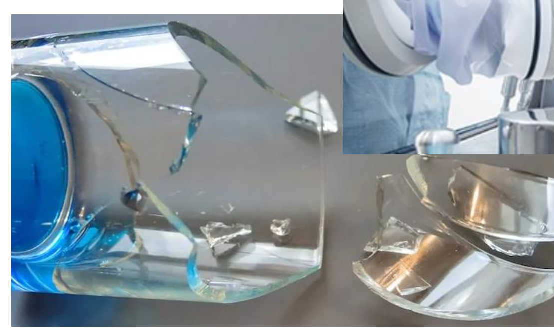
Pictures : google image search

Critical Places of Holes

What do you think, where are the most common holes need to be find?

Critical Places of Holes

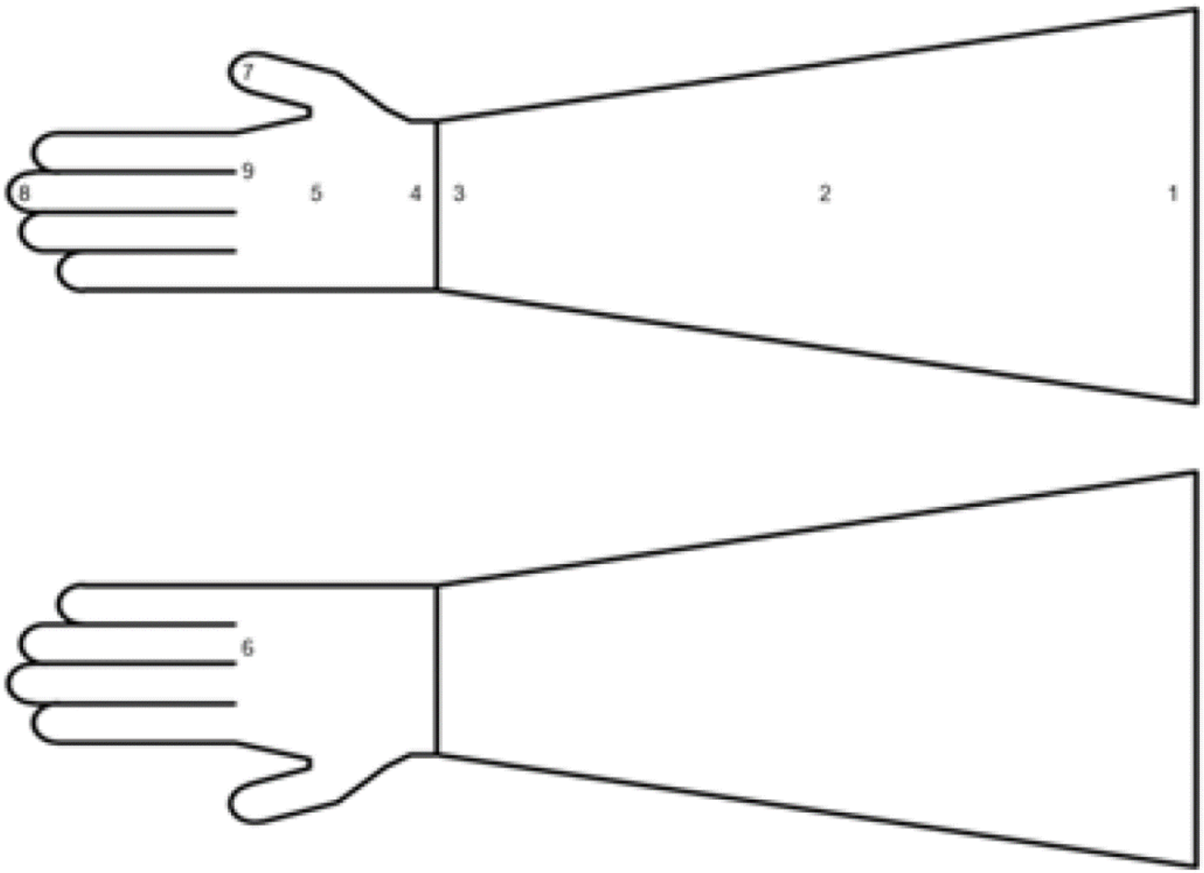
- Parts in direct contact with the product
- Critical points can be:
  - frequent contact areas
  - Fingertips
  - Finger interstices
  - Palm of the hand
- Weak points:
  - Sleeve and shoulder ring connection
  - Connection glove and sleeve
  - Seam (PVC sleeve)
- places which are less easy to stretch



