ILC DOVER

BEYOND BOUNDARIES™

Rapid Large Scale Mixing of Clumped Powder Validated by Testing

OVERVIEW

Mixing powders into liquids efficiently is crucial to productivity in pharmaceutical and biopharmaceutical manufacturing. In some operations, high shear is beneficial, and the resulting heat causes no problems. However, for operations where low shear and high product integrity are required, traditional technologies pose a risk to the quality of the final product.

For these applications, ILC Dover has developed a patented venturi system that nullifies shear and excessive heat, while ensuring complete powder mixing. To prove efficacy, ILC Dover partnered with a large manufacturer to test the system in the manufacturer's plant.

This white paper reviews the technology, operation and testing protocols, and presents the results that demonstrate the venturi system's efficacy for low-shear, low-heat applications.

FIGURE 1

FIGURE 2

TECHNOLOGY-DRIVEN, APPLICATION-PROVEN

cGMP MIXING ADVANTAGES

ILC Dover's JetSolutions JetMixer™ system takes advantage of vacuum created by a patented venturi configuration (Fig.1) to draw powder into the mixing chamber, particle by particle. Because of that, the system offers the following characteristics:

- Virtually no shear forces exerted on the powder, with no product heating, so the powder's properties are preserved
- Particle-by-particle introduction of powder via strong vacuum, which helps prevent bridging and improves mixing
- Efficient powder delivery at viscosities from 1 cP to 10,000 cP
- Rapid mixing and complete dissolution of powder, without clumping
- Very low energy consumption

SYSTEM DESIGN ADVANTAGES

Built around the patented mixing chamber, the complete JetMixer system (Fig. 2) has been designed to provide maximum utility and versatility. System design features include:

- Small footprint and mobile design that allows for the use of one system for several processes
- Couplings that interface easily with flexible or rigid isolators, FIBC discharge stations and more
- Improved ergonomics for better worker safety (operates at floor level, with no need to lift powder to mezzanine-mounted tanks, which reduces the risk to workers of lifting heavy powders)
- Geometry that ensures effective WIP/CIP (wash-in-place/clean-in-place) operations
- Pump, piping and mixing chamber that easily handle viscous solutions
- No-tool disassembly of piping system to speed turnaround

PATENTED VENTURI NOZZLE SYSTEM

The JetMixer system's patented nozzle system creates an accelerated jet that draws a surprising amount of powder into the liquid stream, without introducing clumping, shearing or heating (Fig. 3). The hopper system and constant level of venturi-generated vacuum ensure particle-by-particle induction and mixing, even with high-viscosity fluids. The system works equally well for mixing solid suspensions into liquids or for liquid-liquid mixing. In all cases, the components are uniformly mixed to form a homogeneous fluid.

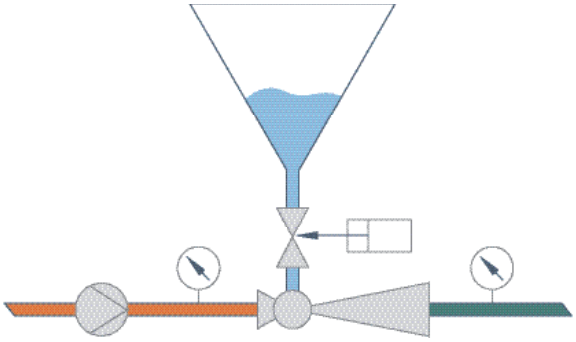


FIGURE 3

SIMPLE SYSTEM COMPONENTS KEEP MAINTENANCE AND OPERATING COSTS LOW

The JetMixer system consists of a limited number of simple components. A pump provides the driving force needed for operation. With only one moving part, the pump is long-lasting, easy to clean and simple to maintain. Energy consumption is also low, which contributes to low system operating costs.

The venturi system and mixing chamber contain no moving parts (Fig. 4), while featuring smooth, polished flow channels with no crevices, edges or other impediments to WIP/CIP operations.

An inherently smooth geometry makes the system particularly suited for cGMP pharmaceutical and biopharmaceutical processes, where CIP is a must and cross-contamination can imperil large amounts of high-value product.

The JetMixer system can handle operating viscosities ranging from 1 cP to 10,000 cP. At the same time, the all-stainless-steel system is robust, and capable of operating at very low vacuum and high process temperatures.

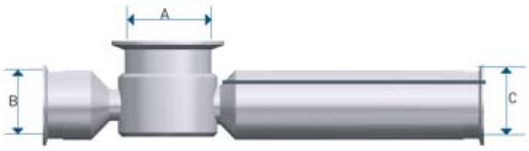
Moreover, since splashing and vapor production are not an issue with the JetMixer system, concerns over powder bridging above the powder feed valve are eliminated.

VERSATILE SYSTEM DESIGN AND RANGE OF SIZES ACCOMMODATE A WIDE VARIETY OF APPLICATIONS

In addition to the standard compact, mobile and fixed skid-mounted forms, the JetMixer system can be easily configured to conform to dust-free or highly contained process environments. Optional provisions can render the system fully compatible with nitrogen blanketing and other inert-gas protection protocols, and jacketing can be provided for heating or cooling, as the process requires.

JetMixer systems are available in seven outflow capacities, ranging from 2 to 100 m3/hr. Powder feed, inlet and mixture outlet sizes vary accordingly and can be easily matched to process requirements (Fig. 5).

FIGURE 4



	PST 25/40/25	PST 40/65/40	PST 50/80/50	PST 65/100/65	PST 80/125/80	PST 100/150/100	PST 125/200/125
A — Powder feeding	40mm	40mm	5	65mm	80mm	100mm	125mm
B — Liquid inlet	25mm	65mm	80mm	100mm	125mm	150mm	200mm
C — Mixture outlet	25mm	40mm	50mm	65mm	80mm	100mm	125mm
Outflow [m³/h]	2	6	12	20	30	65	100
Powder injection [l/h]	10% to 28%	10% to 28%	10% to 28%	10% to 28%	10% to 28%	10% to 28%	10% to 28%

FIGURE 5: JETMIXER SYSTEM SIZE OPTIONS

TURNKEY SYSTEMS TO SOLVE POWDER-HANDLING CHALLENGES

For powders that tend to clump or aggregate, we offer rotating comb systems for fluidization (Fig. 6) or our JetBreaker™ delumping system (Fig. 7). And for particles in suspension, we can provide homogenizers that can be calibrated to produce specific final particle sizes. In fact, we have demonstrated complete delumping and mixing of media and buffers, even at a charging rate of 1,250 kg per hour, when used in conjunction with our drum tipper and JetBreaker delumper. This allows for rapid, efficient mixing of large quantities of buffer to speed time-to-manufacture.

In addition, we can provide our novel EZ BioPac® single-use, closed system for powder handling. This is a proven system that reduces fill time and cross-contamination. The EZ BioPac bags facilitate rapid filling and final-weight adjustment of powders, and offer a separate discharge outlet combined with a unique antistatic polymer that allows for faster, cleaner discharge.

TESTING TO PROVE PERFORMANCE AND PRODUCT PROTECTION

To prove operational efficacy and assess mixing efficiency, ILC Dover cooperated with a major biopharmaceuticals manufacturer to conduct a series of tests mixing three different powders with water. The powders were dextrose, HEPES and sodium chloride (NaCl).

For the glucose test, the temperature of the water was held at approximately 70° C, while the water temperature for the other two powders was approximately 25° C. