



Tours // France
14 & 15 juin 2023



In-use barrier integrity : what's the microbial incidence of glove's pin holes on production isolators ?

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Context



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Isolator: high degree of protection in the pharmaceutical industry

Gloves: main sources of contamination:

integrity: major problem

CHALLENGE

Pharmaceutical manufacturers should
define their own standard operating procedures
for glove testing

 GROUPE
ICARE



Scientific context

How Risky Are Pinholes in Gloves? A Rational Appeal for the Integrity of Gloves for Isolators

Angela Gesler, Alexandra Stärk, Volker Sigwart, et al.

PDA J Pharm Sci and Tech 2011, 85 227-241
Access the most recent version at doi:10.5731/pdajpst.2011.00716



Evaluate the potential risks of microbial contamination and migration through glove pinholes (0.4 to 0.8 mm)

Material: Chlorosulfonated Polyethylene: CSM

Suspension of Brevundimonas diminuta

Even if a high bioburden on the internal face of the defective gloves represents a risk of contamination for the product as well as for the interior of the isolator (Grade A), the bioburden found on these gloves generally presents low concentrations < 20 CFU.cm⁻².

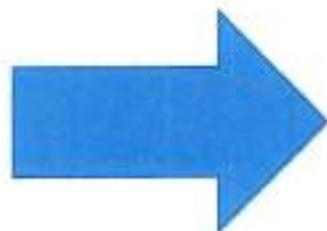
Scientific context

Microbiological study on the management of holes in gloves for isolators

by members of



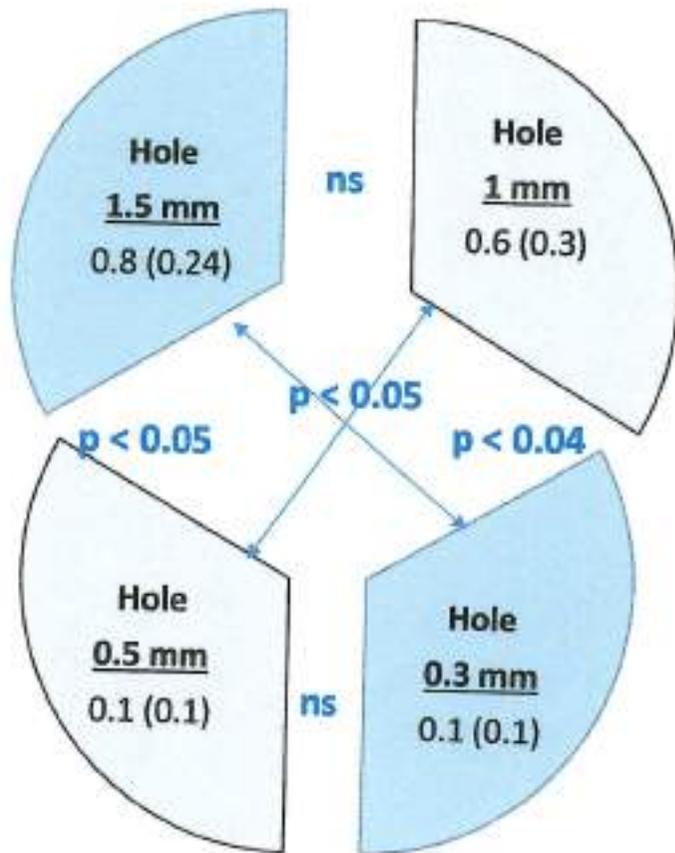
La Vague (2022)



Subjecting isolator gloves to an aerosol containing a *Geobacillus stearothermophilus* microorganism to check their tightness : 1 MP (CSM); 3 hole sizes (1, 2 and 3 mm); fingertip ATCC 7953 (adjusted to 10^6 CFU.ml⁻¹) nebulized

Under a size of hole about 0.6 mm, defective gloves have a low probability to represent a microbiological risk.