Pictures : google image search

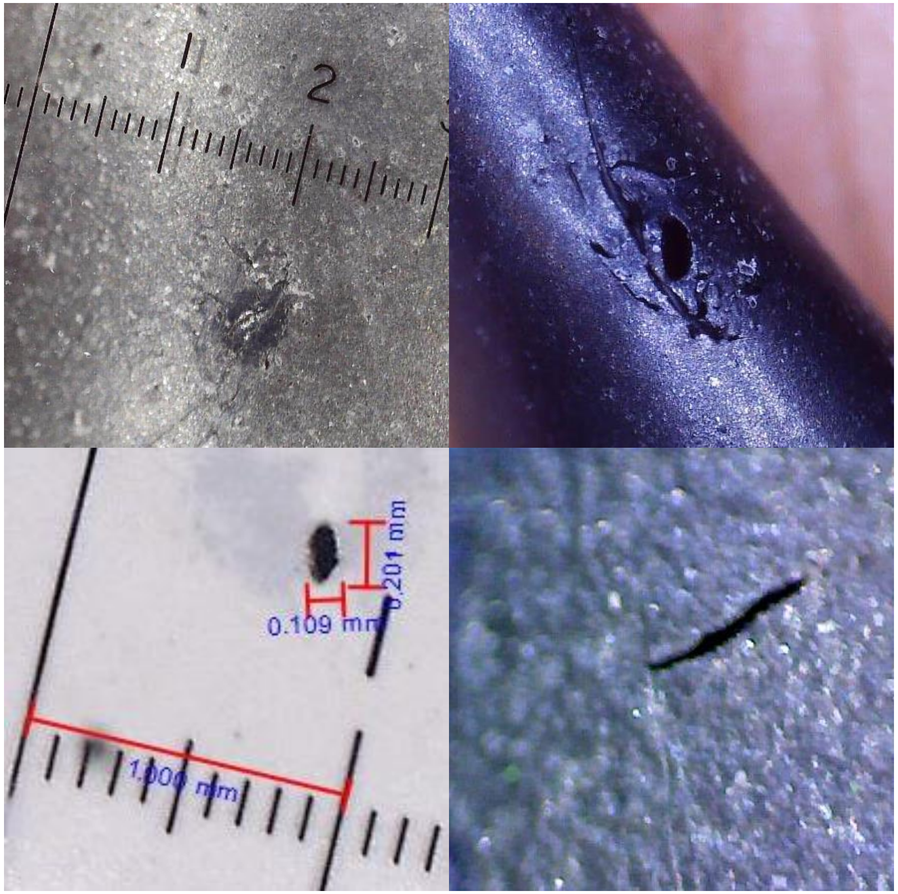
Critical Places of Holes

Critical Places of Holes

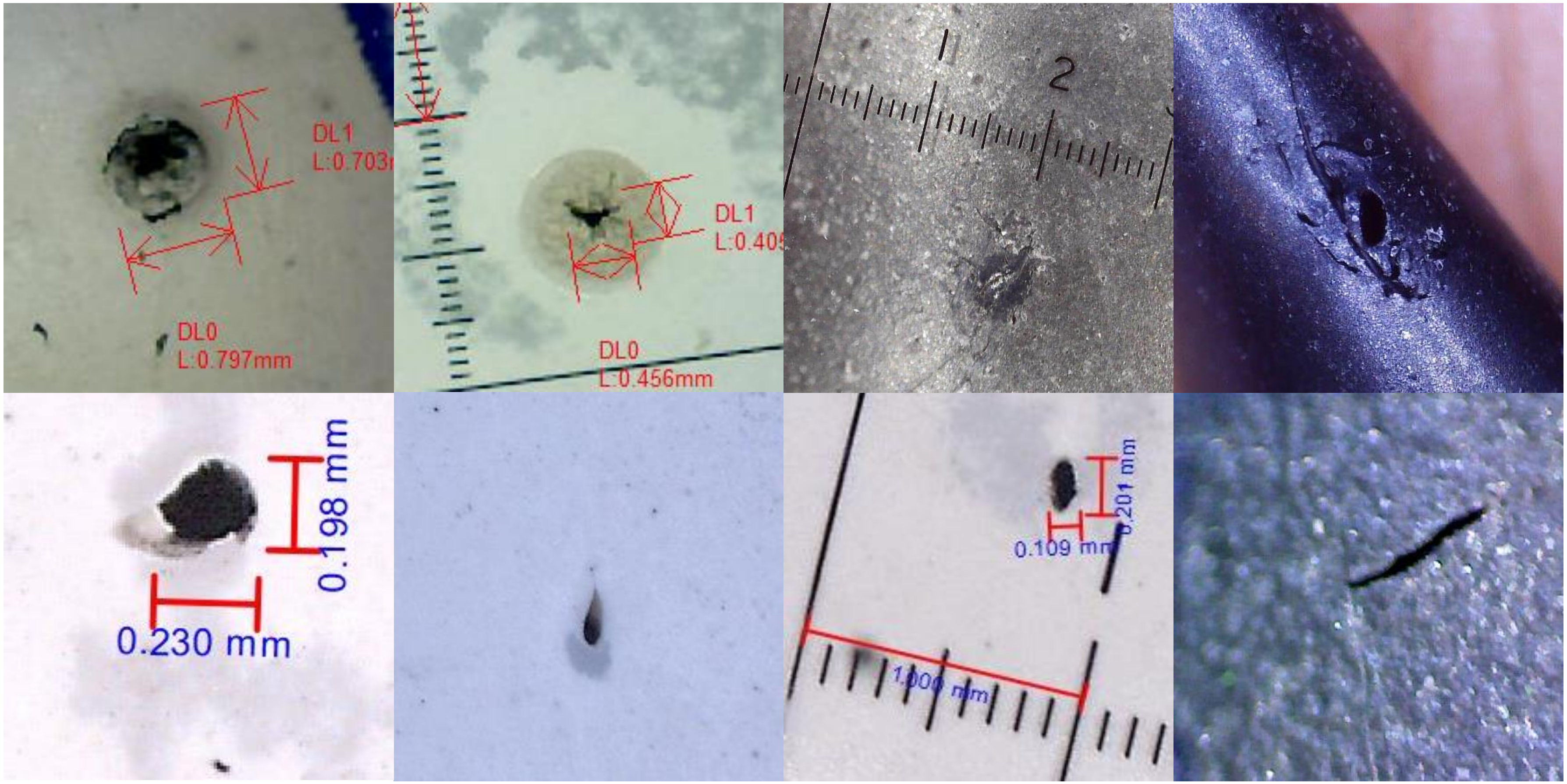


Shapes of Holes

- Holes are difficult to find:
  - Mostly clefts
  - Different orientations
  - Different locations
  - Different sizes
  - Elastic material of the glove
  - Color of the glove
  - Small holes can close again over time



Shapes of Holes



Glove Integrity Test Methods

What about:

… the time between the tests (it is unclear when and how holes occur)?

… small holes which you can not or just hardly see?

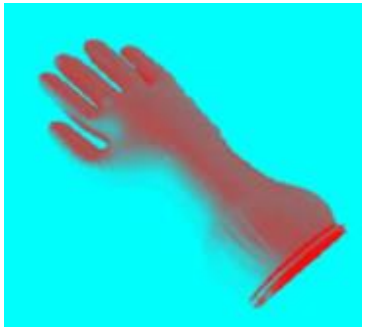
… clafts which overlap/stick together?

… changes in the material due to chemicals and ageing of the glove?

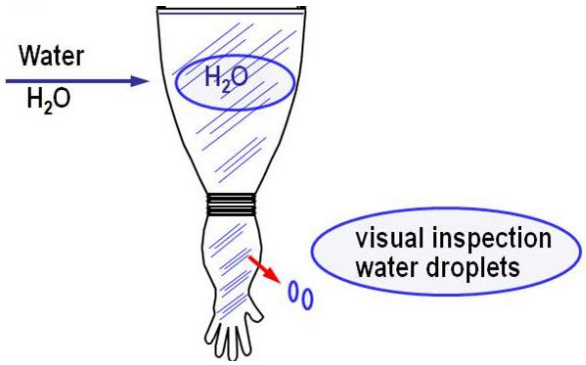
… holes which are difficult to see due to the colour of the material (black glove + very small hole + behind isolator glass)?

