Physicochemical and microbiological stability of Spironolactone oral suspension without potentially harmful excipient

Maxime Petit[1], Sonia Mitreski[1], Julie Forget[1], Hassan Allouchi[2], Elodie Baticle[3], Eric Bailly[4], Stéphanie Provot[1], Xavier Pourrat[1]

1. Pharmacy, CHRU Tours, France 2. Control Laboratory, CHRU Tours, France 3. Bacteriology and Hospital Hygiene Unit, CHRU Tours 4. Parasitology, Mycology and Tropical Medicine Laboratory, CHRU Tours, France

Introduction

- Spironolactone: antihypertensive diuretic widely used in pediatrics
- **No adapted specialty** available
- Prior to this study:
  - Hospital Pharmacy / Health care service
  - **Preparation** and **dispensing** of capsules
  - **Opening** and **dilution** of capsules
  - = Practice with risk of error :
    - Of **administered** dose (dilution, homogenization)
    - **Absorbed** dose (unknown bioavailability)
- Objectives :
  - To develop a **drinkable suspension** of Spironolactone **without Potentially Harmful Excipient (PHE)** from Syrspend® SF PH4 Dry
  - Conduct a **physicochemical** and **microbiological stability study**

Material et methods

- 7 batches are produced :

Conditioning
-Batch 1 to 6 : 10mL amber glass bottles
-Batch 7 : original bottle of Syrspend 200mL

Storage Temperature: Refrigerator / Ambient

Control points according to opening:

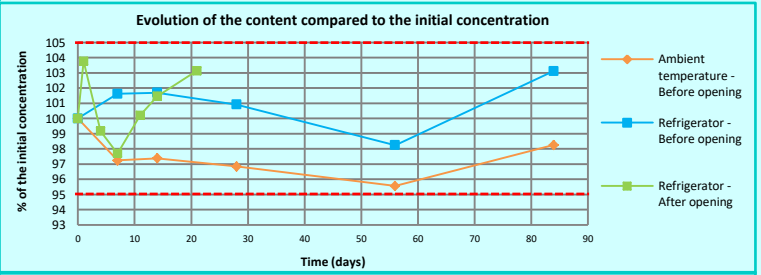
	Refrigerator	Ambient
Before opening (D0 > D7 > D14 > D28 > D56 > D84)	Batches 4-6	Batches 1-3
After opening (D0 > D1 > D4 > D7 > D14 > D21)	Batch 7	

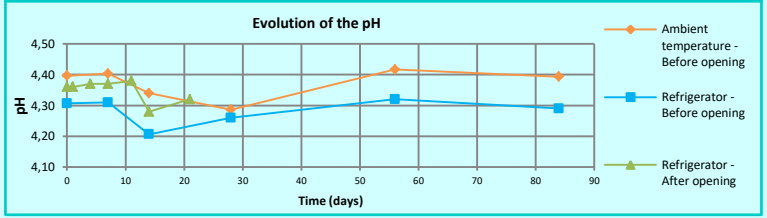
Sampling under the same conditions as the care service

At each control point :

- Physico-chemical controls :
  - **HPLC/UV assay** with stability indicating method
  - **pH** and **osmolality**
  - **Organoleptic** characteristics
- Microbiological controls :
  - **Bacterial** and **fungal** enumeration
  - Specific research of ***E.coli***

Results





- **Osmolality remained <50mosm/kg** throughout the study
- **No** degradation products **detected**
- **No change** in organoleptic characteristics
- **Microbial count below** pharmacopoeia requirements
- **Specific E.coli research** always **negative**

Discussion-conclusion

- Stable preparation **84 days before opening and 21 days after opening** => Allows an **optimal organization** of the production and administration circuit
- **No PHE**: suitable for newborns but means **no preservative** => **microbiological stability** data **essential** + **refrigerated storage** to reinforce this stability
- **The use in the service will be able to start**. The evaluation of the **satisfaction of the nurses** and the **acceptability by the children** is planned
- The use of **this excipient** in oral forms should be **extended to other APIs** to allow **safe administration in pediatrics**

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