

M. Decuyper¹, V. Hay¹, A. Melaye¹, L. Pacqueu¹, L. Negrier^{1,2}, C. Danel^{1,2}, M. Vasseur^{1,2}, M. Bouchfaa^{1,2}, P. Odou^{1,2}

¹ CHU Lille, Pharmacy Institute, 59000 Lille, France

² University of Lille, CHU Lille, ULR 7365 - GRITA - Research group on injectable forms and associated technologies, 59000 Lille, France.

Context

In view of the increase in the number of drug shortages and following the publication of the new BPP, the automation of preparations seems to be an essential alternative for our centre, which has an automatic capsule filler (INCAP SE, Bonapace).

Objective

Développer une formulation de gélules de prednisone 5 mg et qualifier le procédé automatisé permettant la préparation de celle-ci.

Matérials and methods

Production protocol:

300 g excipient powder :

PROSOLV SMCC 90HD® silicified microcrystalline cellulose or VIVAPUR 302® microcrystalline cellulose.

+ Addition of prednisone 5 mg

Automatic mixing at speed 8 for 20 minutes (Inversina 2L, Bioengineering)

First 30 capsules removed

Production of 300 size 2 capsules using the capsule filler

1) Selection criteria:

Powder flow

Fouling of the automatic machine

Core drilling/empty capsules

2) Capability index:

300 capsules

Logiciel R, plateforme Jupyter, librairie qcc, version 2,7

According to capability indicators :

Cp > 1.33: satisfactory situation, process under control

3) Dosage of capsules by HPLC-UV on the mixture (surface, middle, bottom) and on the capsules (start, middle and end of production) n=3

Look for homogeneity during blending and absence of demixing

Acceptance criteria: capsule content between 90 and 110% according to the European Pharmacopoeia.

4) Control card :

Production of approximately 600 capsules divided into batches of 100 capsules. 10 capsules are weighed between each batch of 100 and a control chart is drawn up (R software, Jupyter platform, version 2.7).



Résultats



Hollow in the hopper
Poor flow

VIVAPUR 302®/prednisone



Optimum flow

PROSOLV SMCC 90HD®/prednisone

		Mélange	Gélules
Production 1 PROSOLV SMCC 90HD® /prednisone	Average content (mg)	5,04	5,29
	Average standard deviation (mg)	0,11	0,05
	Bias % par relative to 5 mg	0,83	5,97
Production 2 PROSOLV SMCC 90HD® /prednisone	Average content (mg)	5,08	5,33
	Average standard deviation ((mg))	0,10	0,08
	Bias % relative to 5 mg	1,75	6,67

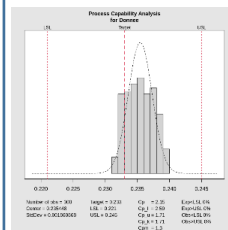
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Dosage of capsules by HPLC-UV

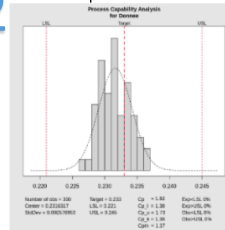


1

2



Production 1
Average mass = 235,29 ±
1,81 mg
Cp = 2,15



Production 2
Average mass = 231,59 ±
2,35 mg
Cp = 1,92

Capability index

PROSOLV SMCC 90HD®/prednisone

4

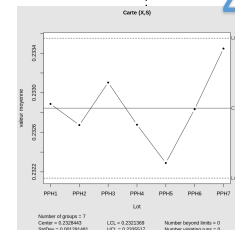


Chart (X,S)
PROSOLV SMCC
90HD/prednisone

✓ Process under control

Conclusion - Discussion

The formulation composed of silicified microcrystalline cellulose and prednisone 5 mg was validated. The data obtained ensure control of the process and high productivity of prednisone 5 mg capsules despite fouling problems. However, the process needs to be improved by adding a lubricant such as magnesium stearate.