Glove Integrity Test Methods

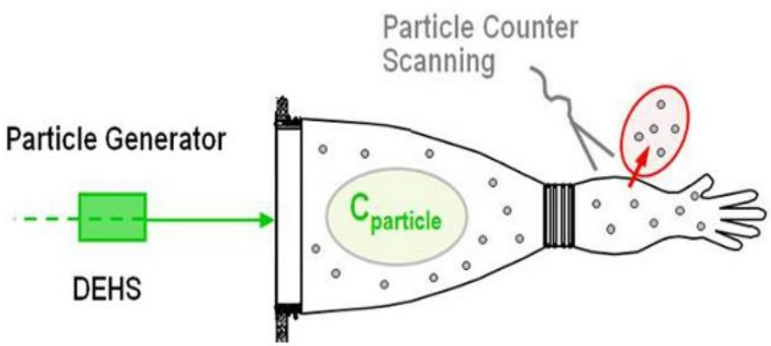
- automatic machine testing:
  - water test
  - particle test
  - ammonia test
  - peracid test
  - helium test
  - flow test
  - pressure drop test
- visual test:
  - untrained operator
  - trained operator



Glove Integrity Test Methods



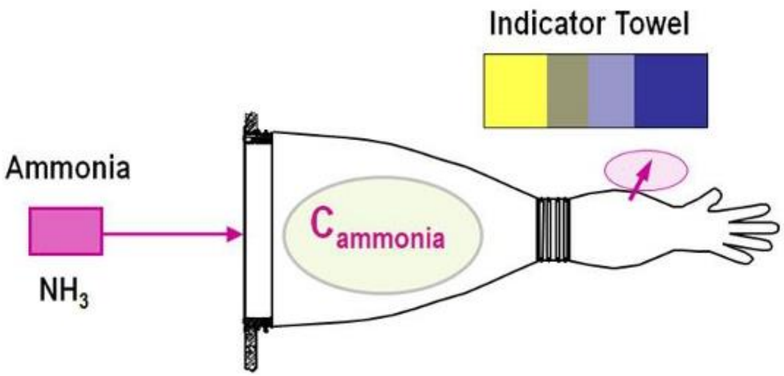
- Water Test
  - 99 % detection rate
  - qualitative method
  - Suitability for routine use: 1

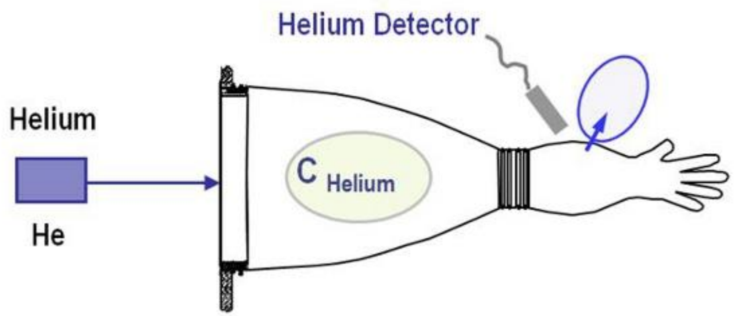


- Particle Test
  - 83 % detection rate
  - qualitative method
  - Suitability for routine use: 1

Source: A. Gessler. How Risky are pinholes in gloves? A rationa appeal for the integrity of gloves for isolators. Vol. 65, No 3, May – June 2011, Page 227 – 241, PDA, Inc. 2011

Glove Integrity Test Methods

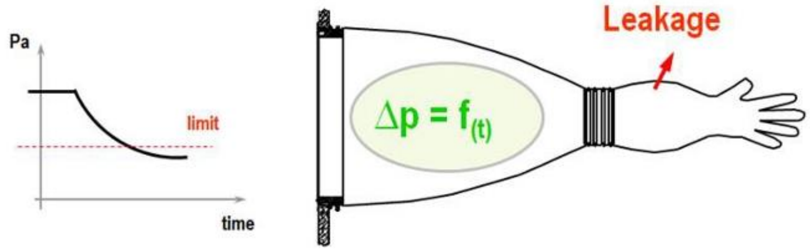




- Diffusional Test
  - 43 – 92 % detection rate
  - qualitative
  - Suitability for routine use: 2

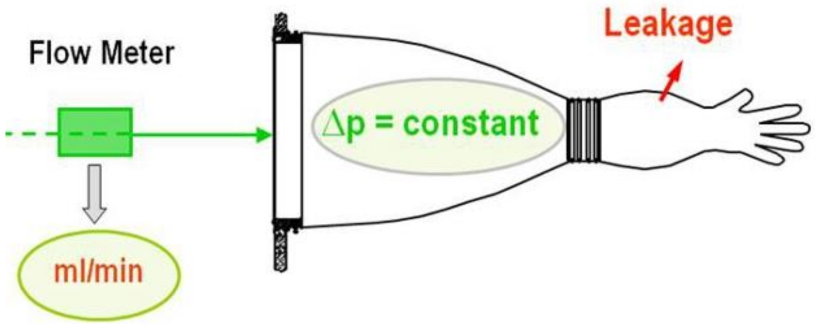
Source: A. Gessler. How Risky are pinholes in gloves? A rationa appeal for the integrity of gloves for isolators. Vol. 65, No 3, May – June 2011, Page 227 – 241, PDA, Inc. 2011

Glove Integrity Test Methods



Pressure drop test

- Measured pressure drop is used to justify the glove integrity
  - 33 – 83 % detection rate
  - quantitative method
  - Suitability for routine use: 9

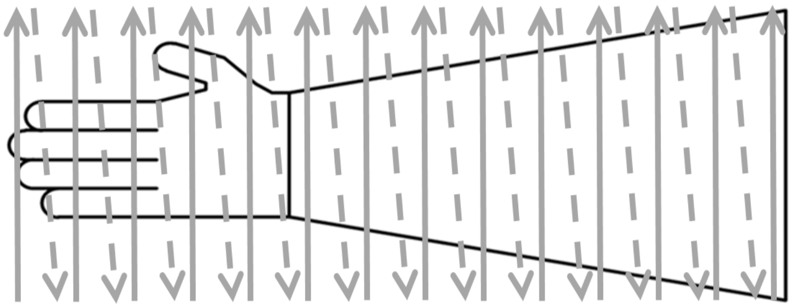


Flow test

- Measured flow is used to justify glove integrity
  - 33 – 92 % detection rate
  - quantitative method
  - Suitability for routine use: 8

Source: A. Gessler. How Risky are pinholes in gloves? A rationa appeal for the integrity of gloves for isolators. Vol. 65, No 3, May – June 2011, Page 227 – 241, PDA, Inc. 2011

Glove Integrity Test Methods



The detection of pinholes is performed visually by:

