Feasibility study of bacterial endotoxin testing in hospital preparations of 10% glycerol / 5% fructose

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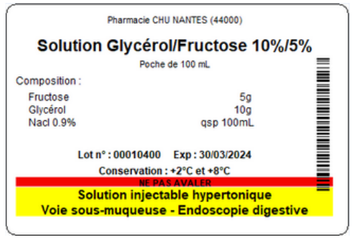
Introduction

In 2023, we initiated the production of injectable **glycerol 10% /fructose 5% (GF)** solutions upon the request of gastroenterologists for the excision of intestinal polyps through interventional endoscopy



The current quality controls include:
- ✓ Sodium determination by ICP-OES*
- ✓ Osmolarity measurement
- ✓ pH measurement
- ✓ Sterility test by membrane filtration (Steritest)

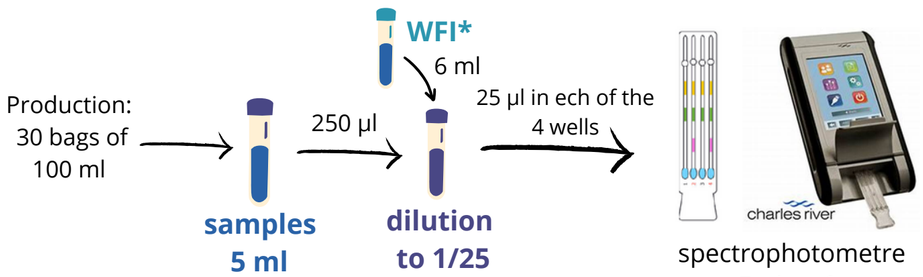
*ICP-AES : Induyctively coupled plasma - optic emission spectroscopy

Objective: Study the feasibility of integrating bacterial endotoxin (EB) testing during routine production to complement quality control of hospital preparation of glycerol/fructose.

Material & Methods

Method D : kinetic colorimetry of the European pharmacopoeia (PE)
(monograph 2.6.14)

- Determination of the **maximale significative dilution (MSD)**
- Determination of the **endotoxin limit concentration (LE)**



spectrophotometre
Endosafe
& dedicated cartridge

*WFI : Water for Injection

Selection of samples → explore **repeatability**
- 3 samples tested 7 days after production
- 1 sample tested 50 days after production

Results

LE determination

Administrated submucosally
› parenteral route

LE = K/M *(thanks to PE)*
K: threshold dose of endotoxin per Kg (K= 100 IU/m²)
M : Maximum recommended dose for product per Kg

Standard patient: 70 Kg, body surface 1.8m², 100ml of GF solution injected
K= (100 x 1.8) /70 = 2.5 UI/ kg
M= 100/70 = 1.42 ml / kg

LE = 1.76 IU/ml

MSD determination

Detection limit of the cartridge is 0.05 - 5 IU/ mL relative to the MSD, corresponding to an actual detection range of 0.05 × MSD and 5 × MSD

Tests performed: MSD 50 and MSD 25

Range obtained must include the LE chosen

MSD = 25
Final detection range used: 1.25 - 125 IU/ml

Manipulation

- 5 minutes handling
- 15 minutes acquisition

Conformity Tests

- Recovery rate 50-200%
- Sample reaction time CV* < 25%
- Spike reaction time CV < 25%
- Positive control included in the cartridge

*CV : Variation coefficient

Results

```
**Endosafe nexgen-PTS rapport de test***
Version: ................ PTS150 V11.0.0
Date / Heure: ........... 17/02/24 00:09
N° série Lecteur: ............ 20331116
Analyste: ........................ CGG
Cartouche: ................... Endotoxin
Température: ... Début: 37.0C Fin: 37.0C
Méthode: ....................... KX-122
Cartouche Lot #: ............... 3913159
Cartouche code Cal: ....... 513936975493
Gamme: ......................... 5-0.05
Temps de Réact. gamme: .... Sec: 139-769
Temps de réact. Puits: >769 226 >769 214
Pente: ..... -0.371 Interception: +2.403
Dilution: ........................ 1:25
Lot échantillon: ................ 10400
Nom de l'échantillon: ............... 4
CV temps Echantillon: ..... 0.0% Réussir
Valeur Surcharge: ........... 1.40 EU/mL
CV temps Surcharge: ....... 3.9% Réussir
% de Recouvrement: ........ 190% Réussir
Test de conformité: ............ Réussir
Conc. Endotoxine: ......... <1.25 EU/mL
$271a67997e8af3f118b402e3fa6ec653c384a390
```

Conclusion

Sample form our tested productions are free from detectable endotoxins at the threshold of 1.25 IU/ml

Feasibility study concluded, encouraging the integration of EB measurement into routine practice:
- short acquisition time
- easy - to use device (*Purchase of the device under study)*
- no additional skills required
- cost of a control : 50€/ cartridge, or 150€ per production batch

For the future ?

Adjustment of production: **Volume of GF solution bags** increased to **250 mL** to meet the clinicians' requirements.

Adjust LE and MSD values to be applied for routine measurement of this new solution volume.