CAPABILITY ANALYSIS OF A POWDER FOR FILLING BY AN AUTOMATIC HARD CAPSULE FILLER

A.MELAYE[1], N.THOMASSET[1], M.DECUYPER[1], L.PACQUEU[1], M.VASSEUR[1 2], M.BOUCHFAA[1 2], P.ODOU[1 2]

1. UNIVERSITY OF LILLE, 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.

COM24 -76922

CONTEXT

"In 2023, 37% of French people say they will have experienced **drug shortages**"

according to Commission of Inquiry into the shortage of medicines and the choices made by the French pharmaceutical industry - Senate - July 2023

SOLUTION

Automated production of hospital preparations

OBJECTIVE

To test the **capability** of powders of different compositions for use in **an automatic hard capsule filler,** as a basis for future preparations.

MATERIALS AND METHODS

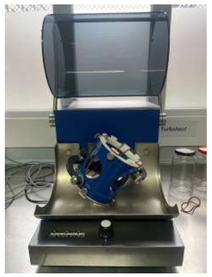
10 powders of 200g → **cellulose** base with **silica** and/or **talc** and/or **magnesium stearate**

Excipients	1	2	3	4	5	6	7	8	9	10
Microcrystalline cellulose (Cooper)	100%	99.3%	99%	98.8%	98.7%	95%	94%	97.5%	96.5%	96.5%
Anhydrous colloidal silica (Inresa) (Max: 1%)		0.7%	1%	1.2%	1.3%		1%			1%
Talc (Cooper) (Max : 30%)						5%	5%			
Magnesium stearate (Inresa) (Max: 5%)								2.5%	3.5%	2.5%

MIXTURE

Three-dimensional blender : **Inversina 2L, Bioenginnering**

- Speed : 8/10
- 30 minutes
- Powders with silicas are sieved before mixing.
- Colorant used: Carmine red



PRODUCTION

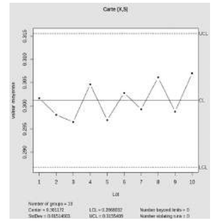
Automatic hard capsule filler: IN CAP-SE, BONAPACE

- Production of 300 capsules of size 0 of each powder divided into sub-batches of 30 units continuously during production.
- 1600 capsules / hour
- Piston adjustment in order of rotation : 3 / 6 / 9 / 12
- Temperature : 18°C ± 1 ; Hygrometry : 56,5% ± 3,75

CONTROL CHART

RMade with R software, qcc library, version 2.7

- Mass of the last 10 capsules of each sub-batch
- Calculate of capability (Cp), deregulation index (Cpk) and Taguchi index (Cpm) from total production



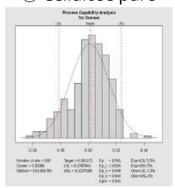
RESULTS

According to capability indicators:

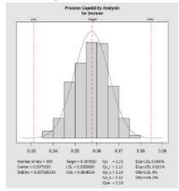
- **< 0.67: Very inadequate, the process is out of control for powder 1 and 6**
- **< 1: Insufficient, all units produced must be controlled for 2, 7 and 10.**
- **< 1.33: Delicate situation where the process may lead to errors for 3, 4, 5, 8 and 9.**

	1	2	3	4	5	6	7	8	9	10
μ (en mg)	301,17	356,95	**357,82**	334,71	340,81	306,77	333,18	**345,30**	364,51	321,73
σ (en mg)	14,73	8,40	**7,38**	7,83	8,14	12,15	8,42	**6,54**	6,98	9,05
Cp	0,54	0,96	**1,13**	1,01	1,1	0,64	0,93	**1,14**	1,03	0.85
Cpk	0,53	0,88	**1,12**	0,99	1,08	0,64	0,92	**1,12**	1,01	0.82
Cpm	0,54	0,94	**1,13**	1	1,09	0,64	0,93	**1,14**	1,03	0.85

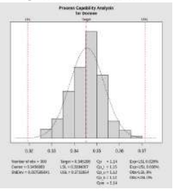
① Cellulose pure



③ Silice 1%



⑧ Stéarate 2.5%



DISCUSSION

Very different capsule weights

Preparations of 1% silica and 2.5% stearate are the most acceptable processes (1 < Cp < 1.33).

Obligatory sampling

Hygrometric and temperature parameters difficult to control

PERSPECTIVES

Modified cellulose

- Better flow
- For industrial process
- Example: PROSOLV SMCC 90HD®, JRS

Dissolution tests

mail : adrien.melaye@chu-lille.fr