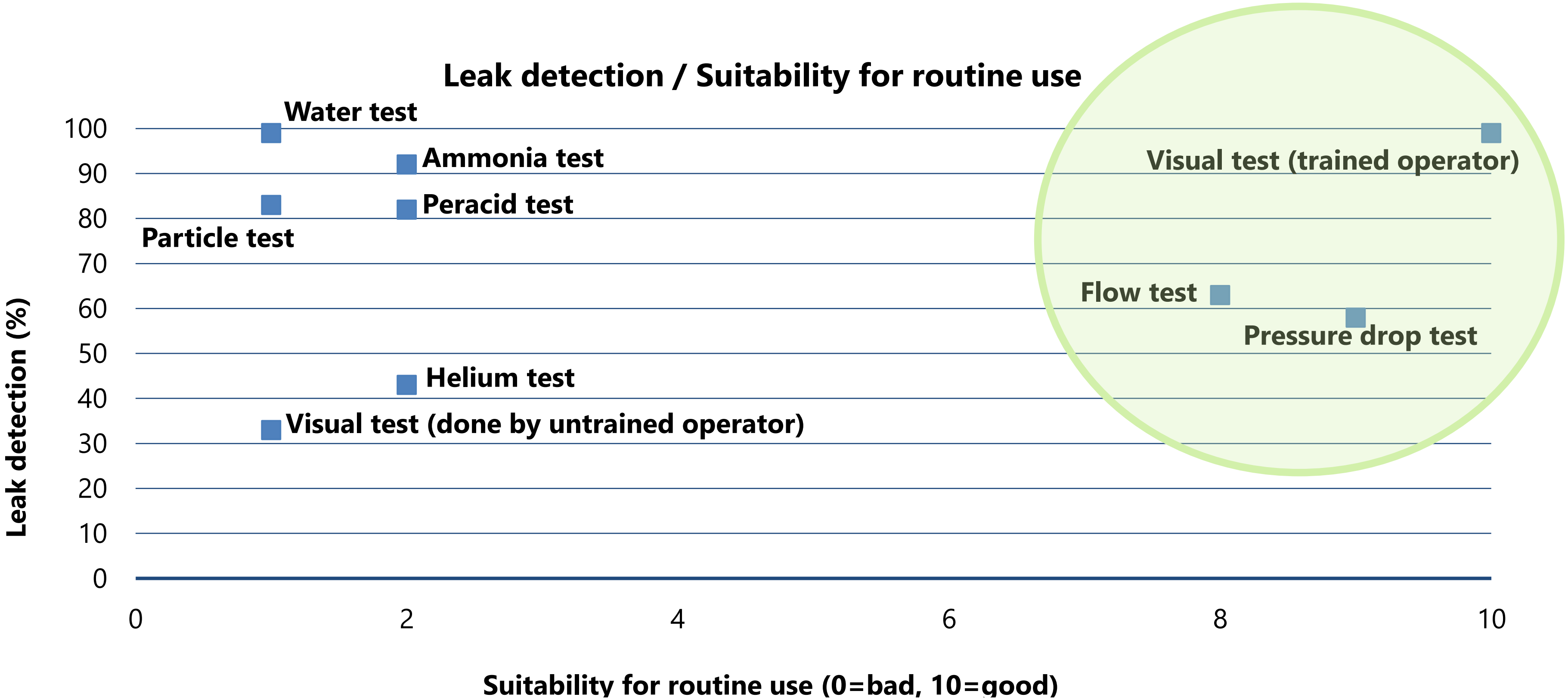
- Trained operator
  - 99 % detection rate
- Not trained operator
  - 33 % detection rate
- Qualitative
- Trained operator
  - Suitability for routine use: 10
- Not trained operator
  - Suitability for routine use: 1

Source: A. Gessler. How Risky are pinholes in gloves? A rationa appeal for the integrity of gloves for isolators. Vol. 65, No 3, May – June 2011, Page 227 – 241, PDA, Inc. 2011

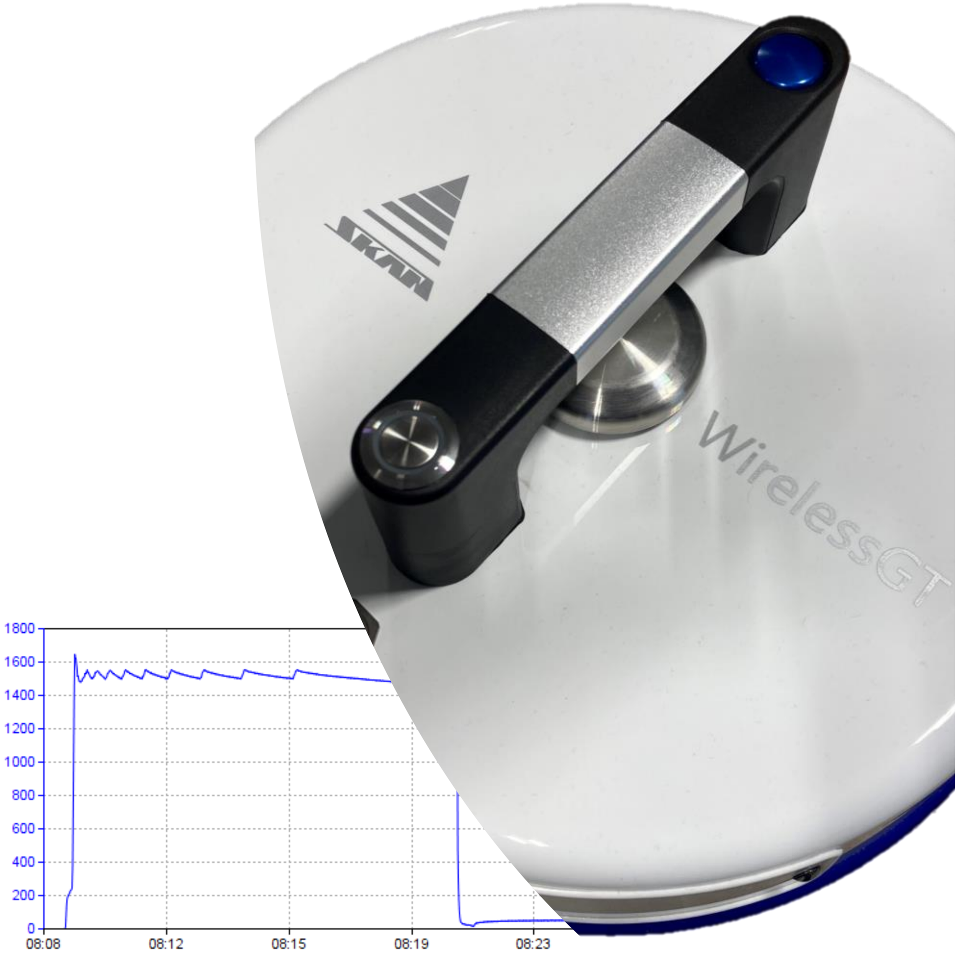
Glove Integrity Test Methods

- **automatic machine testing:**
  - Water test
  - Ammonia test
  - Visual test (trained operator)
  - Peracid test
  - Particle test
  - Flow test
  - Pressure drop test
  - Helium test
  - Visual test (untrained operator)

Glove Integrity Test Methods



Pressure drop test with WGT



Pressure drop test with WGT

- Wireless glove tester (WGT)
  - cGAMP – spezification for pressure drop measurments
  - battery operation
  - no additional hoses
  - monitoring pressure drop for defined time
  - integrity testing in isolator systems
  - suitabel for use in cleanrooms class B,C and D
  - 21 CFR Part 11 compliant and IP54 certified (water and dust tightness)

