



## Introduction

In some severe infections, the dose of **vancomycin** may be 60 mg/kg/day. By manufacturers, the final concentration of vancomycin solutions should not exceed 10 mg/mL.



Body weight : 65 kg  
Daily dose of vancomycin : 4 g  
Dilution in 400 mL of solvent

For patients requiring fluid restrictions, this volume is not adequate.

## Objectives

1. **Impact of an electric syringe pump** on the physical stability
2. **Physicochemical stability studies of vancomycin solutions**
  - **Concentrations** : 62.5 and 83.3 mg/mL
  - **Container**: polypropylene syringes
  - **Solvent**: sodium chloride 0.9% (NaCl 0.9%) - glucose 5 % (G5%)
  - **Storage** : 20-25°C unprotected from light
  - **Analysis** after preparation, and after 6, 24 and 48 hours.

## Materials and Method

### Chemical stability

#### ① RP-HPLC with DAD detector at 280 nm

- **Column**: C18 LiChrospher® 12.5 cm, particle size=5 µm at 30°C
- **Mobile phase**: 8 % of acetonitrile and 92% of KH<sub>2</sub>PO<sub>4</sub> buffer at 0.1M adjusted at pH 3.5 with orthophosphoric acid 85%
- **Flow rate** at 1.5 mL/min
- **Injector temperature** at 15°C
- **Injection volume**: 10 µL

### Physical stability

- **Visual examination** : change of colour, precipitation, gaz formation

#### ② Validation of the method as recommended by ICH Q2(R1)

- **Forced degradation**

Acidic degradation	Alkaline degradation	Heat degradation
HCl 1.0M 16 hours	NaOH 1.0M 60 min	80°C 4 hours

- **Linearity** : standard curve with 5 points : 50-150 µg/mL
- **Repeatability and intermediate precision**

#### ③ pH measurement (Bioblock Scientific pH meter)

- **Subvisual examination** : turbidimetry by spectrophotometry at 350, 410 and 550 nm ( Safas Monaco UV m<sup>2</sup>)

➔ 3 syringes for each condition (S1 – S2 – S3)

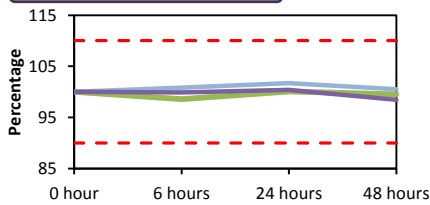
## Results

#### ① Validation : RP-HPLC method

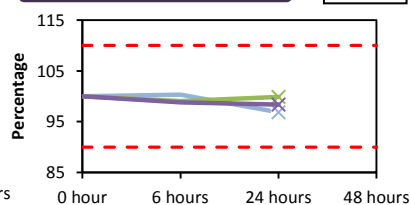
- **Linearity** : R<sup>2</sup>>0.999
- **Repeatability and intermediate precision** : CV<2.5 %

#### ② Chemical stability –HPLC

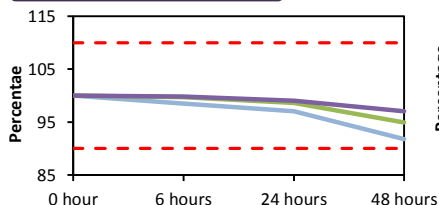
62.5 mg/ mL – NaCl 0.9%



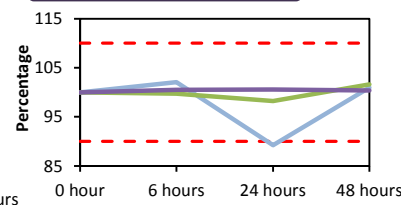
83.3 mg/ mL – NaCl 0.9%



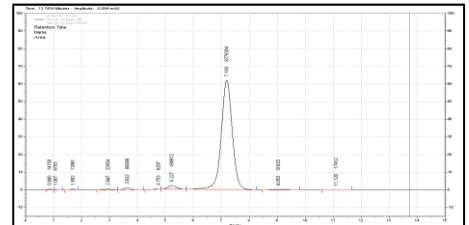
62.5 mg/ mL – G5%



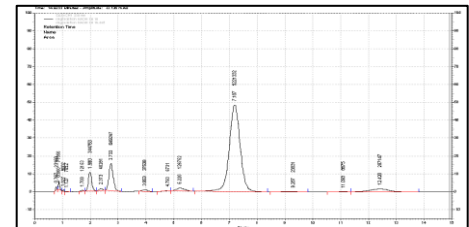
83.3 mg/ mL – G5%



#### ▪ Stability indicating capacity



Chromatogram of vancomycin 100 µg/mL without stressed conditions.



Chromatogram of vancomycin 100 µg/mL after alkaline stressed conditions (NaOH 1.0 M, 1h)

#### pH measurement : ③ Physical stability

- no modification**
  - No impact of the action of an electric syringe pump
  - Visual aspect : precipitation for solutions at 83,3 mg/mL after 48 hours.
- Sub-visual aspect : no modification

## Conclusion

Vancomycin at **62.5 mg/mL** and **83.3 mg/mL** in G5%



Stable for **48 hours at 25°C**  
Unprotected from light



For high concentrations of vancomycin, G5% as solvent is recommended