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COMMITTEE FOR MEDICINAL PRODUCT FOR HUMAN USE (CHMP)

GUIDELINE ON THE SUITABILITY OF THE GRADUATION OF DELIVERY DEVICES FOR LIQUID DOSAGE FORMS

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GUIDELINE ON THE SUITABILITY OF THE GRADUATION OF DELIVERY DEVICES FOR LIQUID DOSAGE FORMS

1. INTRODUCTION

1.1 Objective of the Guideline

This guideline is intended to provide recommendations regarding the graduation of delivery devices for liquid dosage forms. The dosing accuracy and precision as well as the suitability of the measuring device will be discussed in relation to the graduation. The guideline seeks to achieve accurate dosing with little and reproducible variation for liquid dosage forms. Notwithstanding the recommendations given, the delivery device shall comply with relevant parts of the requirements given in the Medical Device Directive 93/42/EEC and with ISO standards, if applicable.

1.2 Background

For solid dosage forms, the dosing accuracy is covered by the requirements for assay and uniformity of content and/or mass of the product. For liquid dosage forms, this is mostly not the case as the recommended dose needs to be administered with a measuring device. Only when dosing accuracy can be assured, it is possible to establish a clear relationship between the clinical state of the patient (effects and side effects) and the prescribed and administered dose.

Therefore, it is important to avoid inaccuracies of dosing due to lack of precision of the graduation. Examples that can be given are unreadable graduation, dislocation of the label when the scale is printed on the label, unacceptable graduation scales in view of the prescribed doses, or risk of overdosing.

1.3 Scope of the Guideline

This guideline addresses items related to the graduation of dosing delivery devices for liquid dosage forms, such as solutions, suspensions and emulsions.

Liquid dosage forms for which dosing devices should be used are among others parenteral preparations or liquid preparations for oral use. The product can be suited for single-dose or multi-dose use. In case of single-dose products a measuring device is needed when not necessarily the whole content of the product will be administered to the patient. The dosing device can be marketed with the medicinal product, e.g. syringes without needles to administer oral liquid preparations, measuring cups, spoons, or beakers, pipette applicators. The dosing device can also be incorporated as integral part of the medicinal product, e.g. pre-filled syringes.

2. GENERAL CONCEPTS

2.1 Manner of graduation

The graduation should be applied to the dosing device in such a manner that accurate and precise dosing is guaranteed. The graduation can be embossed in the material. The graduation can also be printed on the material of the dosing device.

This precision and accuracy of dosing should be guaranteed from release throughout storage until the end-of-shelf life and also during the use of the particular dosing device under the conditions recommended in the SPC. Attention should be paid to the possibility of fading of the printing ink. Glueing of a label with a printed graduation to the dosing device is discouraged, because of the possibility of dislocation of the glued label during storage and use.

2.2 Graduated Scale

The graduated scale should be in line with the dosing advice as stated in section 4.2 "Posology and method of administration" of the SPC. This applies in principle to all administration devices. Attention should be paid to the following items:

- Possibility of the dosing device to supply the minimal and maximal dose per single dose (nominal capacity).
- Suitability of the scale intervals in relation to the dosing advice or the dosage range when doses are stated per kg bodyweight or m^2 body surface.
- Ease of interpretation of the graduated scale: readability of the graduation numbers and/or the graduation lines, distinction between the intervals of the scale.

2.3 Suitability of dosing device for the medicinal product

The suitability of the dosing device for the medicinal product should be addressed. Attention should be paid to the following items:

- Dosing accuracy and precision in relation to the therapeutic window of the drug substance.
- The risk of overdosing in relation to the dosing delivery device. If possible, overdosing should be prevented. If the risk of overdosing cannot be avoided, appropriate care should be taken in the design of the scale graduation to prevent overdosing.
- The physical characteristics of the liquid in relation to the dosing device. The combination should assure accurate and precise dosing. Considerations can be for instance the needle diameter and the particle size of suspensions in injectables, the homogeneity (resuspendability) of suspensions and emulsions prior to and during the application of the dosing device, or residual amounts of liquid in the delivery device after administration of the dose to the patient.

Furthermore, suitability of the dosing device and its graduation for the intended patient population should also be taken into account.

2.4 Acceptance criteria

Acceptance criteria should be in line with European Pharmacopoeia requirements, if applicable (for example Ph.Eur. 2.9.27. Uniformity of mass of delivered doses from multidose containers). For single dose containers the same requirements can be applied as for multidose containers.

In the absence of European Pharmacopoeia requirements acceptance criteria may be present in other accepted pharmacopoeias (e.g. United States Pharmacopeia) or in European and/or International Standards (CEN/ISO). For example, for syringes recommendations are given on tolerances, graduated capacity, and graduated scale in ISO standards. These recommendations can be applied without further justification.