

Case of non-compliant eye drops: investigation on non invisible particles

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CONTEXT



2022: 2.9.53 Particulate Contamination: Non-visible particles in non-injectable liquid preparations
2025: Ophthalmic Preparations (General Monographs)

Production of Insulin Eye Drops: Control of non visible particles

NON-COMPLIANT

OBJECTIVE

Determine the cause of this non compliance

MATERIALS AND METHODS

1 Identifying Causes: The 5M (Workforce, Materials, Methods, Environment, and Materials)

2 Light-blocking particle counter: HIAC 9703+

4 measurements of 5 mL per sample

Raw material, Sterile syringes (10 – 20 – 30 – 60 mL)



DISCUSSION - CONCLUSION

Modification of compounding protocol

Exclude 20 mL syringes.

Medical device vigilance

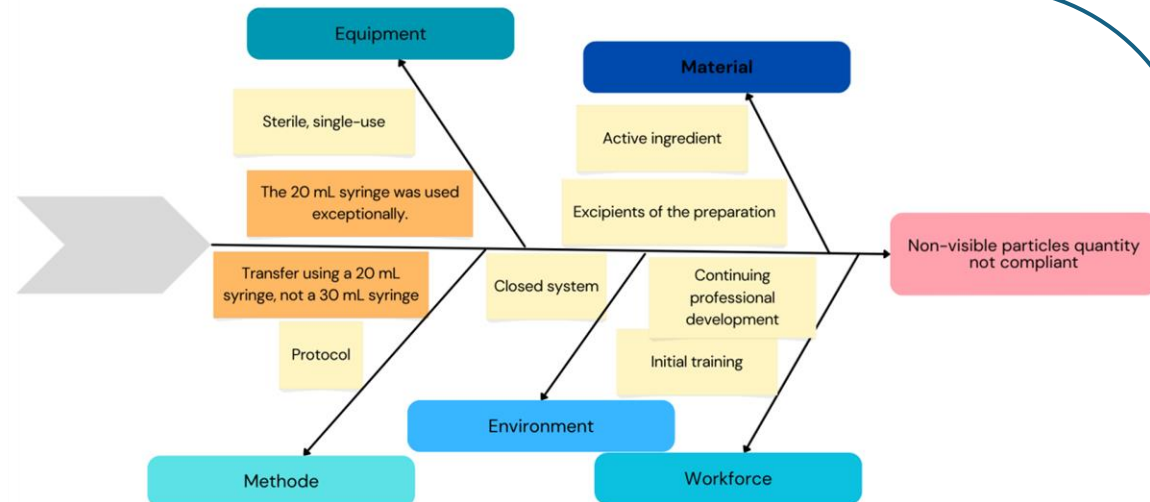
The silicone oil distorts the light-blocking inspection.
Perform the inspection under a microscope.

- Documented interaction between silicone oil and proteins/antibodies
- Quantity of silicone oil administered with the preparation?

RESULTS

1

Identifying causes: method and equipment



2

Material and equipment: Counting non visible particles in eye drops

Material		
Excipient	Particles > 10 µm /mL	Particles > 25 µm /mL
Artificial tears	638 ± 100	12 ± 9
Insulin	393 ± 33	53 ± 16

Equipment		
SUPPLIER A		
Syringe capacity (n=5)	Particles > 10 µm /mL	Particles > 25 µm /mL
10 mL	117 ± 11	1 ± 1
30 mL	37 ± 8	1 ± 1
60 mL	6 ± 3	1 ± 1

SUPPLIER B

Equipment		
Syringe 20 mL (n = 5)		
	Particles > 10 µm /mL	Particles > 25 µm /mL
BATCH A	3098 ± 118	36 ± 17
BATCH B	1729 ± 725	14 ± 2
BATCH C	2109 ± 335	28 ± 7

Particles >10 µm : < 1000/mL
Particules > 25 µm : < 100/mL

COMPLIANT

Particles >10 µm : > 1000/mL
Particles > 25 µm : < 100/mL

NON-COMPLIANT

The source of the particulate contamination is 20 mL syringes