Pressure drop test with WGT

Pressure drop test with WGT

- Requirements for Execution
  - qualified WirelessGT (incl. software and calibration certificate)
  - isolator glove port (or test stand)
  - gloves (+ sleeves)
  - trained users
  - qualified parameters for each glove type to be measured

Pressure drop test with WGT

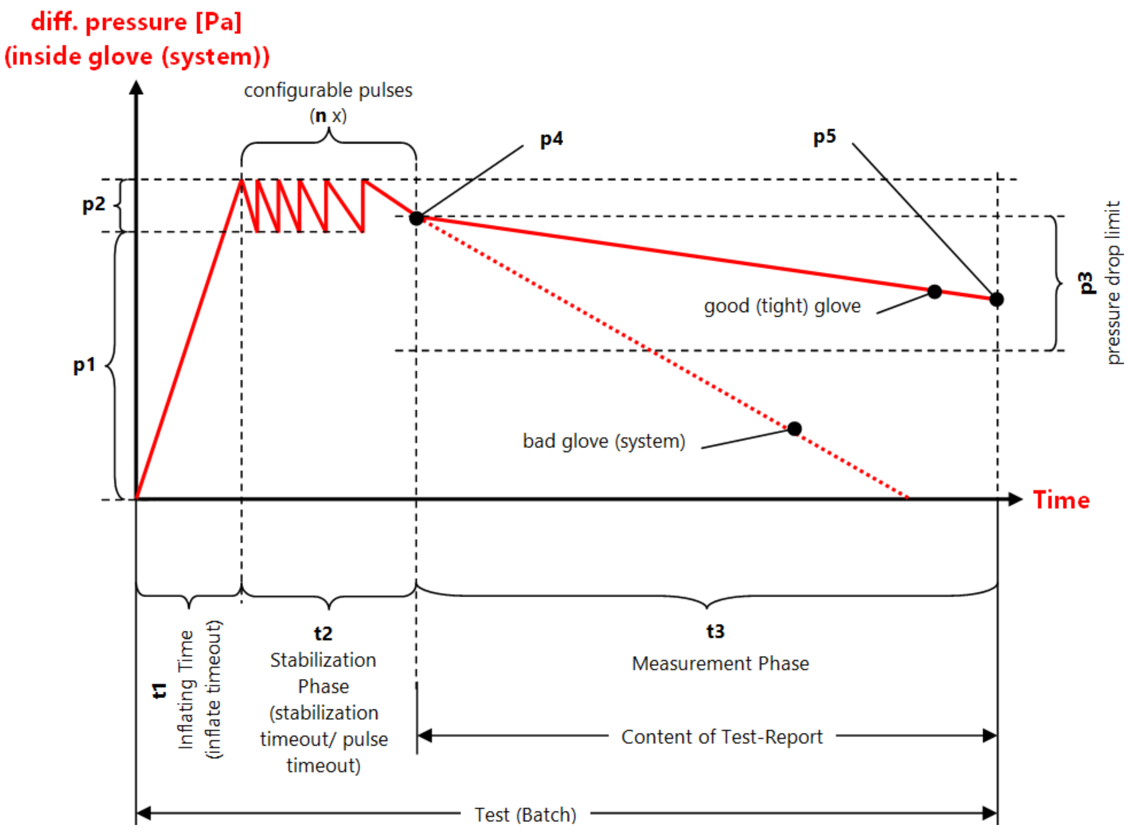
- How to definite the parameters?
  - size of the hole is specified by customer
  - depends on glove material, size and type
  - depends on pinhole size, location, direction and form
  - service from SKAN: parameter development for each glove type
  - service from SKAN: parameter qualification for each parameter set

CONNECTING PEOPLE SCIENCE AND REGULATION®

Pressure drop test with WGT

- Conditions during parameter development:
  - no glove/sleeve is touching anything during the whole test
  - the temperature condition must be stable during the whole test
  - the environmental in a range of +/- 5 K
  - WirelessGT is fitting to the glove port
  - Glove ports are marked with RFID-tags
  - RFID-tags are readable
  - any Wireless Glove Tester is communicating with the software (PC)
  - sealed gloves and gloves with defined pinholes
  - valid for a specific glove and pinhole only

Pressure drop test with WGT



Pressure drop test with WGT

- Paramter Qualification:
  - no validation of WGT
  - done to validate the developed parameter setup of a specific glove type
  - the goal:
    - show a difference between sealed gloves and gloves with reference leaks
  - will be done with leakages on separate locations in the glove
  - for each location the preparation of one glove is necessary
  - parameter qualification is always required.

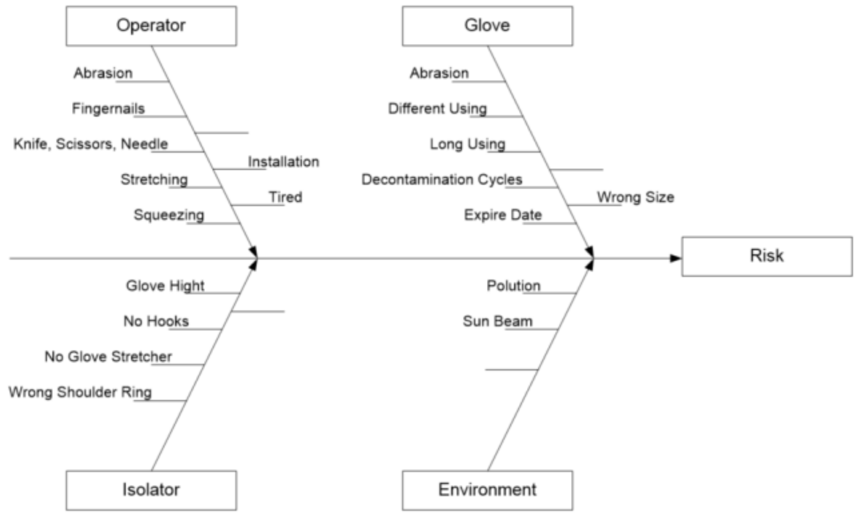
Pressure drop test with WGT

- Summary of parameter development and qualification:
  - information about a pinhole in a glove/sleeve by comparing the pressure drop
  - pinhole is detected when the pressure drop is higher than the pressure drop of a glove with known tightness
  - first: parameter development of the isolator gloves/sleeves
  - Second: qualification of the
  - parameter qualification shows a range of the pressure drop between sealed gloves and leaky gloves
  - parameter qualification should be done on the respective glove ports at the isolator

Glove Risk Management

Glove Risk Management

- **How can the contamination risk trough isolator gloves be minimized?**
- **What is about the isolator contamination status after a pinhole of a certain size occurs?**



