Baxa Corporation

Syringe Filling Accuracy

Technical Paper

Repeatable volume accuracy in syringe filling using the Rapid-Fill Automated Syringe Filling System.

Baxa Corporation
14445 Grasslands Drive
Englewood, CO 80112

tel: 303-690-4204
fax: 303-690-4804
www.baxa.com

Introduction

The Rapid-Fill™ Automated Syringe Filler (ASF) is designed to automate the process of filling, capping and labeling sterile, batch syringes. The Rapid-Fill ASF uses an integrated disposable of banded, capped syringes to accomplish this automation. A band of 200 syringes is loaded onto the drum of the Rapid-Fill ASF and is indexed forward on each fill. Once the source container tube set is primed with fluid and a syringe is in place, the system removes the syringe cap and connects the source container tube set to the syringe. The Rapid-Fill ASF then fills the syringes by pulling their plunger to a specified position, drawing fluid from the source container. The purpose of this evaluation is to demonstrate the repeatable accuracy of syringe volume delivery for the Rapid-Fill Automated Syringe Filler.

Syringe manufacturers are expected to meet ISO 7886, the standard for Sterile Hypodermic Syringes for Single Use, among other published quality and accuracy guidelines. This standard includes the expected accuracy limits for delivery volumes. These limits are stated as ± 5% at half scale and ± 4% at full scale. According to the standard, therefore, if a syringe is filled manually and its air expelled leaving the plunger position on the 10 mL line, the volume dispensed must be between 9.6 and 10.4 mL. Or, if the syringe contains exactly 10 mL, its plunger position must be between the 9.6 and 10.4 mL graduation lines. Since plastic syringes are injection molded, variations in the molded parts are low, relative to the ISO standard. However, the placement of the graduation lines on the syringe barrel may vary significantly relative to the ISO standard.

Assuming that process variations are normal with very good production capability, (that is, a process capability index or Cpk of 1.3) statistics predict the following results from manual syringe filling of a 10 mL volume, using the graduation marks:

- Less than 67% of the volumes would be within ± 0.1 mL
- Less than 85% would be within ± 0.15 mL
- Less than 95% would be within ± 0.20 mL of the desired volume.

When measured against the results above, the Rapid Fill ASF has far greater repeatable delivery accuracy than that expected for the printed graduation lines on a syringe. Therefore, using syringe graduation lines as an indicator of accuracy for the Rapid Fill System, will produce inaccurate and unreliable results.

Testing

The testing described in this paper is designed to provide statistically reproducible measurements for the delivery accuracy of the Rapid-Fill ASF in plastic syringes.

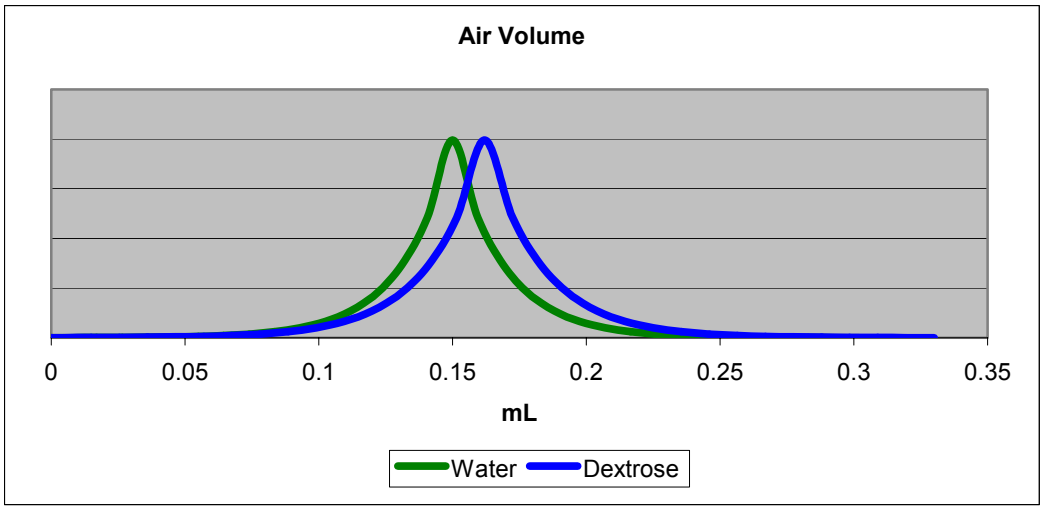
Air Volume

As with all machine-assisted syringe filling processes, a small volume of air remains in the syringe filled by the Rapid-Fill ASF. This air volume is generally small, approximately 0.2 mL. Additional air volume maybe be present when filling syringes with more viscous drugs. Since the total internal volume of a filled syringe includes the air, to achieve an accurate fluid volume the syringe plunger must be pulled to a position greater than the desired dose, i.e., about 10.2 mL for a 10 mL dose.

