Congrès du GERPAC 2024

COM – 30254

Development and validation of a production and a dosage methods of 3D printed tablets containing prednisolone.

Service de pharmacie
CHUV

Context: 3D printer in CHUV pharmacy

- **Project:** development and test of prednisolone in 3D printed tablets in pediatric units

- Formulation : prednisolone 1%
  - 200 mg (2 mg API)
  - 500 mg (5 mg API)

- 1st step:
  - Develop and comparison of 2 protocols of fabrication
  - Identify the best

- 2nd step:
  - Validation of the fabrication protocol with quality control analyses (in- and post-process)
    - Mass uniformity
    - Content uniformity

Comparison of 2 protocols

Manual mixing

- Heat the water bath • 30 minutes
- Heat the CuraBlend • 30 minutes
- Weight all the API
- Mix with mortar and pestle • Quickly !
- Heat the mix • 15 minutes
- Transfer into the syringe

VS

Automated mixing

- Weight all the API • 10 minutes
- Mix with the automate • 10 minutes
- Transfer into the syringe

Manufacturing processes

Manual mixing

- Mix 1 = day 1
  - 200 mg x 25 tablets
  - 500 mg x 25 tablets
- Mix 2 = day 2
  - 200 mg x 25 tablets
  - 500 mg x 25 tablets
- Mix 3 = day 3
  - 200 mg x 25 tablets
  - 500 mg x 25 tablets
- Into blisters and labeled

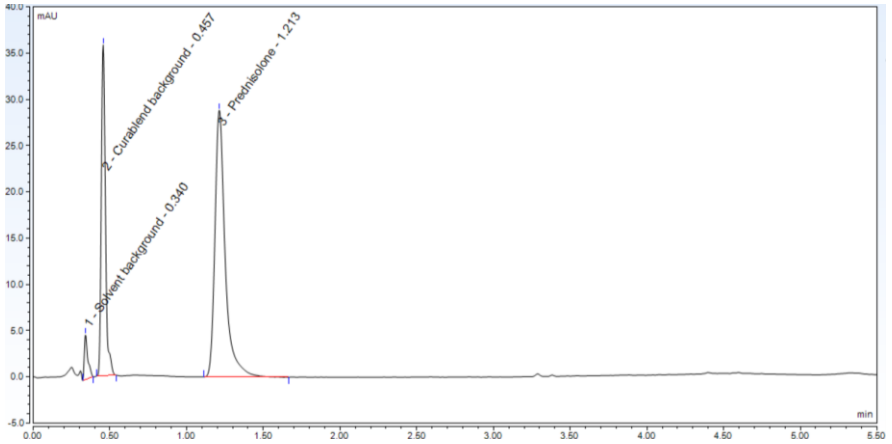
Automated mixing

- Mix 1 = day 1
  - 200 mg x 25 tablets
  - 500 mg x 25 tablets
- Mix 2 = day 1
  - 200 mg x 25 tablets
  - 500 mg x 25 tablets
- Mix 3 = day 1
  - 200 mg x 25 tablets
  - 500 mg x 25 tablets
- Into blisters and labeled

Quality control development

Mass uniformity

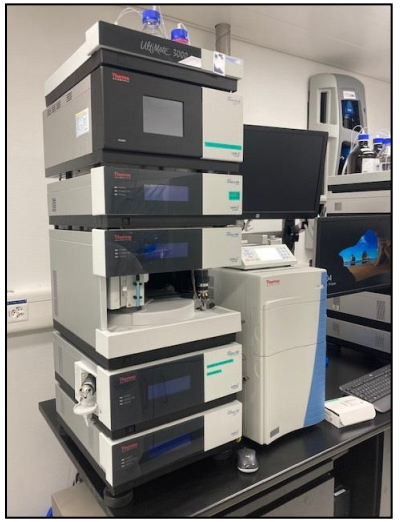
- Collection of masses of all tablets printed



Content uniformity

- Creation and validation of a method of analyses
  - In accordance with ICH Q2R2

ICH harmonisation for better health



- HPLC coupled with a diode array detector (DAD)
  - Column BEH C18 (Acquity™ Premier VanGuard™ FIT, 1.7 µm, 2.1 mm X 50 mm)
  - UV 280 nm
  - Mobile phase H2O/ACN

