

USP Requirements for Volumetric Instruments

How to Work with Different Standards in the Lab



Companies producing pharmaceutical products for the US market are monitored by US authorities, e.g. the FDA (Food and Drug Administration) and have to meet the requirements of the USP (United States Pharmacopeia). Besides many instructions for analytical procedures the USP defines the equipment to be used for these processes. However, the differences between USP and DIN EN ISO can pose a difficult task for work with glass volumetric instruments in European labs.

Section 31 outlines the requirements for volumetric instruments to be utilized. A most important requirement of the USP is the mandatory use of glass volumetric instruments with accuracy according to class A. Due to some clauses this seemingly easy demand eventually turns out to be difficult to understand.

On the one hand, the requirements for volumetric flasks, transfer pipets, micro-burets, and graduated burets in the USP refer to ASTM standards. On the other hand, for graduated pipets and graduated cylinders the USP specifies explicitly their requirements in the aforementioned section 31. Moreover, class A

error limits required by USP as well as the described nominal capacities are different from the correspondent ISO data. This diversity hampers an easy and appropriate work with glass volumetric instruments in European laboratories, if they have to follow the demands of the USP. Thus, the subsequent sections will explain the important requirements, namely nominal capacity (Figure 1) and error limits (Figure 2) for all types of USP glass volumetric instruments and compare these data with the relevant DIN EN ISO standards.

First of all, some general remarks that should be considered:

- Minimum and maximum capacities stated in the respective USP/ASTM and ISO standards should be interpreted as sharp limits. Therefore additional nominal capacities below or above these limits cannot refer to any of these standards.

- Since the construction specifications of USP/ASTM and ISO differ completely, manufacturers usually just focus on the usability of

volumetric instruments: the class A error limits for the types and sizes described by USP/ASTM.

- For volumetric instruments with nominal capacities not stated in a standard, the USP/ASTM standards typically refer to specifications of the next smaller capacity. In contrast ISO standards refer to specifications of the next nearest capacity (or prescribe to keep fundamental specifications like shape and some important dimensions).

- According to ISO standards for 'Ex' adjusted volumetric instruments (pipets and burets) class AS – with S for swift delivery – is defined as highest quality grade. USP/ASTM standards do not contain such a specification. They just define class A for highest quality grade of volumetric instruments.

Transfer Pipets and Graduated Pipets

For transfer pipets the USP refers to the ASTM standard E 969. Contrarily to DIN EN ISO 648 transfer pipets with two marks are not mentioned in the ASTM E 969. Hence, this kind of volumetric instruments should not be used for applications supervised by US authorities (FDA). Specifications of transfer pipets with one mark in accordance with ISO are only included for the nominal capacities 0.5, 1, 2, 5, 10, 20, 25, 50 and 100 ml, while ASTM standard E 969 defines the capacities 3, 4, 6, 7, 8, 9, 15, 30 and 40 ml in addition to the aforementioned values. The majority of nominal capacities for transfer pipets have to meet the same error limits whether in accordance with ASTM or ISO. Just class A ASTM error limits of transfer pipets with nominal capacities of 1, 2, 4, 5, 6 and 7 ml are tighter than class AS ISO error limits. The 0.5 ml transfer pipets represent a particular case as the class AS ISO error limit of this pipet is the only one to be tighter than the class A ASTM error limits.

The USP defines the specifications for graduated pipets with nominal capacities 1, 2, 5, and 10 ml as well as the respective class A error limits directly in the section 31. In contrast to the DIN EN ISO 835 just type 2 graduated pipets are mentioned. As a consequence the commonly known types 1 and 3 pipets should not be used for applications supervised by US authorities. Class A USP error limits of the 5 and 10 ml graduated pipets are tighter than class AS error limits of the correlated ISO standard, while the 2 ml graduated pipet exhibits the same error limit with reference to both standards. The 1 ml graduated pipet represents another particular case as the class AS ISO error limit of this pipet is tighter than the class A USP error limit.

Flasks, Cylinders, Burets

For volumetric flasks the USP refers to ASTM standard E 288, which does

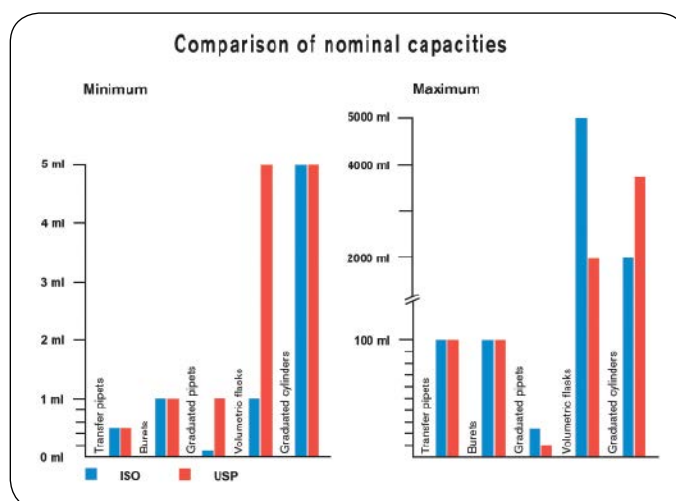


Fig. 1: Comparison of minimal (left) and maximal nominal capacities (right) defined by USP/ASTM and ISO

not state nominal capacities below 5 ml and above 2000 ml. Hence, the commonly known 1 and 2 ml trapezoidal flasks and the 5000 ml bulb-shaped flasks should not be used for applications supervised by US authorities. The USP refers to the ASTM

standard E 288, which describes tighter class A error limits than the comparable DIN EN ISO 1042 for all sizes of volumetric flasks.

Specifications for graduated cylinders are mentioned in section 31 of the USP. In comparison with

the respective DIN EN ISO 4788 4 sizes, namely the capacities 5, 10, 100, and 250 ml, show the same error limits. Class A error limits of the other 5 nominal capacities (25, 50, 500, 1000, and 2000 ml) defined by USP are tighter than the corresponding limits of the ISO standard. Please note that class A error limits for mixing cylinders are the same as for graduated cylinders regardless whether they are with reference to USP or ISO.

For burets the USP refers to ASTM standards E 287 for graduated burets (nominal capacities from 10 to 100 ml) and E 1189 for micro-burets (nominal capacities from 1 to 10 ml) while the respective DIN EN ISO standard 385 describes specifications for nominal capacities from 1 to 100 ml. Class A error limits of USP/ASTM are the same as the class AS error limits of ISO. However, they may differ with regard to the commonly known 25 ml buret, which is not described by USP/

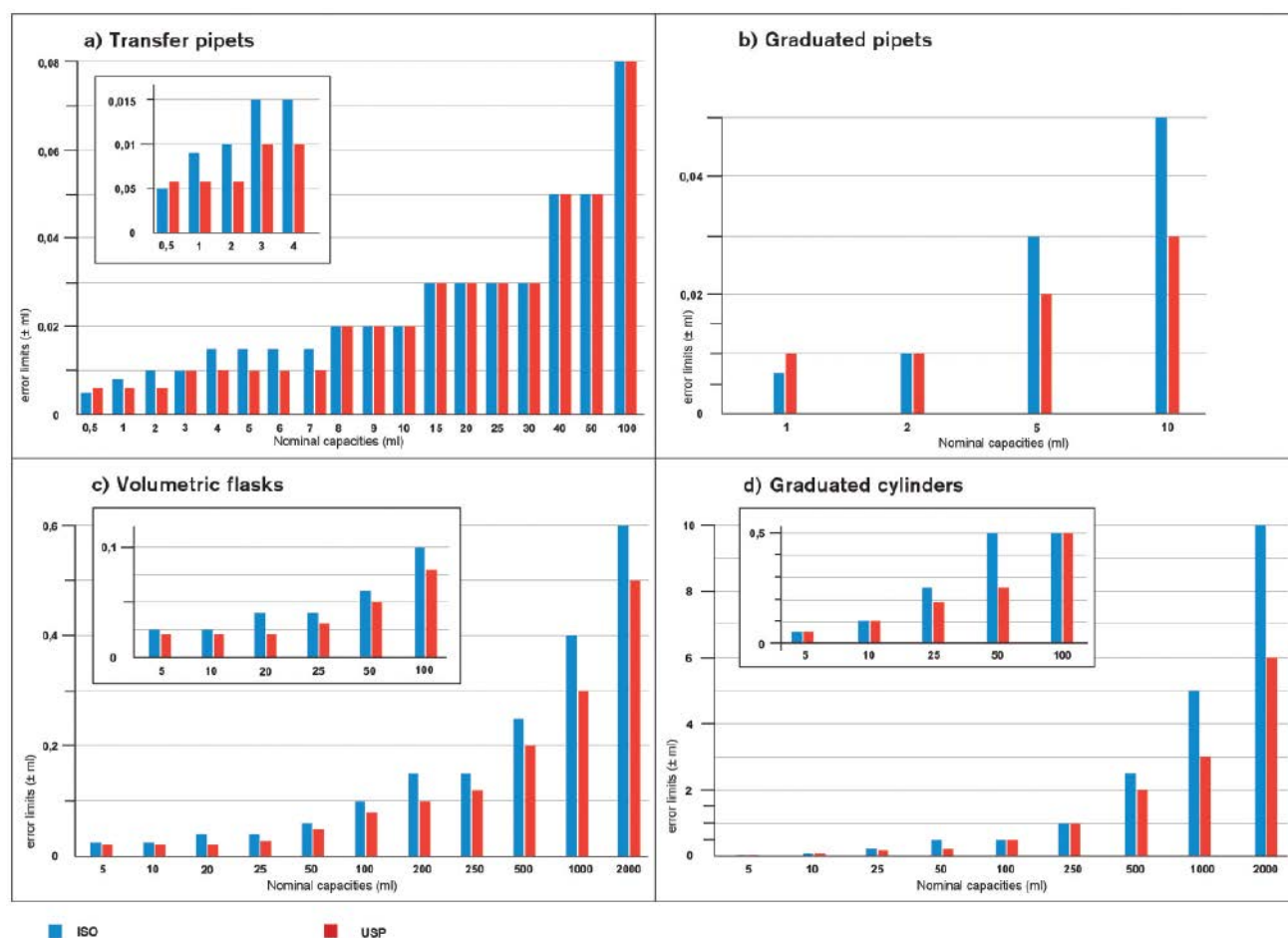


Fig. 2: Error limits of highest quality grade volumetric instruments in accordance with USP/ASTM (class A) or ISO (class A or AS): a) transfer pipets: Capacities 3, 4, 6, 7, 8, 9, 15, 30 and 40 ml are not stated in ISO; b) graduated pipets; c) volumetric flasks: Capacity 20 ml is not stated in USP/ASTM; d) graduated cylinders. Please note general remark 3 for capacities not stated in a standard.

ASTM with a subdivision of 0.05 ml and, thus, should not be used for applications supervised by US authorities. All other kinds of class AS ISO burets can be used if they are marked with the inscription USP.

Summary

As mentioned at the start of this report, the diversity of commonalities and differences hampers an easy and appropriate work with glass volumetric instruments for end-users in European laboratories, if they have to follow the requirements of the USP/ASTM. Some manufacturers have modified their production lines to be able to offer volumetric instruments that fulfill both the class A error limits required by USP/ASTM, and the construction specifications of the respective DIN EN ISO standards. Usually changes are made to the certificates which refer to the USP/ASTM standards and, therefore, to the class A error limits demanded by USP/ASTM. More-



Fig. 3: Examples for inscriptions of 5 ml transfer pipet in accord with ISO (left) or USP/ASTM (right)

over, the DIN EN ISO standards are also printed on these certificates as the construction specifications and maximal permissible errors are met as well. It is possible to confirm smaller values for the maximal permissible errors, because standards prescribe only the maximal permissible error. Hence, in the particular

cases of 1 ml graduated pipet and the 0.5 ml transfer pipet, whose class AS ISO error limits are smaller than the class A USP/ASTM error limits, the smaller one can be chosen.

To differentiate between volumetric instruments in accordance with class A error limits required by

USP and highest quality grade (class A or AS) following ISO, manufacturers print USP on the volumetric instrument (Fig. 3) and deliver either batch or individual certificates with USP and/or ASTM references. For applications supervised by US authorities like the FDA these USP volumetric instruments should be chosen instead of the ISO volumetric instruments. The calibration could be done in accordance with the established working plans as the DIN EN ISO 4787 shall be used for volumetric instruments whether according to USP/ASTM or ISO standards.

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