Glove Risk Management

Annex 1

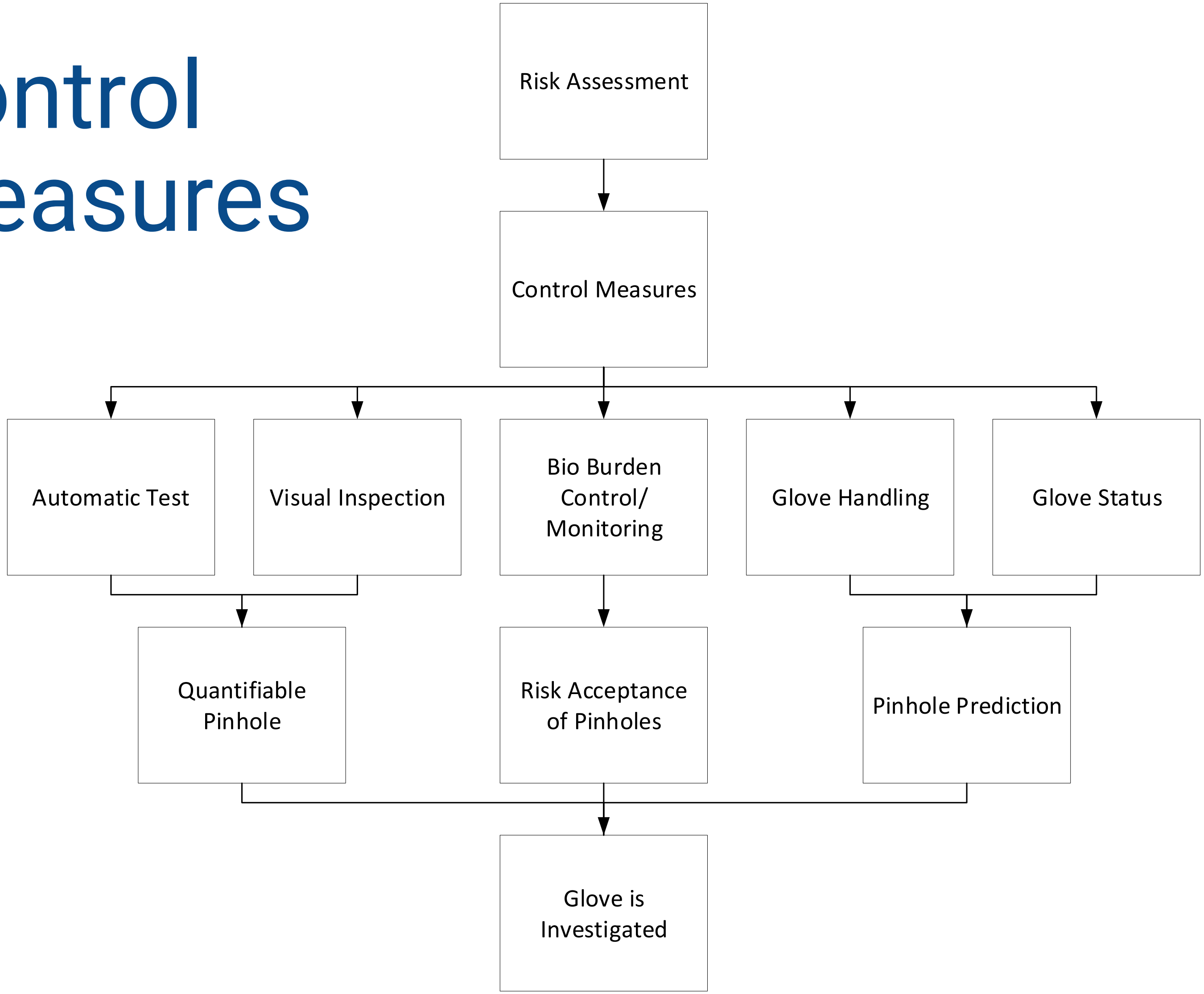
- Contamination Control Strategy:
  - Monitoring measures
  - Measures should be updateable
  - Periodic measures

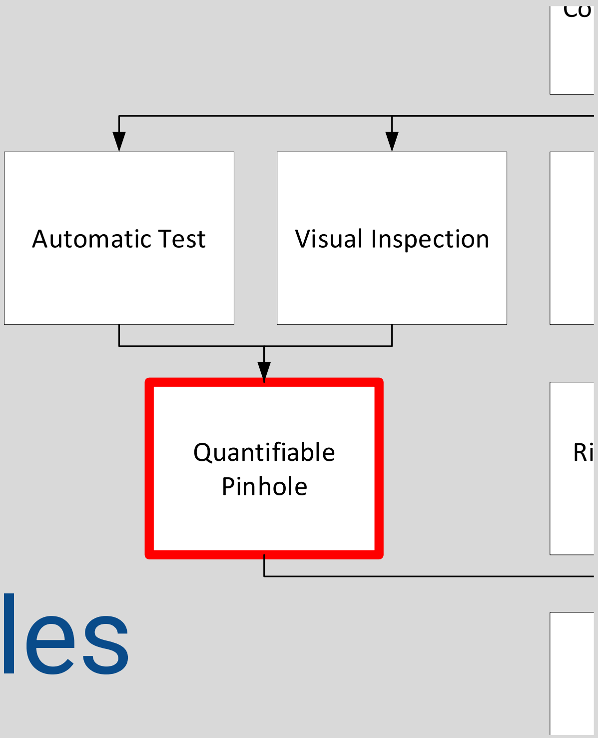
- Leak Test should be present at defined intervals
- Gloves should be disinfected
- Generally glove integrity testing should be performed at a minimum frequency of the beginning and end of each batch or campaign
- Additional glove integrity testing may be necessary depending on the validated campaign length.
- Glove integrity monitoring should include a visual inspection associated with each use and following any manipulation that may affect the integrity of the system.

Task: Control Measures

Describe different control measures which reduces the contmination risks

Control measures





Quantifiable Pinholes

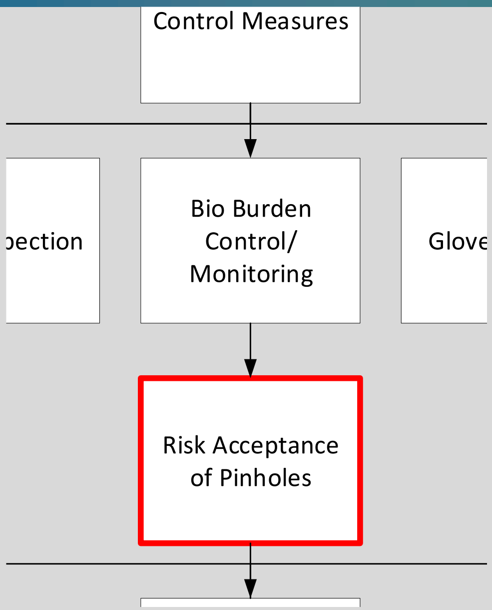
Quantifiable Pinholes

The verification of pinholes of a certain size in isolator gloves. This evidence is given momentary (while a test is actual performed) or over a period (between two tests).

