PHARMACOPOEIAL HARMONISATION

The Pharmacopoeial harmonisation section contains proposals for monographs and general chapters, new or revised, elaborated under the pharmacopoeial harmonisation procedure (see chapter 5.8 of the European Pharmacopoeia). Once these texts have undergone the harmonisation procedure and have been adopted, they will be included in the European Pharmacopoeia and the other pharmacopoeias of the Pharmacopoeial Discussion Group (PDG).

There may be differences between the title of a monograph/general chapter in the Ph. Eur. and in the corresponding draft harmonised text depending on the official nomenclature system used by each pharmacopoeia (for example, the INN).

It is stressed that these proposals have not been adopted by the European Pharmacopoeia Commission and must not be regarded as official texts.

BRIEFING NOTE

This draft corresponds to Revision 2, Stage 2, ver. 1 (based on the Pharmacopoeial Discussion Group (PDG) working procedure) within the pharmacopoeial harmonisation process. The coordinating pharmacopoeia is the Ph. Eur.

The draft harmonised text presented below is published for information. Comments are invited on the revision proposal for the Ph. Eur. general chapter Test for extractable volume of parenteral preparations (2.9.17), which is published in the Texts for comment database (Pharmeuropa 36.2) and shows how this draft harmonised text would affect the current Ph. Eur. general chapter. The Procedure for commenting on Pharmeuropa drafts is located in the Useful information section. Only comments sent before end of June 2024 will be considered for the preparation of the final version of the harmonised text.

The following changes are proposed:

– The testing procedure has been updated, eliminating the requirement for a specific number of test samples to conduct the test. Due to different tolerances regarding the fill volume during production and the performance of the filling equipment, the number of containers to be tested is to be determined using a suitable statistical approach.

– The requirement for the use of a specific syringe and needle has been removed. The size of syringe and needle to use is to be read from the product label to better mimic the clinical practice.

Two sentences have also been deleted from the Single-dose containers section, with the effect that:
– pooling of volumes is no longer allowed when measuring the extracted volume from small containers, since it is important that each container fulfils this requirement;
– direct emptying is no longer described for small volume parenterals in single-dose containers with a capacity of 10 mL or more to better mimic the clinical practice.

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TEST FOR EXTRACTABLE VOLUME OF PARENTERAL PREPARATIONS

Suspensions and emulsions are shaken before withdrawal of the contents and before the determination of the density. Oily and viscous preparations may be warmed according to the instructions on the label, if necessary, and thoroughly shaken immediately before removing the contents. The contents are then cooled to 20-25 °C before measuring the volume.

SINGLE-DOSE CONTAINERS

~~Select 1 container if the nominal volume is 10 mL or more, 3 containers if the nominal volume is more than 3 mL and less than 10 mL, or 5 containers if the nominal volume is 3 mL or less.~~ Determine an appropriate number of containers to be tested, based on the number of units available and a suitable statistical approach. ~~Take up~~ Following the instructions on the label, extract the total contents of each container selected into a suitable, dry syringe ~~of a capacity not exceeding 3 times the volume to be measured, and~~ fitted with a suitable needle, e.g. a 21-gauge needle not less than 2.5 cm in length. Expel any air bubbles from the syringe and needle, taking care not to spill out any product. T~~t~~hen discharge the contents of the syringe without emptying the needle into a ~~standardised~~ calibrated dry cylinder (graduated to contain rather than to deliver the designated volumes) of such ~~size~~ a capacity that the volume to be measured occupies at least 40 per cent of its graduated volume. Alternatively, the volume of the contents in millilitres may be calculated as the mass in grams divided by the density.

~~For containers with a nominal volume of 2 mL or less, the contents of a sufficient number of containers may be pooled to obtain the volume required for the measurement provided that a separate, dry syringe assembly is used for each container. The contents of containers holding 10 mL or more may be determined by opening them and emptying the contents directly into the graduated cylinder or tared beaker.~~

The volume in each container tested is not less than the nominal volume ~~in case of containers examined individually, or, in case of containers with a nominal volume of 2 mL or less, is not less than the sum of the nominal volumes of the containers taken collectively~~.

MULTIDOSE CONTAINERS

For injections in multidose containers labelled to yield a specific number of doses of a stated volume, select one container and proceed as directed for single-dose containers using the same number of separate syringe assemblies as the number of doses specified.

The volume extracted into each syringe is such that it ~~each syringe~~ delivers not less than the ~~stated~~ dose stated on the label.

CARTRIDGES AND PREFILLED SYRINGES

Determine an appropriate number of containers~~for testing~~ to be tested, based on the number of ~~samples~~ units available and a suitable statistical approach. ~~Select 1 container if the nominal volume is 10 mL or more, 3 containers if the nominal volume is more than 3 mL and less than 10 mL, or 5 containers if the nominal volume is 3 mL or less.~~ If necessary, fit the containers with the accessories required for their use (needle, piston, syringe) and transfer the entire contents of each container, without emptying the needle into a dry tared beaker by slowly and ~~constantly~~ continuously depressing the piston. ~~Determine~~ Calculate the volume in millilitres calculated as the mass in grams divided by the density.

The volume measured ~~for~~ in each of the container testeds is not less than the nominal volume.

~~PARENTERAL INFUSIONS~~ LARGE-VOLUME PARENTERALS

Determine an appropriate number of containers ~~for testing~~to be tested, based on the number of ~~samples~~ units available and a suitable statistical approach. ~~Select one container.~~ Transfer the contents of the container into a calibrated dry ~~measuring~~ cylinder of such a capacity that the volume to be ~~determined~~ measured occupies at least 40 per cent of its~~the~~ nominal volume ~~of the cylinder~~. Measure the volume transferred. Alternatively, the volume of the contents in millilitres may be calculated as the mass in grams divided by the density.

The volume in each container tested is not less than the nominal volume.