

Baxa Corporation

Fluid Dynamics and the EM2400

Technical Paper

An investigation and analysis of the impact of specific gravity on ingredient exchange while filling TPN bags with the Baxa automated compounder.



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Introduction

Baxa Corporation designs, builds, markets and supports state-of-the-art automated compounders and software for mixing multi-ingredient parenteral solutions. The Exacta-Mix 2400 Compounder (EM2400), introduced in December 2001, represents the most advanced technology for automated compounding and medication safety in the industry.

This paper describes the impact of fluid dynamics on ingredient exchange, the software changes that were made to minimize this exchange on the EM2400 and how the compounder's performance was measured and tested to ensure the integrity of the final compounded solutions.

Scope of Investigation

This investigation applies to the use of the EM2400 Compounder with fluids of varying specific gravities. Its intent is to demonstrate that differences in specific gravities provide a driving force for fluid exchange in the EM2400 Fluid Inlets. The testers then use worst-case examples of specific gravities and delivery volumes to determine where the system is most vulnerable to specific gravity differences by quantifying the maximum delivery of unintended ingredients through this mechanism.

Potassium phosphates (Kphos, 3mMol/mL phosphorus) and sterile water with methylene blue dye have a relatively large specific gravity differential (1.32 and 1 respectively). Therefore when methylene blue, a dye indicator in water, is in the valve manifold and Kphos is in the inlet line, opening the valve should result in methylene blue flow up the Kphos inlet line. Presence of methylene blue in the Kphos inlet line supports the theory that the differential in specific gravity is the mixing mechanism. Since methylene blue is dark blue, it will be visually evident as it travels up the inlet line. The contents of the inlet line will be pumped into a collection container for evaluation via spectrophotometry, which provides a means of identifying and quantifying the amount of dye in a mixture, based on light absorption at various wavelengths along the UV-visible scale.

Other factors that affect fluid exchange are time (how long the ingredients are exposed to each other) and the fluid interface area in the valve. Both of these factors need to be minimized, and EM2400 Operating Software Version 1.03 addresses these requirements by:

Valve Closure – The valve no longer remains open during an alarm condition. (e.g., air detection, occlusion detection, pump lid open, user-selected pause). If the user chooses to resume operation, the compounder will continue under normal operation.

Valve Partial Opening for Low Speeds - For deliveries at volumes less than 10 mL, the compounder only partially opens the valve.

Test Method

Testers pumped 10 mL of a low-specific gravity fluid (methylene blue mixed with sterile water) into the EM2400 Valve Body prior to pumping a high-specific

gravity ingredient (Kphos – potassium phosphate). The 10 mL volume is slightly greater than the volume of the valve body manifold, thus ensuring that the entire manifold filled with the low-specific gravity ingredient.

Next, 0.2 mL of the high-specific gravity ingredient was pumped. This represented the smallest delivery volume that could be made in order to actuate the valve. This places the delivery volume in the $\pm 10\%$ range, or ± 0.02 mL. Since the mechanism driving the fluid exchange is specific gravity, the volume is constant and therefore the volume of the low-specific gravity ingredient entering the high-specific gravity inlet is the same volume as the high-specific gravity ingredient entering the valve body manifold. The valve then closed, and the fluid was flushed to the collection container (Figure 1, Fluid Section B).

In a second delivery cycle, 10 mL of the high-specific gravity source ingredient was pumped, followed by a 30 mL flush with sterile water, to ensure that any ingredient exchanged was captured in the collection container. The 10 mL volume was selected, as it is greater than four times the volume of the micro-inlet tubing. This ensured that any exchanged residual low-specific gravity fluid was flushed out of the 175 Micro-Volume Inlet (Figure 1, Fluid Section A). This delivery was analyzed for content using spectrophotometry.

