



IntelliFill® i.v. Syringe Accuracy



INTRODUCTION

IntelliFill i.v. fills doses into syringes that are intended primarily for manual use. When a syringe is used manually, users tend to treat the markings on the syringe as if they are completely accurate. However, the accuracy of syringes is governed by an ISO standard (ISO 7886-1) that permits a defined range of error in the accuracy of those markings.

When a syringe is filled by the IntelliFill i.v., the markings on the syringe are not used to measure the fluid; the mechanisms used to fill the syringe are expected to be more accurate than those markings may be.

The result is that a properly filled syringe may appear to be improperly filled when the markings on the syringe are used to make that determination.

RESPONSIBILITIES

Pharmacies have the responsibility for developing and enforcing their own policies and procedures regarding visual checking of syringes produced by IntelliFill i.v. The information in this document is intended to assist them in this regard.

ISO 7886-1 ACCURACY LIMITS

Table 1 – Capacity tolerance, dead space, scale dimensions and test forces

Nominal capacity of syringe, V mL	Tolerance on any graduated capacity		Maximum dead space mL	Minimum overall length of scale to nominal capacity mark mm	Scale Internal mL	Increment between graduation lines to be numbered mL	Forces for leakage testing (see annex D)	
	Less than half nominal capacity	Equal to or greater than half nominal capacity					Side force (±5%) N	Axial pressure (gauge) (±5%) kPa
V<2	± (1.5% of V+2% of expelled volume)	± 5% of expelled volume	0.07	57	0.05	0.1	0.25	300
2<V<5	± (1.5% of V+2% of expelled volume)	± 5% of expelled volume	0.07	27	0.2	0.5 or 1	1.0	300
5<V<10	± (1.5% of V+2% of expelled volume)	± 4% of expelled volume	0.075	36	0.5	1	2.0	300
10<V<20	± (1.5% of V+2% of expelled volume)	± 4% of expelled volume	0.10	44	1.0	5	3.0	300
20<V<30	± (1.5% of V+2% of expelled volume)	± 4% of expelled volume	0.15	52	2.0	10	3.0	200
30<V<50	± (1.5% of V+2% of expelled volume)	± 4% of expelled volume	0.17	67	2.0	10	3.0	200
50<V	± (1.5% of V+2% of expelled volume)	± 4% of expelled volume	0.20	75	5.0	10	3.0	200

IntelliFill i.v. operates using a Terumo 10 mL syringe. According to Table 1 (above) in ISO 7886-1, this means that the Terumo syringe (in the group of syringes whose volume is in the range $10 \leq V < 20$) has the following accuracy specifications:

- If the volume to be delivered is ≤ 6 mL, the percent variance is computed as $\pm (0.18 \text{ mL} + 1\% \text{ of volume})$
- If the volume to be delivered is > 6 mL, the percent variance is $\pm 4\%$

The following table shows the permitted error and the resulting percent error for a range of volumes between 0.5 mL and 11.5 mL:

Volume	Variance	Percent
0.5	0.19	37.5%
1	0.20	20.0%
1.5	0.20	13.5%
2	0.21	10.5%
2.5	0.22	8.7%
3	0.23	7.5%
3.5	0.23	6.6%
4	0.24	6.0%
4.5	0.25	5.5%
5	0.26	5.1%
5.5	0.26	4.8%
6	0.27	4.5%
6.5	0.26	4.0%
7	0.28	4.0%
7.5	0.30	4.0%
8	0.32	4.0%
8.5	0.34	4.0%
9	0.36	4.0%
9.5	0.38	4.0%
10	0.40	4.0%
10.5	0.42	4.0%
11	0.44	4.0%
11.5	0.46	4.0%

Depending on the volume, a syringe that appears to be accurately filled to visual inspection may be off by as little as 0.19 mL or as much as 0.46 mL.

When a Terumo syringe is pulled to the 10 mL volume, it may actually hold as little as 9.6 mL or as much as 10.4 mL.

When a Terumo syringe is pulled to 1 mL, it may contain as little as 0.8 mL or as much as 1.2 mL.

Table 1 also indicates that the graduations that would apply to the Terumo 10 mL syringe would have major graduations at 1 mL increments with five sub-markings (0.2 mL increments). This would generally be taken to mean that a human could read the scale to a precision of ± 0.2 mL.

INTELLIFILL i.v. ACCURACY VERIFICATION

IntelliFill i.v. verifies syringe filling by weighing the syringe. The balance used for this purpose is accurate to ± 0.01 g which, for water, translates to ± 0.01 mL.

The pumping mechanism used to deliver the solution into the syringe moves over the range of 10 mL in 40,000 steps, representing a resolution of 0.00025 mL per step. A failure to move 100 steps is barely in the detectable range for the scale. Variance in the delivery system comes from hysteresis in the disposable components of the delivery system and in the pump itself.

The theoretical weight of any syringe is determined by the formula:

(Volume X Density) + SyringeTareWeight

This presumes that syringe tare weight is effectively a constant and, for any given drug, density is a constant. To the extent that this is true, the weight of the syringe can be used to verify the delivery of fluid into the syringe. Given that the weight can be measured to 0.01 g, this represents an ability to assess volume that is, at least theoretically, more sensitive than the ability of the human eye to discern volume on the syringe.

Variance in the weight comes primarily from two sources, the actual drug solution-specific gravity, and the dry weight of the syringe:

- **Drug Solution Density** – The drug solution density can show variation if the drug is reconstituted. Variation can come from the amount of powder in the vial (manufacturers are allowed as much as 15% variance in this number), and in the amount of diluent placed in the vial. Density (or specific gravity) is not a routinely reported value for drug solutions, so customers must determine this value for themselves. This adds further variance to the process.
- **Dry Weight of the Syringe** – IntelliFill i.v. loads syringes in a band, which prevents tare weighing of each syringe before filling. As a result, the weight verification system must use a statistically derived tare weight for the syringe dry weight that includes the weight of the syringe, its attached band, attached label and cap.

Baxa determines this statistically derived mean weight by processing (but not filling) 500 syringes on at least two IntelliFill i.v. devices and then computing the variation as four times the standard deviation of the mean weight. This variance consistently falls in the range of ± 0.15 to 0.20 g. Obviously, if there is a labeling failure that requires application of an additional label to the syringe, this further affects the tare weight of the syringe.

The weight verification system applies a site-defined, drug-specific weight variance for each syringe. This variance is expressed as a percentage of the delivered volume.

Therefore, as the dose in the syringe gets smaller, the effect of the variance in the dry weight of the syringe and/or the variance in the actual density of the drug solution becomes more significant. As a result, the software may reject syringes that are accurately filled.

CONCLUSION

Human visual acuity on a Terumo 10 mL syringe is limited to approximately 0.2 mL, presuming the scale is placed accurately.

Scale placement is permitted to vary by as little as 0.2 mL and as much as 0.46 mL.

Syringe tare weight variance may vary by 0.2 mL.

As a result, IntelliFill i.v. syringes that appear to be filled within ± 0.2 mL should be considered accurately filled.

IntelliFill i.v. is manufactured for Baxa Corporation by FHT, Inc.

¹ International Standards Organization. "Sterile hypodermic syringes for single use – Part 1: Syringes for manual use. ISO 7886-1:1993.