# Optimization and stability study of compounded oral suspension of spironolactone at 5mg/ml for infants

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## Background

An oral suspension formulation of spironolactone at 5mg/ml in InOrpha® (for its safety profile) is proposed for neonatal use. This formula sedimentates rapidly (caking), impacting on appropriate use of oral suspension

## Objective

The aim is to optimize the oral suspension of spironolactone in InOrpha® and assess its stability.

## Material & Method

**Galenic optimization**

Added 0.2% xanthan gum (m/V) to the formula in InOrpha®.

**Dosing method**

Stability indicating method via HPLC-UV

**Stability study**

2 conditions: 22°C ± 3°C and 5°C ± 3°C

Triplicate analysis at D0, D15, D30, D60, D90, D120, D135 before opening and at D0, D15, D30, D37 after opening (with daily sampling of oral suspension)

The parameters monitored are:

- Dosing of spironolactone and detection of degradation products
- Organoleptic characteristics, sedimentation (concentration in unstirred bottle), viscosity (rotary rheometer), density (hand refractometer), pH (potentiometry) and osmolality (osmometer)
- Microbial enumeration test and specific detection of E.coli according to the European Pharmacopoeia

## Results

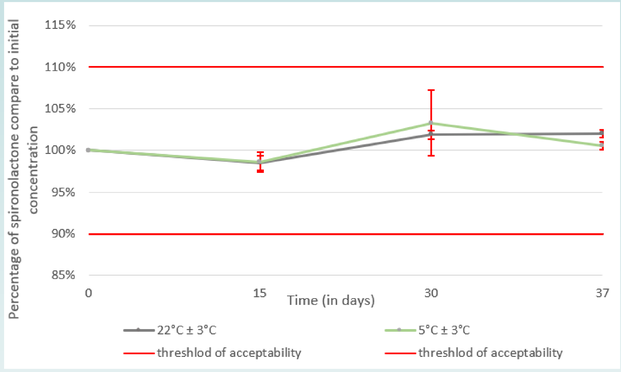


Table 1: Percentage of spironolactone compare to initial concentration until D37, after opening bottle

### Chemical stability

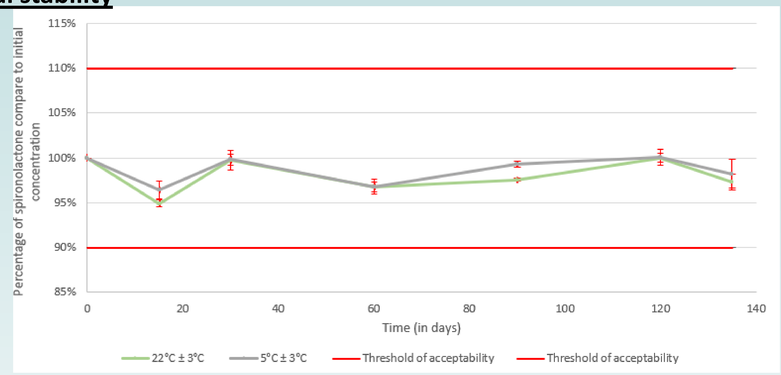


Table 2: Percentage of spironolactone compare to initial concentration until D135, before opening bottle

No degradation products.

### Physical stability

Organoleptic characteristics: No change in color and odor for ambient and cold

Sedimentation: concentration of spironolactone within acceptability limits set at ± 5% deviation up to D135 in ambient and cold

No change and no difference for density (≈ 1.014), pH (≈ 4.76) and osmolality (≈ 185 mosmol/kg) in ambient and cold

Stable viscosity but difference beetwen ambiant and cold ( ≈ 218mPa.s at 5°C ± 3°C and 133mPa.s at 22°C ± 3°C)

### Microbiological stability

Validation of environmental fertility (monograph 2.6.12)

The microbial enumeration test before and after opening vials (monograph 2.6.12) : compliant with validation thresholds

The search for specified micro-organisms (monograph 2.6.13) : no *E.coli*

## Conclusion/ Discussion

✓ Optimization of the galenic formulation with the addition of a safe excipient for pediatrics. Sedimentation is no longer observed at 4 months post-production at 22°C ± 3°C and 5°C ± 3°C .

✓ Physico-chemical and microbiological stability of oral suspension has been demonstrated for a shelf-life of 135 days before opening (i.e. 4 effective months) and 37 days after opening (i.e. 1 effective month) at 22°C and 5°C.

➡ Conservation at room temperature to simplify storage.