



COMPARISON OF MANUFACTURING PROCESS ROBUSTNESS: FROM A MANUAL TO AN AUTOMATED METHOD

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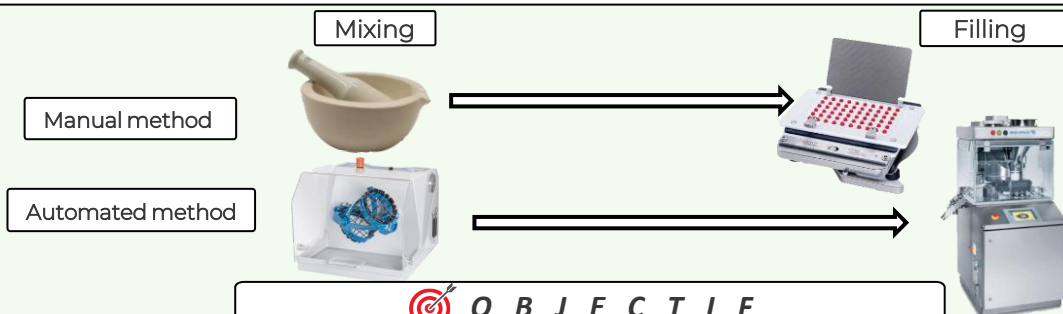
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KEYWORDS

Tablets, Quality Control, Drug Compounding

CONTEXT

The annual volumes of hospital-compounded 5mg melatonin preparations(> 20 000 units/year) led us to switch from a **manual capsule-filling** method (CAP) to an automated tablet compression method (TAB).



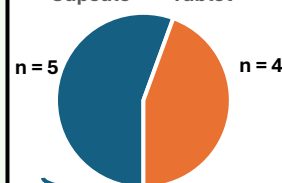
OBJECTIF

To compare the robustness of the two manufacturing processes.

MATERIALS AND METHOD

9 complying batches analysed

■ Capsule ■ Tablet



Manufactured between 01/01/2025 and 03/31/2026

Assessment criteria:

- Values from mass uniformity testing, evaluated on 20 units for each batch (*Ph. Eur. 11th edition, 2.9.5*)
- Values from content uniformity testing, evaluated on 10 units for each batch (*Ph. Eur. 11th edition 2.9.6*)

Statistic analysis using: **Minitab**

Robustness assessed by calculating capability indexes:

- Cp: evaluates overall process robustness
 - Cpk: evaluates process centering relative to a target value
- Specifications: $\pm 10\%$ around the target values



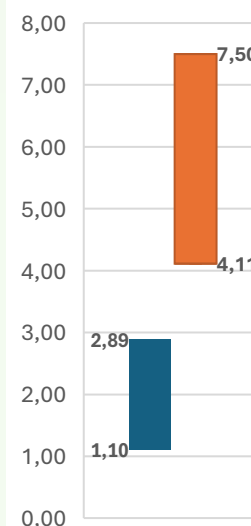
RESULTS

Mass Uniformity (MU)

Cp inter-batch :
Capsule: 1,63
Tablet: 3,99

Intra-batch Cp range

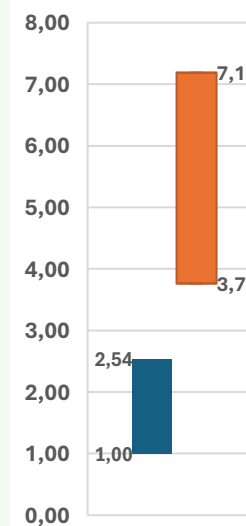
■ Capsule ■ Tablet



Cpk inter-batch :
Capsule: 1,63
Tablet: 3,95

Intra-batch Cpk range

■ Capsule ■ Tablet

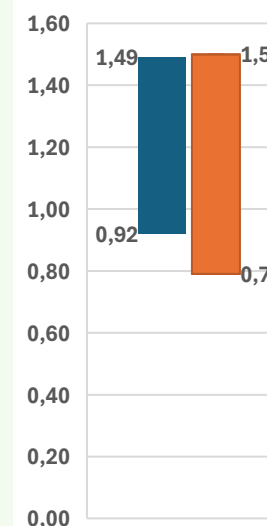


Content Uniformity (CU)

Cp inter-batch :
Capsule: 0,99
Tablet: 1,07

Intra-batch Cp range

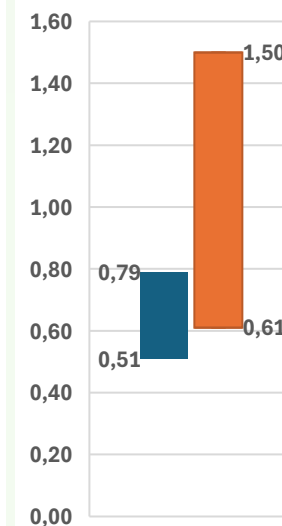
■ Capsule ■ Tablet



Cpk inter-batch :
Capsule: 0,55
Tablet: 0,92

Intra-batch Cpk range

■ Capsule ■ Tablet



DISCUSSION - CONCLUSION

Automation has **significantly improved process capability** for the MU. It also led to an **improvement in Cpk**, and to a lesser extent Cp, regarding CU. Industrial standards generally consider a **process** to be **robust** when **both indexes values exceed 1.3**. These targets were achieved with both processes for MU. However, for CU, only one TAB batch was compliant, highlighting insufficient control of the mixing step. **An analysis of critical factors** related to raw materials and the mixing process appears necessary.

Although these requirements specifications are stringent for hospital production, the annual volumes manufactured justify the implementation of process performance indicators and support a **product quality review approach**, as introduced in the 2023 French Good Preparation Practices (*Bonnes Pratiques de Préparation*).