Effect of hole size on 10 gloves



UFC/sampling



From 0.5 mm to a hole of 0.3 mm, no difference in passage of *S. aureus*

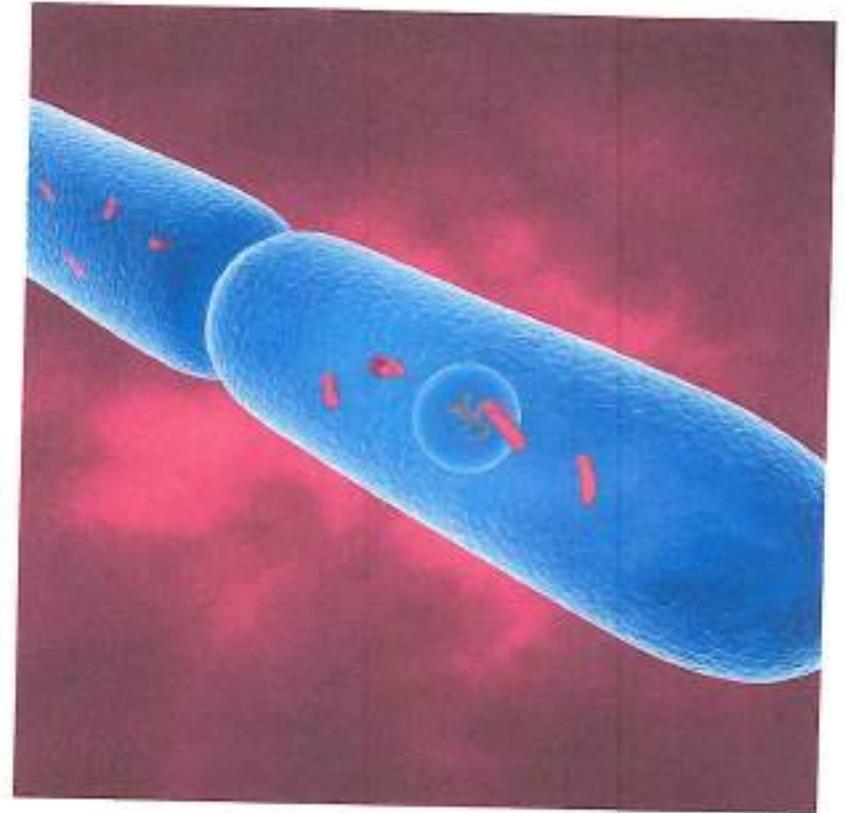
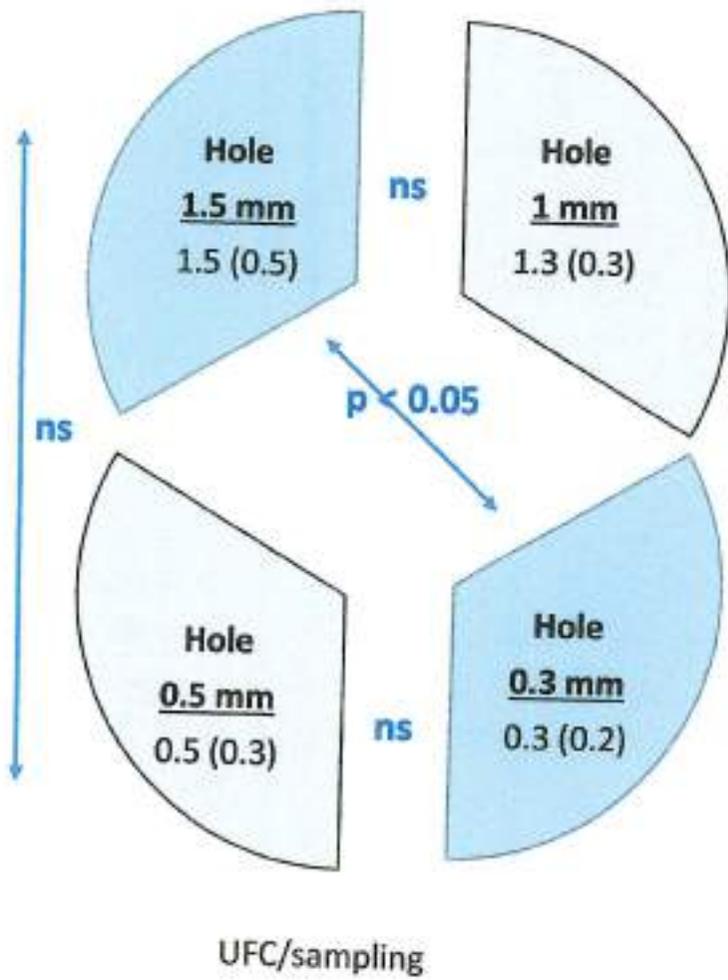
Bacillus subtilis

