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## Context

## State of play



- Production of 21,000 bags of anti-cancer drugs/year
- Maximum storage time of the bags : 7 days
- Préparation on D-1 of the administration, in case of deprogramming, reallocation of the preparation if physico-chemical stability:
  - 2,9 % ddeprogramming of which 15% of preparation are reallocated

## Recommendations

- USP 797:** Conservation outside of any sterility testing for preparation:
- European Guidelines 2011** on Stability Studies for Cancer Drugs<sup>1</sup> : recommends sterility assessment in case of long-term conservation and for bacterial growth-promotion preparations (proteins)

Ambient temperature	+2°C à 8°C
48 hours	14 days

## Rationale

- Rituximab
- Good physico-chemical stability (28 days<sup>2</sup>) in 0,9% NaCl
  - Protein**

No inhibitory effect of Rituximab according to the literature<sup>3,4</sup>

## Objective

↑ of the maximum shelf life to 28 days

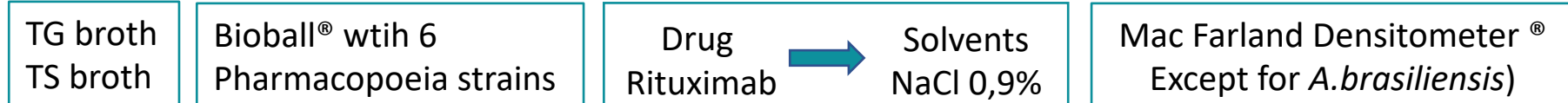
↑ in the reallocation rate

Reduction in the number of bags destroyed + Economic gain

## Material and method



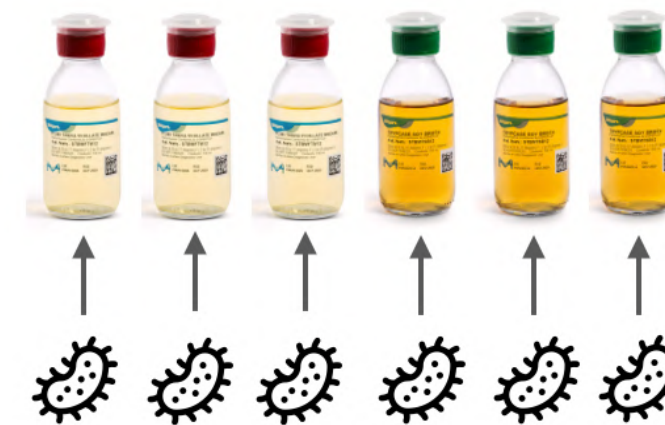
## Material



## Culture characteristics of European Pharmacopoeia strains for microbiological stability study

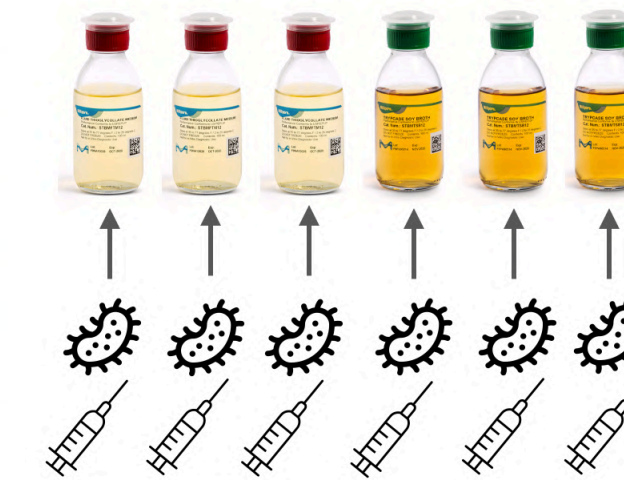
Pharmacopoeia 9.0 strains	Solid growth medium	Liquid growth medium	Incubation time (D)	Incubation temperature (°C)
<i>S.aureus</i> ATCC 6538	Blood agar	Thioglycolate (TG)	3	35
<i>P.aeruginosa</i> ATCC 9027	Blood agar	Thioglycolate (TG)	3	35
<i>C.Sporogenes</i> ATCC 19404	Blood agar	Thioglycolate (TG)	3	35
<i>B.subtilis</i> ATCC 6633	Blood agar	Triptycase soya (TS)	3	35
<i>C.albicans</i> ATCC 10231	Chromagar plate	Triptycase soya (TS)	5	35
<i>A.niger</i> ATCC 16404	Chromagar plate	Triptycase soya (TS)	5	31

## Fertility testing

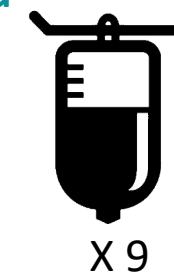


**Method:** 100µL of a 10<sup>3</sup> UFC/mL suspension of each strain added to the broths  
**Objective:** to test the fertility of the broths = **positive control (TP)**

## Testing the applicability of the method



**Method:** similar to sterility test + 10 mL of Rituximab (4mg/mL): performed in triplicate  
**Objective:** to test the absence of inhibitory character of the drug



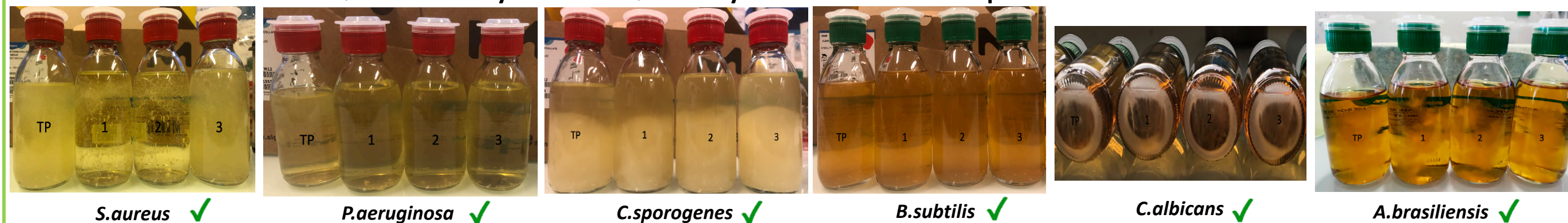
## Stérility test

**D0:** 3 bags: 10 mL of drug in 2 TS and 2 TG  
**D 14 and D 28 :** same with different bags

**Method:** 9 bags of Rituximab (1mg/mL) At D0: addition of 10 mL in 2 TG and 2 TS of each of 3 bags → **incubation 14 days. Operation repeated at D14 and D28, testing 3 new bags each time**  
**Objective:** to test for the absence of bacterial growth

## Results

**Test of applicability of the method: comparable growth between TP and broths containing Rituximab**  
 → no inhibitory character → sterility test can therefore be performed



## Results of the reading at Mac Farland

Day	MO	TP (McF)	N°1 (McF)	N°2 (McF)	N°3 (McF)
D3	<i>P. aeruginosa</i>	0,9	0,9	0,8	0,8
	<i>S. aureus</i>	4,4	3,6	3,6	4,4
	<i>C.sporogenes</i>	5,5	6,5	6,1	6,0
	<i>B.subtilis</i>	0,9	0,9	1,0	0,9
D5	<i>C. albicans</i>	3,9	3,7	3,7	3,7

## Result of the sterility test

Absence of turbidity in all pockets tested

## Conclusion

Lack of inhibitory character

Conducting the sterility test

No bacterial growth

Extension of the shelf of Rituximab bags

## Prospects

Study only representative of one day of production → **implementation of a routine control**

**Extrapolation** of results to other monoclonal antibodies ? → monoclonal antibodies with similar profiles and formulations can be extrapolated