

Development and validation of a sterility test method by membrane filtration of ceftazidime 5% eye drops

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Introduction

The sterility test of ceftazidime 5% eye drops prepared in our unit is currently performed by **direct seeding** on Trypticase-Soja and Sabouraud agar. According to the European Pharmacopoeia (EP), the **membrane filtration method** is chosen as soon as the nature of the product allows it.

→ **Objective = To develop and validate the sterility test by membrane filtration of ceftazidime 5% eye drops.**

Material and Method

Membrane filtration steps

- Pre-wetting of the membrane
- Filtration of the eye drops
- Rinsing of the membrane
- Culture and incubation of the membrane



Bibliographic research
 +
 Exchange with different centers

Which parameters to test?
 → Development of 3 methods

Testing of each method on 3 eye drops with a *Pseudomonas aeruginosa* strain (Bioball®)

↘ Determination of optimal parameters

Validation of the method according to the EP
 (applicability test by 3 operators)



Results

Parameters to test ?

- Flushing fluid volumes
 - Pump speeds
 - Types of flushing fluid
 - Types of membrane
- Fixed according to supplier's recommendations
- Peptone water (F1)
 Peptone water + polysorbate 80 (F2)
- Cellulose Ester (CE)
 Polyvinylidene fluoride (PVDF)



Test Method	Eye drops			Positive control
	N°1	N°2	N°3	
1 = F1 + EC	+	-	-	Growth of <i>P.aeruginosa</i>
2 = F1 + PVDF	+	+	+	Growth of <i>P.aeruginosa</i>
3 = F2 + PVDF	+	+	+	Growth of <i>P.aeruginosa</i>

Method 3 is chosen for method validation

↓
 Microbial growth comparable to positive controls at D5 for each of the 6 microbial strains and for each operator.

Discussion and conclusion

- Test (3) is preferred because the **polysorbate 80, surfactant, favors the elimination of antimicrobial activity** and the thinner **PVDF membrane** (120µm) than the EC one (150µm) **reduces the risk of ceftazidime adsorption**. This risk is also reduced thanks to the **pre-wetting which saturates the pores** of the membrane and to the **rapid filtration of the eye drops**.
- The method is **validated** and will be used routinely to control the sterility of ceftazidime 5% eye drops.
- The next steps are the realization of a **microbiological stability study** of ceftazidime 5% eye drops and the **development of the method on other reinforced antibiotic eye drops**.