Concentration inoculum (UFC/inoculum)	Surface sampling (UFC/assay)	Air Sampling (UFC/assay)
Hole 1.5 mm: $7.4 \cdot 10^7$ Hole 1 mm: $6.5 \cdot 10^7$ Hole 0.5 mm: $8.6 \cdot 10^7$ Hole 0.3 mm: $7.8 \cdot 10^7$	Hole 1.5 mm: 5.7 (0.7) Hole 1 mm: 1.4 (0.5) Hole 0.5 mm: 0.6 (0.2) Hole 0.3 mm: 0.1 (0.1) ***: $p < 0.001$ (1 vs 1.5; 1.5 vs 0.3; 1.5 vs 0.5)	Hole 1.5 mm: 174.0 (31.5) Hole 1 mm: 73.9 (13.7) Hole 0.5 mm: 13.3 (3.8) Hole 0.3 mm: 0.4 (0.3) ** : $p < 0.01$, 1 vs 1.5 $p < 0.001$ 0.5 vs 0.3; 1.5 vs 0.3; 1.5 vs 0.5
Negative Control: $1.0 \cdot 10^8$	Negative Control : 0	Negative Control : 0

From 0.5 mm to a 0.3 mm hole

- no statistical difference in surface deposition
- statistical difference in air sampling ($p < 0.001$)

Effect of hole size on 10 gloves



From 0.5 mm to a hole of 0.3 mm, no difference in passage of *B. subtilis*

DISCUSSION

Gloves: effective barrier to microbial contamination

- Below 0.4 mm (Gessler et al, 2011)
Suspension of Brevundimonas diminuta



Preliminary study

Microbial contamination increases from a hole size of 0.6 mm
Suspension of Geothermophilus stearothermophilus

In this study

- 0.5 mm is the critical hole size above which contamination increases



Practical considerations

Class B

Air : 10 UFC.m⁻³

Nebulization 1.0.10⁷ in 0.5m³ → 2.0.10⁷ in 1m³

Class C

Air : 100 UFC.m⁻³

Class D

Air : 200 UFC.m⁻³

	<i>B. subtilis</i> nébulization 2.0.10 ⁷ UFC/m ³				<i>S. aureus</i> nébulization 2.0.10 ⁷ UFC/m ³			
	Experimen- tal results	Estimated colonies for B class	Estimated colonies for C class	Estimated colonies for D class	Experimen- tal results	Estimated colonies for B class	Estimated colonies for C class	Estimated colonies for D class
1.5mm	174	8.7.10 ⁻⁵	8.7.10 ⁻⁴	1.7.10 ⁻³	33.0	1.7.10 ⁻⁵	1.7.10 ⁻⁴	3.3.10 ⁻⁴
1.0mm	73.9	3.7.10 ⁻⁵	3.7.10 ⁻⁴	7.4.10 ⁻⁴	34.4	1.7.10 ⁻⁵	1.7.10 ⁻⁴	3.4.10 ⁻⁴
0.5mm	13.3	6.7.10 ⁻⁶	6.7.10 ⁻⁵	1.3.10 ⁻⁴	0.6	3.0.10 ⁻⁷	3.0.10 ⁻⁶	6.0.10 ⁻⁶
0.3mm	0.4	2.0.10 ⁻⁷	2.0.10 ⁻⁶	4.0.10 ⁻⁵	0	/	/	/

Thank you for your attention



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