European Medicines Agency

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CONCEPT PAPER ON THE DEVELOPMENT OF A COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE (CHMP) GUIDELINE ON DOSING DELIVERY OF INJECTABLE LIQUIDS

Scope and introduction

This concept paper addresses the dosing delivery of injectable liquid dosage forms. It may also be applicable to oral delivery systems. It primarily focuses on the manner of graduation of (multidose) syringes and the graduation scale. Other related aspects such as the injectability of liquid suspensions (needle diameter and particle size) may be addressed.

Problem statement

Some EU member states have granted Marketing Authorisations to injections where the graduation is printed on a label that is glued to the plastic of the syringe, rather than printed on or embossed into the plastic. This approach may cause inaccuracies of dosing, due to lack of precision of the graduation, the exact placement of the label on the syringe, and possible displacement of the label during storage or use. Moreover, the graduation scale should be acceptable in view of prescribed doses. The problem with graduation on syringes is not only theoretical because in daily practice problems have lead to product recalls.

Anticipated benefit to industry and other interested parties

It is to the benefit of each patient, to receive the prescribed dose with little and reproducible variation. Only when this can be assured, it is possible to establish a clear relationship between the clinical state of the patient and the prescribed dose and unexpected side effects and insufficient effect can be acknowledged and attributed to the dose.

For solid dosage forms this aspect is covered by requirements for the assay of the drug product. For liquid dosage forms, this is mostly not the case as these dosage forms need an administration device. Additional guidance on the dosing accuracy of the device itself and for use of the device are on the one hand necessary, but on the other hand presently missing for one of the most critical dosage forms: injectables.

Anticipated benefit regulatory authorities

Consistent European guidance on the way to assess the dosing delivery of injectable liquid dosage forms, with focus on the graduation of syringes.

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Discussion

The discussion will primarily focus on the graduation of a multidose syringes, including.

- The acceptable manner of graduation: by gluing on a label, by printing/embossing in the syringe itself, by both or by both under specified conditions?
- The precision of the delivered dose and its compatibility with the dosing instructions in the SPC
- The risk of overdosing with multidose containers when only parts of the contents are to be used.

Recommendations

- To develop a guideline on the graduation of syringes and related aspects
- To liaise with BWP as this also affects biotech/biologicals
- To liaise with ad hoc GMP Inspectors Working Party for feedback
- To liaise with EN/ISO organisations if necessary in view of consistency
- Literature search
- Possible recommendation to EP
- Considerations of impact on ICH Q8

Timetable

To be added into QWP Work Programme 2004-2005. Draft guideline for consultation planned to be finalised in February 2005 with 6 months consultation period.

Resource requirements for preparation

The guideline has a narrow scope, therefore resource requirements will be limited.

Impact for industry and other interested parties

The final opinion may result in stricter requirements with a need to review its application to already marketed products

Impact assessment for regulatory authorities

Evaluation of present-day assessment policies and future harmonisation

References

None