Quality in pharmaceutical compounding for paediatric patients

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Background and Purpose
Licensed medicines for children are rare. As a result, pharmacy preparation plays a crucial role in this vulnerable patient group but its quality must be assessed carefully. Our hospital pharmacy prepares various capsules for children by crushing and diluting licensed products. For the requested low concentrations, high and sometimes serial dilutions are necessary. We follow good pharmacy practice and use uniformity of mass as our routine quality control.

Material and Methods
Simulating standard concentrations, procedures and quantities, capsule samples were produced by each member of the production team.

We chose sodium chloride as the "active" compound for its accessibility, cost and detectability with one of our standard analytical methods (fig.1). Means, minimum and maximum values for chloride (in % of the labeled concentration) were identified.

The capsules were analysed for uniformity of mass (PH.EUR.6 2.9.5) and for uniformity of content (PH.EUR.6 2.9.6). Subanalysis were conducted using altered uniformity of content criteria. (fig. 2+3)

Results
22 samples, each containing 50 capsules of either 0,1 mg or 1 mg concentration were produced by 11 members of our production team.

All samples (100%) met the PH.EUR.6 2.9.5 requirements for uniformity of mass. 4 (18%) of the samples failed the PH.EUR.6 2.9.6 criteria for uniformity of content.

The mean content of the labeled concentration was 89% (53,1-105,5%).

Subanalysis of the two different sample concentrations were carried out using altered PH.EUR.6 criteria (labeled instead of mean concentration) and are depicted in table 1 and 2.

Table 1 shows that in the 1 mg group (n=11), 3 (27%) conformed to the altered PH.EUR.6 criteria, 3 (27%) were eligible for further analysis and 5 (46%) disaccorded. The average content was 86,1% (78,1-95,3%) of the labeled concentration.

As for table 2: out of the 0,1 mg group (n=11), 2 (18%) met the altered PH.EUR.6 criteria, 2 (18%) allowed further analysis and 7 (64%) failed. The average content was 83,5% (53,1-105,5%) of the labeled concentration.

Conclusion and Discussion
Our study indicates that a routine check of conformity of mass is not sufficient for quality assurance of our preparations. It also showed that the dilutions don’t seem to result in acceptable concentration ranges in the capsules. This conclusion was drawn when we used labeled concentration instead of mean concentration for PH.EUR.6 testing, which in our view is more appropriate for vulnerable patient groups such as children. A re-evaluation of the products and our production methods is planned. We will do uniformity of content testing using original extemporaneously prepared capsules instead of sodium chloride dummy capsules. A change to alternative dosage forms will also be evaluated.