It contains:

– Physical/automatic glove test

– Visual inspection



Risk Acceptance of Pinholes

Risk Acceptance of Pinholes

- Based on «How Risky Are Pinholes in Gloves? A Rational Appeal for the Integrity of Gloves for Isolator» (A. Gessler et al, PDA, Inc. 2011)
- Defined pinhole sizes (approx. 0.4 mm)
- defined pinhole locations
- Defined bioload on gloves (value defined by monitoring)
- No contamination on touched parts inside the isolator

Risk Acceptance of Pinholes

As result:

- ➢Less bio burden
- ➢Small pinholes
- ➢Less contamination risk

Risk Acceptance of Pinholes

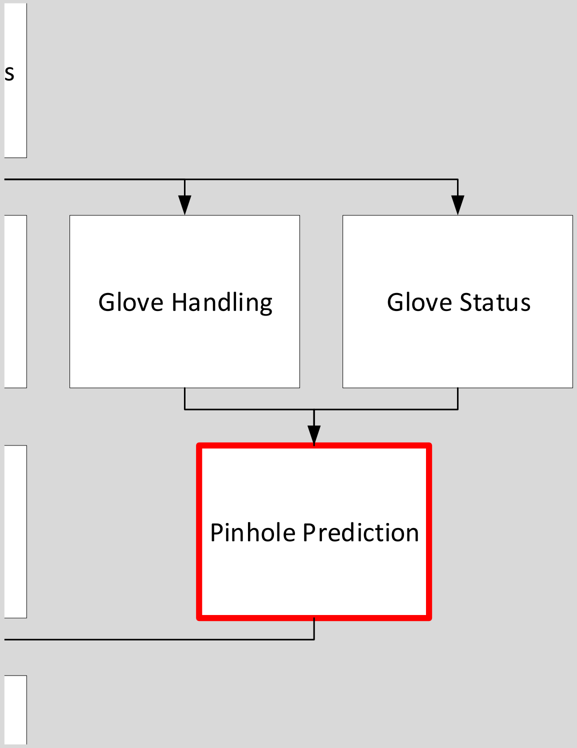
- This control should include:
- Bio burden monitoring on both sides of the glove
- Bio burden control by frequently cleaning of the glove
- Data recording and trend analysis

Risk Acceptance of Pinholes

Benefits:

- Bio burden data of all gloves
- Bio burden control adjustments
- Defined “cleaning status”
- Arguments for decisions after pinhole

Pinhole Prediction



Pinhole Prediction

- General overview about the glove
- Each glove is separated in its task:
  - E.g. maintenance use only or process relevant or for unexpected interventions

- This category is devided in two control measures:
  - Glove status
  - Glove handling

Pinhole Prediction

Glove Status

Pinhole Prediction – Glove Status

- Recording all interventions on each glove
- Define the task of each glove
- Only users with necessary authorization have access to certain gloves (depending on glove task)

Pinhole Prediction – Glove Status

- Task of the glove
- installation date
- expiry date
- who installed the glove
- who uses the glove
- when was the glove used
- glove integrity tests (e. g. amount of pinholes, pinhole locations)
- change intervals
- reason for change
- bio burden

Pinhole Prediction

Glove Handling

Pinhole Prediction – Glove Handling

- Precautionary measures on the isolator
  - Glove port size
  - Glove type
  - Glove port location
  - Type of glove stretchers
  - Positioning of parts inside the isolator

Pinhole Prediction – Glove Handling

- Precautionary measures by the operator
  - Operator training
    - Do not wear rings, jewelries, watches
    - Wash hands, cut fingernails
    - Handling in general
    - Do not touch sharp edges (e. g broken glass) with the glove
    - Avoid over stretching
    - Correct assembling of the glove
    - Touch surfaces as little as possible
  - Defined working hours (tired)
  - Operator monitoring and adjust training courses
  - Report issues
  - Reducing stress

Pinhole Prediction

Benefits:

- Glove exchange frequency can be adjusted – different task, different exchange frequency
- Get info about which glove or user is more related to issues on the glove
- Helps to improve the process on the glove
- Helpful after getting pinholes to make decisions about the isolator contamination status
- Operators a trained
- Operators helping to reduce pinholes in gloves
- Controls are present before pinholes are occur

Risk Minimizing

Example

Risk Minimizing - Example

- Risk matrix
- Risk description/analysis
- Risk rating
- Risk reduction with controls

Risk Minimizing - Example

Risk Matrix

p. of o. \ e. of l.		minimal dirt	dirt	abrasion	leakage	contaminated
		1	2	3	4	5
often	5	C	C	C	C	C
possible	4	B	C	C	C	C
seldom	3	B	C	C	C	C
impossible	2	A	B	C	C	C
virtually impossible	1	A	A	B	B	C

Risk Minimizing - Example

Risk Rating

source	number	hazard	scenario	probability of occurrence	extent of loss	risk
1. Operator	1,01	cutting in the glove (breakage of glas, sharp edge, scissors, knife, needle, etc.)	after cutting in the glove there will be a leakage	5	4	20
	1,02	the glove is overstreched by user	the glove will be destroyed, maybe a leakage	4	4	16
	1,03	abrasion through false handling	the glove lost there properties, it is easier to get a leakage or dirt can be accumulated	3	3	9
	1,04	user has dirty hands	glove will be polluted, after getting a leakage the isolator can be contaminated	5	2	10
	1,05	tired	if the operator is tired, they will do more failures in the glove handling	2	4	8
	1,06	stressed	handling to rude because production must be running	3	4	12
	1,07	glove is wrong installed	the glove dont fit to the assembly = leakage	3	4	12
	1,08	squeezed	there will be a leakage	2	4	8
2. Glove	2,01	the glove is used over a long time	abrasion	4	3	12
	2,02	leakage during process after to long use of the glove	isolator is contaminated	3	5	15
	2,03	the expire date is over	the glove will loss there properties (easier to get leakage)	2	3	6
	2,04	the glove label is not readable	traceability of used glove not given	2	3	6
	2,05	the glove had to many cycles of decontamination	the glove will loss its properties (easier to get leakage)	3	3	9
	2,06	after detection of a leakage it is not asssured that a contamination happened/or occured during the process	the product will be contaminated	2	5	10
	2,07	one or more gloves have a higher abrasion	the gloves have a different abrasion	4	3	12
	2,08	leakage before process	isolator will be contaminated	4	5	20
	2,09	leakage while isolator is closed and decontaminated	isolator will be contaminated	4	5	20
	2,10	It is not sure how big the pinhole is	isolator will be contaminated	4	5	20
	2,11	leakage after process	isolator will be contaminated or is contaminated	4	5	20
3. Isolator	3,01	no hooks	the glove will be squeezed = leakage (position isnt defined)	3	4	12
	3,02	no glove stretcher	the glove will be cover the suface from the bottom by the dekkontamination cycle = isolator contaminated	3	5	15
	3,03	the glove position isnt ergonomically designed	the user will be overstrech the glove	3	4	12
4. Environment	4,01	the glove wasn't measured with contact plates	contaminated isolator	2	5	10
	4,02	polution of the glove (inside isolator)	isolator is contaminated	3	5	15
	4,03	polution of the glove (outside isolator)	isolator can be contaminated after a leakage	5	5	25

