DEVELOPMENT OF A SAMPLING METHOD TO VALIDATE THE CLEANING PROCESS OF AN AUTOMATIC HARD CAPSULE FILLER

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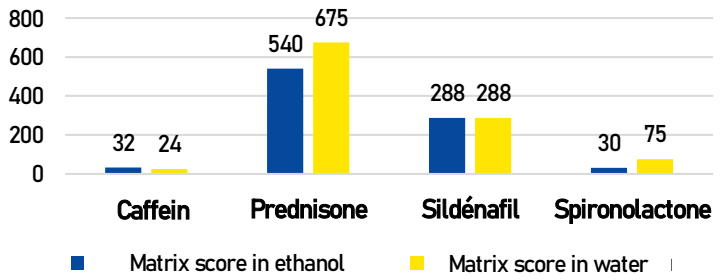
INTRODUCTION - OBJECTIVE

- Our establishment wishes to respond to the increase in **demand** and **drug shortage** by resorting to preparations. The 2023 Good Preparation Practices allow us to increase batch sizes.
- We have equipped ourselves with an **automatic hard capsule filler** (*INCAP SE, Bonapace*) to automate preparations.

With the increase in capsule production, our aim is to develop a method for **validating the cleaning process** between two productions of different molecules.

RESULTS

Choice of "worst case" molecule



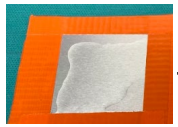
Sampling méthod

Of the 18 points initially selected, the sampling plan identified 5 critical sampling points:

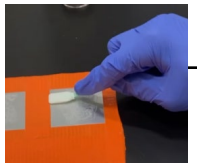
- **Dosing disk**
- **Hopper**
- **Discharge chute**
- **Capsule moulds**
- **Sealing slide**

Validation of the sampling method

Deposition of 200uL of prednisone at a known concentration in methanol, followed by drying



2 swabs desorbed in 10 ml ethanol for 15 minutes



Analysis of the recovery rate for 12 measures and 3 operators

Average recovery = **82.0 ± 9.3**
Covariance of repeatability = **11.0%**
Covariance of reproducibility = **11.3%**

MATERIALS & METHODS

Good Manufacturing Practice recommends that the cleaning process be validated by :

Swabbing

The use of a '**worst case**' approach to **choose the molecule** used for monitoring

For each molecule considered in the capsule filler we analysed :

- Cleanability estimated by log P
- Solubility in water and ethanol (solvents considered for cleaning)
- Toxicity
- Therapeutic activity without effects and LD50

For each criterion, a score from 1 to 5 was assigned, enabling a total score to be calculated for each molecule, the one with the highest score being the 'worst case'.

Drawing up a **sampling plan**

Using a **matrix study**, the following criteria were used to estimate the critical points: difficulty of cleaning, surface porosity, routine accumulation and direct contact with the raw material.

Validation of the **sampling method**

A methodology for sampling aluminium was studied by modifying several parameters: deposition volume, number of swabs, solvent used, desorption time until a recovery **rate of over 70% was obtained**.

The residual quantities swabbed were determined using **high-performance liquid chromatography coupled to a diode array detector**.

DISCUSSION - CONCLUSION

- The sampling method has been **validated for aluminum surfaces** and **needs to be extended** to each material in the capsule filler: plastic and cast iron.
- Taking these samples will then enable us to validate the capsule filler cleaning process.
- Finally, the methodology developed will also enable us to **validate the operators** during the cleaning stages and **monitor the process.**