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Stability study of hydrocortisone 1mg/mL oral suspension for neonatal use

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INTRODUCTION

The **neonatal department** uses therapies that require adjustments in dosage and formulations, including hydrocortisone (HCT) which prevent bronchopulmonary dysplasia in premature newborns. At present, HCT capsules are opened and diluted extemporaneously, highlighting the **need for a ready-to-use oral suspension**.

The aim of the study was to **produce an oral suspension of hydrocortisone free from excipients with known effects** (EKE) framed by microbiological and physicochemical stability studies.

MATERIAL & METHODS

	Batches	Constitution	Storage condition	Opening & manipulation	Checkpoints Physicochemical & microbiological controls
	1-2-3	30 amber vials of 20mL (10 vials each)	RT	NO	Day 0, 7, 14, 28, 56 and 84
	4-5-6	30 amber vials of 20mL (10 vials each)	4°C	NO	
	7	1 amber vial of 200mL	RT	YES	Day 0, 4, 7, 11, 14 and 28
	8	1 amber vial of 200mL	4°C	YES	
Worst case scenario	**9**	10 amber vials of 30 mL	4°C up to excursion	NO	Day 7 or 14 after a 12- or 24-hour temperature excursion
	10-11-12-13	4 amber vials of 200mL (1 vial each)	4°C up to excursion	YES	

RT : Room temperature / 4°C : Refrigerated temperature

Concentration of HCT oral suspension set at **1mg/mL** using the EKE-free Syrspend SF PH4 Dry vehicle

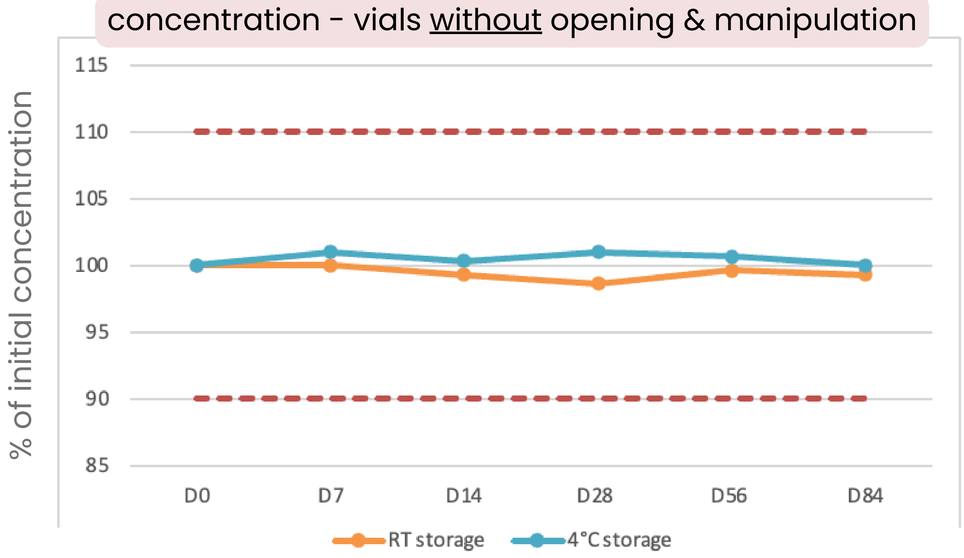
Batches with opening & manipulation (7, 8, 10-14) are used to reproduce sampling conditions in neonatal department.

Physicochemical & microbiological controls :

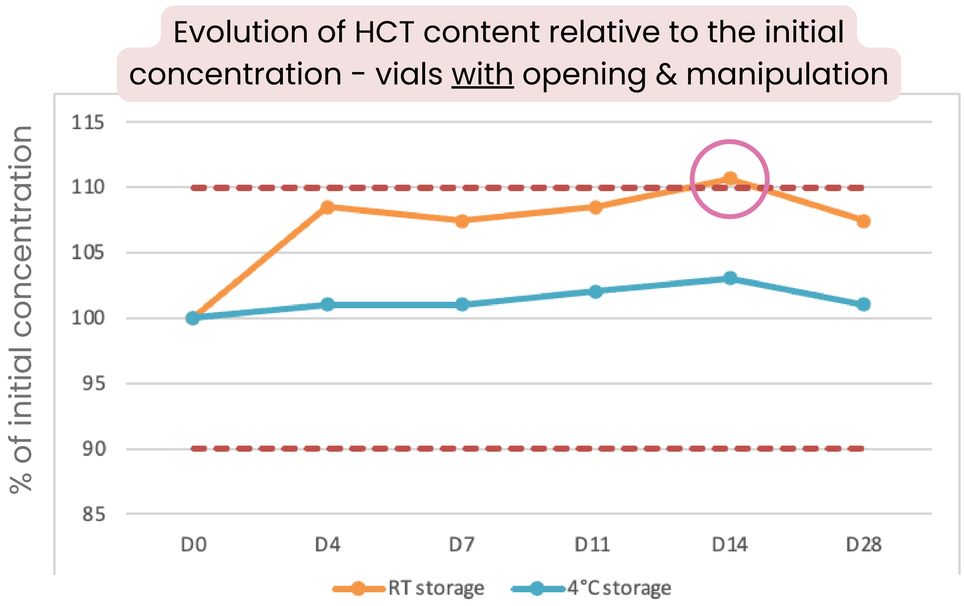
- An **HPLC/UV assay** was carried out with measurement of **pH**, **osmolality** and **visual inspection**.
- Bacterial and fungal enumeration included specific testing for **E.coli** *(in accordance with European Pharmacopoeia 11th edition)*.

Stability was defined as an average content between 90 and 110% of the initial drug content.

Evolution of HCT content relative to the initial concentration - vials without opening & manipulation



Evolution of HCT content relative to the initial concentration - vials with opening & manipulation



RESULTS

Physicochemical stability :

- **HCT content** was between 90 and 100% of the initial concentration of 1mg/mL up to 84 days at 4°C without opening, and up to 28 days with opening. At RT one measurement on D14 of the batch with opening had a 10,64% deviation.
- **pH** : stable with or without opening at RT and 4°C.
- **Osmolality** : stable and <50mosm/kg for all study conditions except for a RT without opening vial at D56 (20,93% deviation).

Visual inspection : presence of two phases with the need for homogenization before each sampling.

Microbiological quality :

- With the exception of two measurements at 4°C on D14, for which external contamination is suspected, **microbiological quality was compliant**.
- E.coli testing was negative.

Worst case scenario

Physicochemical stability was not affected after 12 or 24-hour temperature excursions.

CONCLUSION

This study enables us to store HCT oral suspension without EKE at **4°C for 3 months**.
Once opened, it should be stored at **4°C** and used within **14 days**. Drinkable suspension makes HCT administration safer and can now be deployed in neonatal department.