Therefore, the first accuracy measurement verified was the air volume created when filling syringes with the Rapid-Fill ASF. Testers measured the volume of air in 264 syringes filled on five different machines, using 45 different tube sets. Two different liquids, water and 20% dextrose, were used to represent a range of IV fluid viscosities. Air volume raw data results are shown in the table below.

Air Volume Statistical Data (mL)			
Water		**20% Dextrose**	
Average	Standard Deviation	Average	Standard Deviation
0.162	0.0419	0.150	0.0379

The normal bell-shaped curve for this data is shown in the graph below.



Fluid Volume

The Rapid-Fill ASF uses the syringe plunger position to determine total volume filled. Therefore, if an operator enters the value of 10.2 mL for desired volume (to accommodate both fluid and air), the plunger will be pulled to the volume of 10.2 mL and the delivered fluid volume will be 10 mL. The repeated accuracy of the pulled plunger position is very tight. However, variations in syringe plunger length and barrel diameter will affect volume variation for a given plunger position.

The second accuracy measurement performed was designed to ensure the repeatable accuracy for fluid volumes in syringes filled by the Rapid-Fill System. For the test, 1,800 syringes were filled with water and 20% dextrose. Five machines and 90 tube sets were used for fill volumes of 1, 10 and 12 mL.

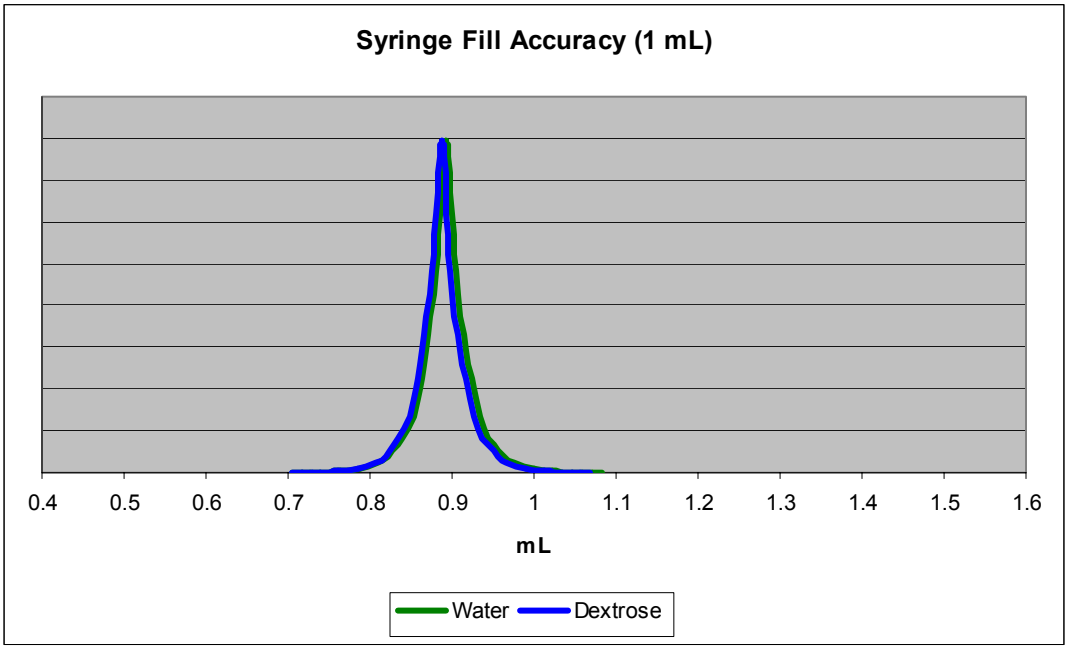
The table below shows the statistical values for the data.

	Accuracy Statistical Data			
	Water		**20% Dextrose**	
mL	Average	Standard Deviation	Average	Standard Deviation
1	0.893	0.0472	0.887	0.0454
10	9.909	0.0436	9.785	0.0445
12	11.903	0.0478	11.738	0.0544

