Pediatric syrups : impact of the API row material on the final preparation volume

Cécile REHN[1], Céline MARIE[2], Zamzame CHARIFFOU[2], Céline FOULIER-VIE[2], Makrem BEN REGUIGA[1]

•[1] : Pharmacist; [2] : Pharmacy technicians, Central Pharmacy, Centre Hospitalier de Mayotte, France

Background

- Our hospital pharmacy produces yearly several compounded magistral pediatric syrups (n=700 in 2019)
- The production method in based the volumetric Quantum Satis (QS) method: Diluent is added on API powder in a measuring cylinder and its volume is assessed at each production to reach a final volume
- A short retrospective traceability data analysis showed possible variabilities of diluent volumes used for a same final product. A variable dilution volume means a variable endpoint API concentration

We intend to produce these preparations with anticipated larger quantities, called "Hospital Preparations", these products are submitted according to the French regulations to qualitative and quantitative quality controls (QC), including API concentration assay

Objectives

- To assess the impact of API weighing method on the variability of final volumes and if needed, standardizes and validate the weighing preparation process by including the potential impact of the API volumetric characteristics

Methods and Results

The study was carried out with 12 API, 108 preparations were produced and graphed in BPPREP® software :

- RM powder is weighed on a Mettler Toledo precision scale and is stirred into a small dlient volume volume (Syrspend®, Fagron, France)
- The final volume is measured in a 100 mL measuring cylinder
- The measure of the final volume is compared to the volume of the weighed syrup so as to assess the volume shift factor

- 3 technicians were involved in the experiments, preparing each one 3 samples 60 mL for each formulation (one/day, 3 days)
- The data regarding API and syrups weighing and volumes were graphed in the BPPREP software

- They allowed to assess the volume shift factors by means of accuracy and repeatability (CV) % :
  → [m ± CV], compliant if < 5 %

Raw material	Solution concentration (mg/ml)	Results [m ± CV] (%)
ursodesoxycholic acid	30	[6.01 ± 0.6]
Amiodarone	1	[-0.2 ± 0.32]
Amlodipine	1	[-1.11 ± 0]
Baclofen	10	[-0.54 ± 0.16]
Hydrocortisone	1	[-1 ± 0.48]
Isoniazid	10	[-0.59 ± 0.32]
Melatonin	1	[-1.2 ± 0.32]
Propranolol	1	[-1.35 ± 0.16]
Spironolactone	2,5	[-1.61 ± 0.16]
Sulfadiazine	100	[2.61 ± 0.78]
Thiamin	100	[4.75 ± 0.46]
Topiramate	5	[-1.35 ± 0.65]

Rate (%) of Diluent Displacement Factors per MP as a Function of Solution Concentration

Conclusion

- Among the 12 molecules studied, 11 did not lead to major changes in the final volume with non-significant shift factors and no predictable impact on the final QC
- Only the URS has a significant shift factor leading to an expansion of the diluent beyond 5 %, with a large bias
- For URS, a specific production weighing process should be specifically set up, and margins of acceptation of QC results including the variability of the volume of RM from a preparation to another.