

# Interest of an analytical control by UV spectrophotometry for the control of phenobarbital compounded preparations.

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## Introduction

Phenobarbital (PHB) is an antiepileptic frequently used in pediatric population for the treatment of epilepsy. To overcome the lack of marketed specialties suitable to this category of patients, hospital pharmacy units realized compounded of PHB capsule preparations (CP). Currently, in our unit their control is based on the European Pharmacopoeia mass uniformity (UM) test (2.9.5). Nevertheless, the risk assessment of PHB CP is in support of enhancing its control. The objective of this work is to evaluate the interest of a control by UV spectrophotometry (UV spectro) for the control of PHB CP.

## Material and method

The developed method was validated according to the ICH Q2 (R1) recommendations. Its linearity was verified for concentrations ranging from 0.007 to 0.06 mg.ml<sup>-1</sup> ( $r = 0.9996$ ).

Accuracy and precision were tested on 2, 20 and 100 mg controls. The coefficients of variation were less than 4% and the bias value for all 3 dosages ranged from -1.08 to -3.33%.

### Experimental conditions:

- 1 Dilution in methanol 50 % (v/v)
- 2 Dilution in phosphate buffer (pH = 3.9)

Detection at 239 nm

The results of the UM test and the UV spectro assay were collected and compared.

	Categorie 1	Categorie 2
Dosage in phenobarbital	< 2 mg (CP < 2 mg)	2 mg < CP < 25 mg (CP > 2 mg)
Interval acceptance UV spectro	± 15 % *	± 10 %

\* According to European Pharmacopoeia, uniformity test of content of single-dose preparations assay B (2.9.6)

## Results

	Categorie 1: CP < 2 mg	Categorie 2: CP > 2 mg
Number of CP manufactured between December 2018 and June 2020	2	35
CP non-compliant according to UM	None	
CP non-compliant according to UV spectro	None	28,5 % (n=10)

## Discussion and conclusion

The NC rates according to UM and UV spectro assay thus demonstrate the value of the determination of PHB content. On the other hand, the level of CP > 2 mg NC observed is consistent with the overall NC level found in our unit for batch preparations controlled according to the uniformity test of content of single-dose preparations (24% NC).

UV spectro is an analytical method of choice for the control of CP; the relatively short analysis times allow to include it in their manufacturing and control circuit.

Then, these results demonstrate the interest of routine control by UV spectro of PHB CP, but they must be verified on a larger number of CP especially for CP ≤ 2 mg.