Risk Minimizing - Example

source	number	hazard	scenario	probability of occurrence	extent of loss	ri[sk]
1. Operator	1,01	cutting in the glove (breakage of glas, sharp edge, scissors, knife, needle, etc.)	after cutting in the glove there will be a leakage	5	4	20
	1,02	the glove is overstreched by user	the glove will be destroyed, maybe a leakage	4	4	16
	1,03	abrasion through false handling	the glove lost there properties, it is easier to get a leakage or dirt can be accumulated	3	3	9
	1,04	user has dirty hands	glove will be polluted, after getting a leakage the isolator can be contaminated	5	2	10
	1,05	tired	if the operator is tired, they will do more failures in the glove handling	2	4	8
2. Glove	2,05	the glove had to many cycles of decontamination	the glove will loss its properties (easier to get leakage)	3	3	9
	2,06	after detection of a leakage it is not asssured that a contamination happened/or occured during the process	the product will be contaminated	2	5	10
	2,07	one or more gloves have a higher abrasion	the gloves have a different abrasion	4	3	12
3. Isolator	3,01	no hooks	the glove will be squeezed = leakage (position isnt defined)	3	4	12
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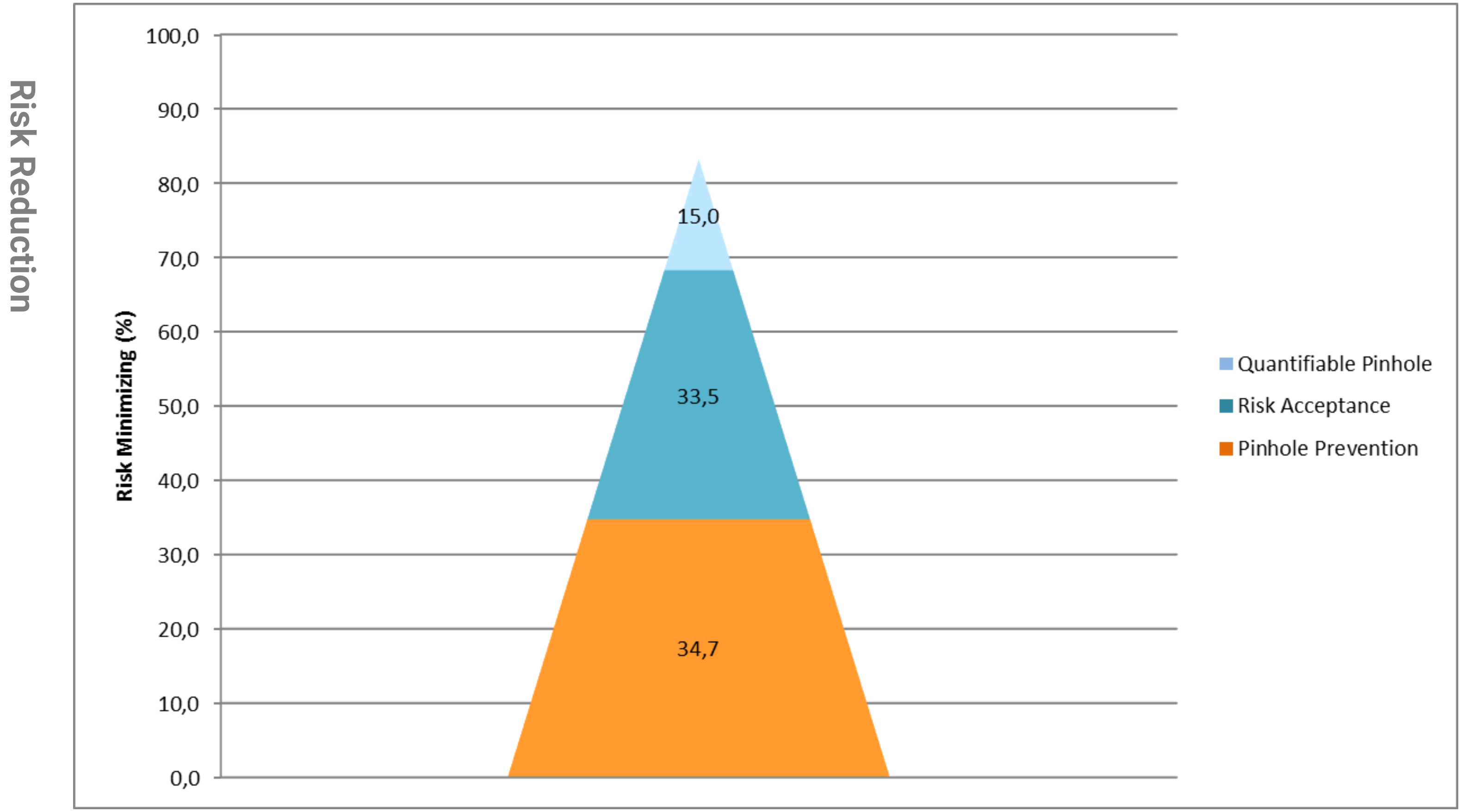
	3,03	the glove position isnt ergonomically designed	the user will be overstrech the glove	3	4	12

Risk Minimizing - Example



Conclusion

- To reduce the contamination risk in isolators:
  - Gloves (glove location) shoulb be known and described by its different task on the isolator
  - Not the leak test alone reduces the risk, but is a important part on the whole process of risk reduction
  - Controls should be present and have to fulfill as minimum the following categories:
    - Pinhole prediction
    - Risk acceptance of pinholes
    - Quantifiable Pinholes
  - All control measures should be adjustable after a monitoring over a long period
- To have a answer after a pinhole occurs:
  - Monitoring data
  - Trending analysis
  - Active controls

Summary

- Glove Requirements
- Glove Types
- Selecting appropriate glove
- Glove Substitution
- Glove contamination Risks
  - Sources
  - Holes (critical places & shapes)
  - Test methods
  - Risk Management
  - Control Measures
    - Quantifiable Pinholes
    - Risk acceptance
    - Pinhole prediction

Thank You for Your Attention!

Any Questions?

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