Validation of an automated method for cyclophosphamide reconstitution and comparison with the manual process

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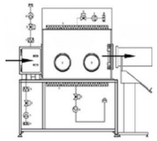
CONTEXT

Injectable cyclophosphamide : powder for reconstitution.

In our hospital — Campaigns of 30 vials



by hospital pharmacy technicians (HPTs) + automatic agitation (30 minutes) →

Arrival of the APOTECACHEMO robotic system :

Automating cyclophosphamide reconstitution ?

→ **Time consuming, requires anticipation**

Objective

- Define and validate a robotized reconstitution method
- Compare it to the current manual method

MATERIALS AND METHODS

1.Determination of the optimal dissolution duration with the robotic system

- **4** durations tested
- **4** vials per attempt
- Accepted or rejected via visual inspection

→ The duration selected is tested again **3** times to be validated.

2. Ensuring the absence of chemical contamination with the robotic system

Reconstitution with NaCl + **fluorescein**

Vials manually agitated inside a bag for 30 sec

→ **exposure under UV light :**

- Vials
- Robotic area
- Wipes

On 3 batches of 4 vials, by 2 operators

A positive control is conduced.

COMPARISON

3. Reconstitution campaign duration: overall timing of the procedure

From: Creating the batch file
To: Placement of the vial into the storage area

The measured durations are **normalized per vial** for comparison.

4. Drudgery and musculoskeletal disorders risks: use of questionnaires

- ☐ Based on the Santé Publique France "Eval Risk TMS" questionnaire
- ☐ 1 questionnaire by method
- ☐ 7 questions

0 point → 11 points increasing drudgery

5. Accuracy: statistical analysis

Gravimetric control after reconstitution

Student's t-test: comparison of the mean of deviations from the expected vial weight.

RESULTS

1 Determination of the dissolution duration:

- 5 minutes (shortest duration, recommended by the manufacturer)
- 6 minutes
- 7 minutes
- **7 minutes and 30 seconds** = no visible particles left (3 times) → **duration validated**

→ particles in solution

2

No visible traces were detected on any observed elements with the fluorescein test:

- Vial surface and septum
- Wipes used to clean the agitator and septum
- The preparation area

The **positive control is conclusive** and confirms the validity of the test.

	Current manual method	Robotic method
Average duration per vial 3	**4.5 min** (135 minutes for 30 vials)	10 min (40 minutes for 4 vials)
Drudgery and TMS risks 4	7.8/11 (n = 10 HPTs)	**1/11** (n = 4 HPTs) — Only 4 HPTs trained
Accuracy 5	For 120 vials: 1.05% (+/- 0.66)	For 32 vials: **0.58%** (+/- 0.21)
	P-value < 0.05: significantly higher accuracy of the automated reconstitution	

DISCUSSION / CONCLUSION

This work enabled the validation of a robotized reconstitution method:

- Less physically demanding
- More accurate
- Free from chemical contamination

than the manual method.

PERSPECTIVES

- Further optimization of **campaign duration**
- A **particle counter** has been acquired → detection of non-visible particles in solutions.
- In addition to the fluorescein test → robotic chemical contamination test