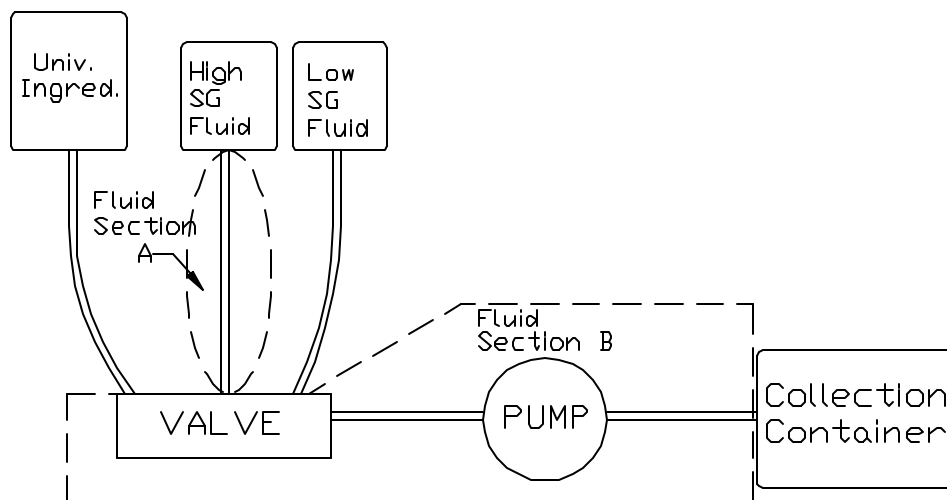


Figure 1

Since the fluid mechanism can be shown to be a constant-volume displacement due to the specific gravity difference, the measured amount of unintended low-specific gravity ingredient in the second collection (Figure 1, Fluid Section A) represents the same volume as the extra high-specific gravity ingredient from the first collection (Figure 1, Fluid Section B). It is more accurate to measure the amount of unintended ingredient than to measure extra ingredient delivered since any delivery has an accuracy tolerance applied to it as well. The tolerance for an individual ingredient delivery may prevent detection of extra ingredient delivered due to specific gravity differences.

To measure ingredient mixing during an alarm condition, testers dispensed 10 mL of low-specific gravity fluid (methylene blue mixed with sterile water) into the valve body. They then dispensed 10.01 mL of Kphos, which caused the valve

position to be wide open and is considered a worse-case condition. The pump cover was opened after the Kphos valve opened. This alarm condition causes the valve to close. Next, the valve set was flushed with sterile water. Then 10 mL of Kphos was pumped into the collection container, followed by a 30 mL flush with sterile water to ensure that any ingredient exchanged was captured (Fluid Section A). This delivery was analyzed for content using spectrophotometry.

Test Results

Ingredient exchange was verified by spectrophotometer analysis of the fluids pumped into the collection container under careful laboratory conditions. A statistically significant (90% confidence/ 90% reliability) number of data points were collected using multiple EM2400's, 724 Valve Sets and 175 Micro Volume Inlets and the mean and standard deviation of ingredient volumes exchanged under normal operating and alarm conditions were calculated.

The table below summarizes the raw data results during normal operation under worst case conditions:

Delivery Volume	Accuracy Range	Exchange Volume Mean	Standard Deviation	# of Data Points
0.2 mL	± 0.02 mL or 10%	0.0068 mL	0.0022 mL	24

The table below summarizes the raw data results during an alarm condition under worst case conditions:

Delivery Volume	Accuracy Range	Exchange Volume Mean	Standard Deviation	# of Data Points
10.01 mL	± 0.3 mL or 3%	0.0328 mL	0.0072 mL	24

Conclusion

The testing demonstrates that specific gravity differences do provide a driving force for fluid exchange in the EM2400 Fluid Inlets. Under the worst-case scenario of pumping ingredients with the greatest difference of specific gravities at delivery volumes where the system is most sensitive to specific gravity differences, the amount of ingredient volumes exchanged, both during normal operation and under alarm conditions, falls within the EM2400 accuracy specifications for a given delivery volume.