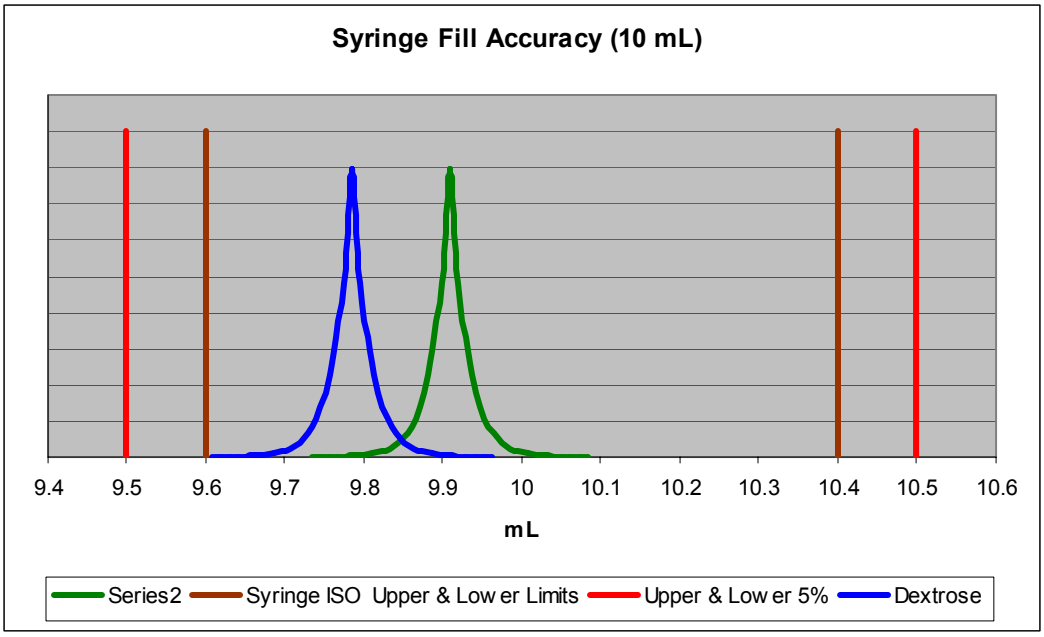
The maximum standard deviation for the tested syringes was 0.544 mL. With this result, statistic analysis predicts the following accuracy for delivered volumes:

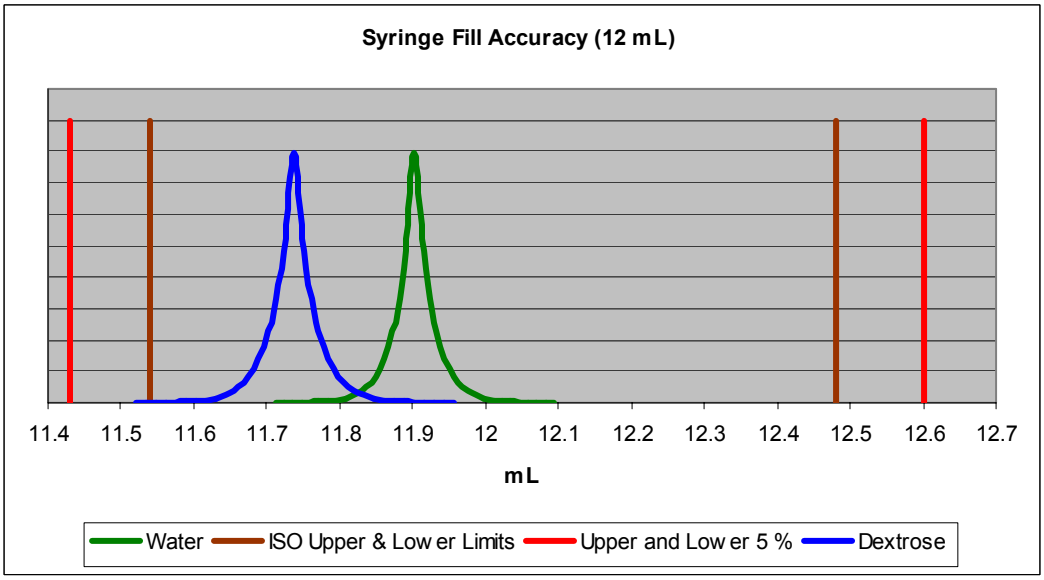
- Greater than 93% within ± 0.1 mL
- Greater 99.4% within ± 0.15 mL
- 99.98% ± 0.20 mL

The following charts demonstrate how the Rapid-Fill ASF's tested syringe filling accuracy compares to the ± 5% pharmacy guideline and the ISO standard. The charts show individual results for 1, 10 and 12 mL fill volumes at both extremes for drug viscosity, i.e., water and 20% dextrose. The charts also include the results for water and dextrose fill volumes without taking into account the air volume, i.e., where the requested fill volumes were 1, 10 and 12 mL, respectively. These values indicate the impact of the air volume in the syringe. Increasing the requested fill volume by 0.1 to 0.25 mL to account for the air in the syringe would have produced curves aligned with the requested delivery volume.



NOTE: Since syringes are generally not used at volumes less than half scale, the 5% and ISO standard lines were omitted on this chart.





Conclusion

Testing demonstrated the repeatable accuracy of the Rapid-Fill Automated Syringe Filler for volumes from 1 to 12 mL. Data clearly show that delivery accuracy using the Rapid-Fill ASF is well within acceptable pharmacy guidelines for both water and viscous fluids. This accuracy is shown for fills taking syringe air volume into account. Therefore, operators using the Rapid-Fill ASF as outlined in the Operator Manual can expect to deliver accurate fluid volumes in plastic syringes.

The Rapid-Fill ASF fills syringes by pulling their plunger to a designated length. So, there is no pump calibration to perform and check during setup. Further, the plunger pulling mechanism does not drift, so users have a high degree of confidence that a defined batch, i.e., drug and fill-volume setting, will produce accurate, repeatable delivery volumes, from the beginning to the end of the run.