

# IMPLEMENTATION AND QUALITY CONTROL OF A 5% FRUCTOSE AND 10% GLYCEROL STERILE SOLUTION FOR DIGESTIVE ENDOSCOPY

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## Background

Endoscopic Mucosal Resection (EMR) and Endoscopic Submucosal Dissection (ESD) are innovative digestive endoscopic approaches allowing “*en bloc*” tumours removal - which facilitates histological analysis and lowers risks of local relapse.

To ease complete tumour removal, both techniques require submucosal fluid injections.

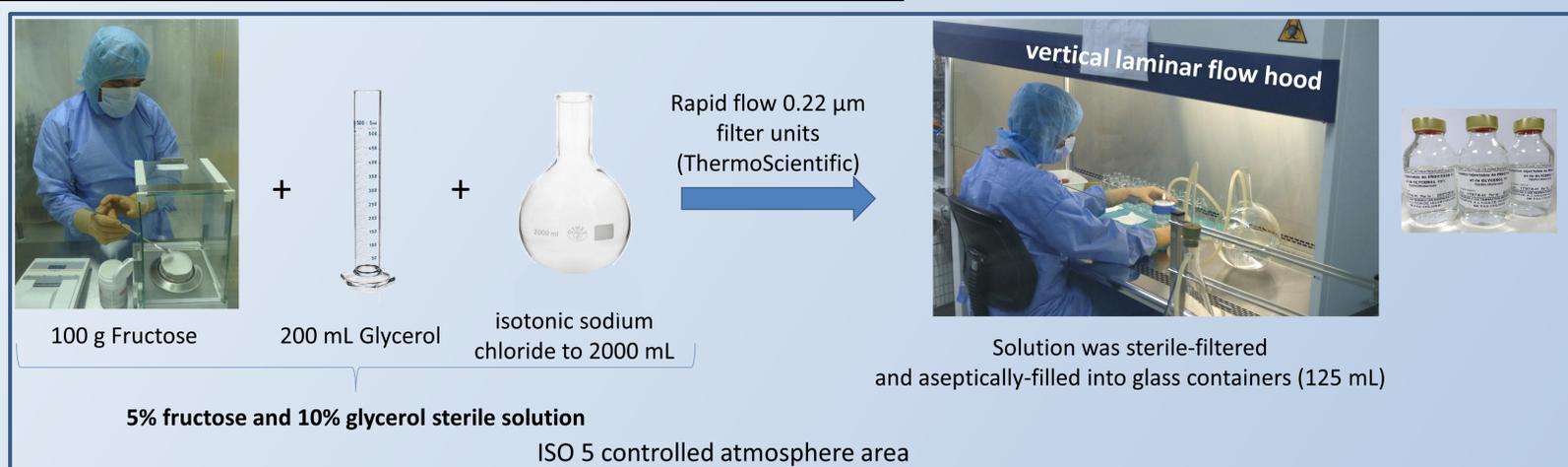
Nevertheless no ready-to-use commercial solutions for submucosal injection are available.

## Purpose

To implement a simple production of a ready-to-use 5% fructose and 10% glycerol sterile solution (FGSS) for submucosal injection and appropriate quality controls.

## Material and Methods

### FGSS aseptical compounding according to the Good Manufacturing Practices:



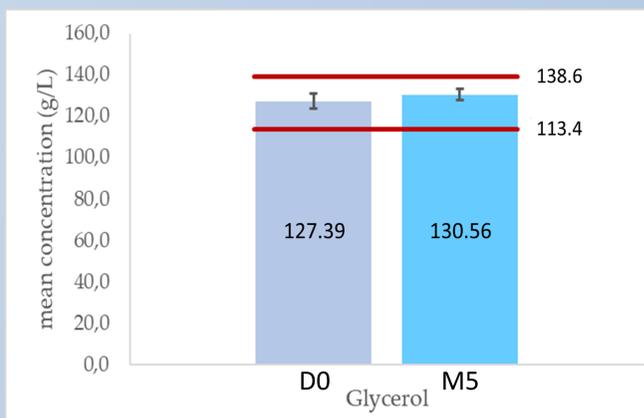
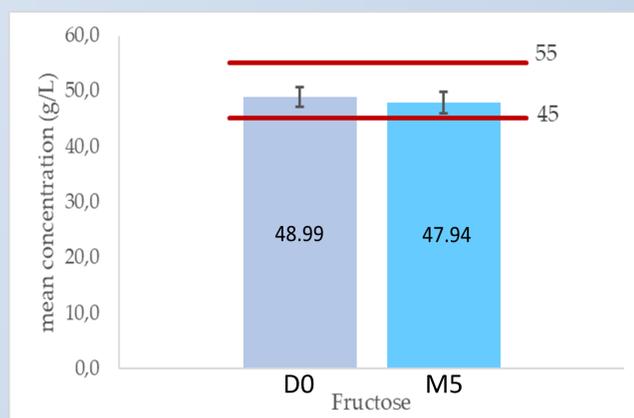
Alternative method, using terminal sterilization (121°C for 20min), was also tested.

**Quality controls:** Performed on three vials (beginning-middle-end of production).

- Fructose and glycerol concentrations
  - Colorimetric-enzymatic methods adapted on a chemistry analyser (Konelab Prime 60i®, ThermoScientific)
- Fructose degradation products: 5-hydroxymethylfurfural (5HMF) and 2-furaldehyde (2FA) concentration
  - HPLC-UV method (Ultimate 3000®, ThermoScientific)
- Sterility assay
- Endotoxin testing
  - Kinetic chromogenic method (Endosafe®- PTS, Charles River)
- Sub-visible particles contamination
  - European pharmacopoeia (EP) 2.9.19 light-obscurtion method (APSS 2000®, Particles Measuring Systems)
  - EP Threshold: respectively 25 and 3 particles/mL for particles size  $\geq 10 \mu\text{m}$  and  $\geq 25 \mu\text{m}$
- Visual aspect
- pH (HI5222®, Hanna Instruments)
- Osmolality (Advanced Instruments osmometer 3320®, Advanced Instruments)



## Results



Results mean [min-max]	D0	M5
Particles > 10 µm (particle/mL)	9.99 [5.50-16.50]	9.08 [2.50-17.17]
Particles > 25 µm (particle/mL)	0.37 [0.17 - 0.67]	0.30 [0.17 - 0.67]
pH	6.31 [6.26 - 6.36]	6.55 [6.06 – 7.25]
Osmolality (mOsm/kg)	2330 [2312-2348]	2269 [2238-2295]

At D0 and M5, both 5HMF and 2FA concentrations were below our method's limits of quantification (3.39 and 1.69 ng/mL respectively). When using moist heat sterilisation method, solution became lightly yellow and 5-HMF was 19.61 mg/L.

## Discussion

- pH and osmolality remained stable
- Sterility was preserved with no change in visual aspect
- Fructose and glycerol concentration remained in the acceptance limits (theoretical concentration  $\pm 10\%$ )
- Fructose degradation products:
  - Not detected with sterile filtration
  - 5HMF concentration above EP threshold (2.5 mg/L) with moist heat sterilisation
- Bacterial endotoxin free
- Sub-visible particles contamination : below EP 2.9.19 threshold

## Conclusion

Our compounding method is simple, optimised to limit 5HMF production, and can be implemented in any hospital. Produced FGSS complies with the EP quality requirements.

We developed the first specific and sensitive method for 5HMF and 2FA concentrations measurement in a FGSS preparation.

