Flocculation of etoposide preparations: what are the influencing factors?

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BACKGROUND

At Lille University Hospital : Production of 400 bags of etoposide (ETO) are produced per year, with concentrations ranging from 0.14 and 9.24 mg/mL in 0.9% NaCl.

★ Concentration that were subject to non-conformities in 2024

Cmin: Minimum concentration produced Cavg: Average concentration of production Cmax: Maximum concentration produced

- 11 non-conformities occured in 18 months: bags flocculated before their expiration date

→ **Pump occlusion alarms, uncertainty regarding the administered dose, emergency replacement of the bag**

Identify factors that may influence the occurrence of flocculation.

MATERIALS & METHODS

A preliminary analysis varying different parameters was carried out:

Raw Material (RM)

- Variation in RM used Accord®, Hikma®, Viatris®, Teva®
- Impact of Polysorbate 80
- Impact of PEG300

Preparation process

- Filling speed: variation in the injection device (needle and Chemolock® ICU Medical)
- Variation in final ETO concentration (0.1; 0.2; 0.4; 0.8; 2; 10 mg/mL)
- Presence or absence of air in the final packaging
- Variation in final packaging: bag or syringe

Final storage conditions :

- Room temperature (64.4-68°F)
- Refrigerator (35.6-46.4°F)
- Incubator (91.4°F)
- Storage temperature variations:

RESULTS

115 bags were produced.

Factors that do not affect flocculation:

- Filling speed
- Excipients

Facteurs favorisant la floculation :

- Storage temperature variation
- Concentrations between 0.4 and 10 mg/mL

CONCLUSION & OUTLOOK

Following this initial screening of numerous factors, an experimental plan should be put in place, varying the two factors that appear to promote flocculation. The bags will be prepared using the two diluents mentioned in the summary of product characteristics of the ETO (0.9% NaCl or 5% glucose).