Results

Production of 200 mg tablets

Manual mix

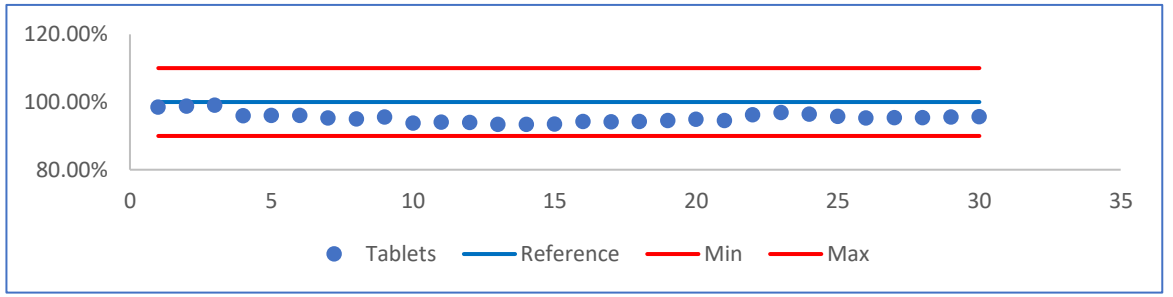
	Mix 1	Mix 2	Mix 3
Mass uniformity	Conform	Conform	Conform
Mean	199.2 mg	200.2 mg	199.6 mg
	99.6 %	100.1 %	99.8 %
Standard deviation	2.07 mg	4.47 mg	6.33 mg
	1 %	2 %	3 %

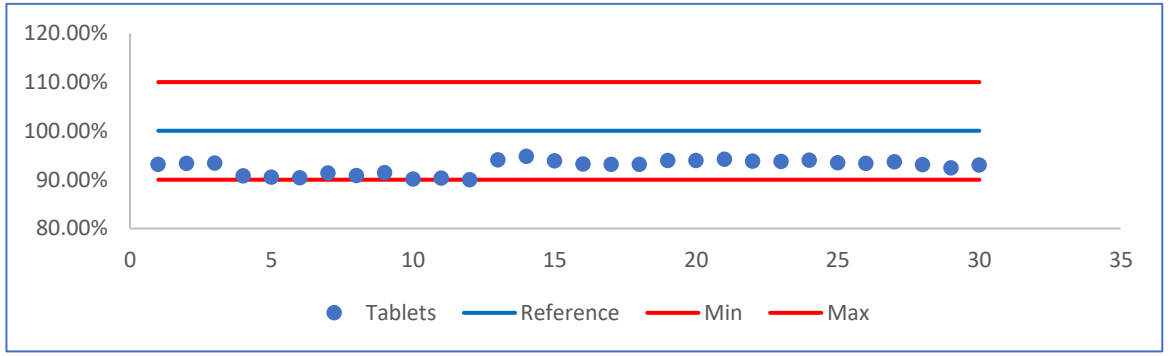
Automated mix

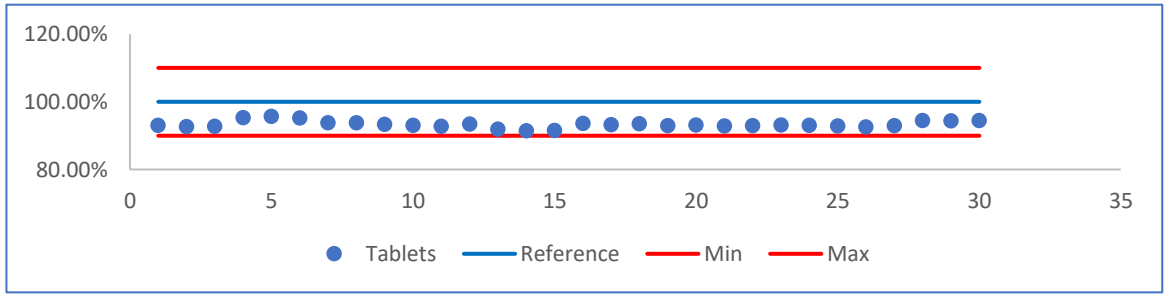
	Mix 1	Mix 2	Mix 3
Mass uniformity	Conform	Conform	Conform
Mean	202,4 mg	203,3 mg	200.5 mg
	101,2 %	101,7 %	100.2 %
Standard deviation	3.1 mg	4 mg	2.44 mg
	1.6 %	2 %	1.2 %

Results – *content uniformity with automated mix*

	Content uniformity	Average	Standard deviation
Mix 1	Conform	95.4 %	1.5 %
Mix 2	Conform	92.7 %	1.5 %
Mix 3	Conform	93.3 %	1.0%







Conclusion

Manual mixing

- ~ 90 minutes to be ready to print
- Mixing part more difficult
- Homogeneity
  - Depending on an operator
- Mass uniformity : conform
- Dosage uniformity :
  - To be determined

Automated mixing

- ~ 30 minutes to be ready to print
- Mixing part much easier !
- Homogeneity
  - Depending on a machine
- Mass uniformity : conform
- Dosage uniformity : conform
  - Standard deviation < 3% !
- Feasible in routine