Optimization of the control of compounded capsule preparations: feedback on the implementation of an acceptance value for the mass uniformity test

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Introduction

The control of compounded capsule preparations (CCP) in hospital pharmacy units is mainly based on the mass uniformity (UM) test (2.9.5) of the European Pharmacopoeia (Pharm. Eur.). In 2017, out of the 187 CCP manufactured in our pharmacy unit, none were non-compliant (NC) according to UM test.

In order to improve their control, an acceptance value of the UM (VA_{UM}), has been developed based on the acceptance value described by the Pharm. Eur. for the uniformity test (UT) of dosage units (2.9.40). The objective of this work is to assess the impact and relevance of VA_{UM} for CCP control.

Material and method

The VA_{UM} considers the percentage difference (E) between the average capsule mass observed and the theoretical mass calculated from the manufacturing data, and the coefficient of variation (CV) of the sample (CV_{UM}).

$$M_{théo} = \frac{(\text{Mass}_{PA} + \text{Mass}_{Excipient})}{\text{Size of the batch}} + Mass_{capsule\ empty}$$

$$E\% = \frac{(\overline{M_{obs}} - M_{théo})}{M_{théo}} \times 100$$

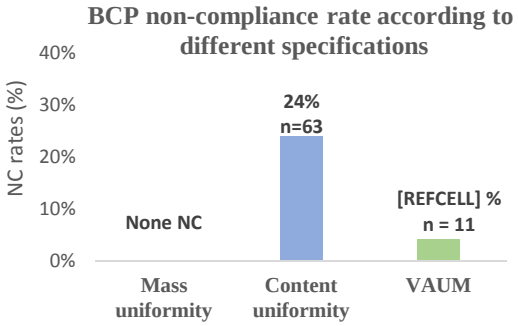
$$VA_{UM} = \text{Abs}(100 - \text{E}\%) + (\text{k} \times CV_{UM})$$ with k=2

A retrospective review of the controls of CCP and batch capsule preparations (BCP) manufactured between March 2018 and March 2020 was carried out:

- On BCP, the NC rates according to UM test and VA_{UM} were compared to those obtained from UT test
- On CCP, the NC rates according to UM test and VA_{UM} were compared.

Résults

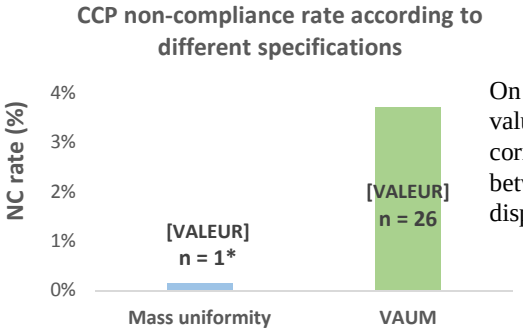
Over the period under study, 263 BCP were manufactured.



	VA_{UM} Compliant (VA_{UM} < 11)	VA_{UM} Non-compliant (VA_{UM} > 11)
Content uniformity conpliant	n = 197 **TN = 74,9 %**	n = 3 **FP = 1,14 %**
Content uniformity non-compliant	n = 55 **FN = 20,9 %**	n = 8 **TP = 3,04 %**

** TN (true negative), FN (false negative), FP (false positive), TP (true positive)*

Over the same period, 694 CCP were realized.



On the 26 CCP NC according to VA_{UM}, values of VA_{UM} were between 11.1 and 37 corresponding to a raw material loss between -2.5% and -32.81% and a dispersion between ± 8.7% and ± 20%.

* With a VA_{UM} of 20,7

Conclusion

On BCP, the low NC rate observed with VA_{UM} compared to the rate obtained with the UT test can be explained by the difference of the factors considered by these 2 controls. The VA_{UM} considers the filling uniformity and manufacturing errors such as addition or loss of raw material. However, unlike the UT, it does not evaluate the homogeneity of the mixture. Nevertheless, on CCP, the VA_{UM} has permitted the detection of 3.7% of CCP NC against 0.15% for the UM test. The VA_{UM} thus allows to complete the UM test which only evaluates the dispersion of the filling and does not consider the theoretical mass related to the quantities used. On the other hand, these results showed a low FP rate making it possible to use VA_{UM} routinely without unnecessary re-manufacturing. Then, the VA_{UM} represents an interesting specification, enhancing the control of CCP and improving their level of safety by simply using a scale.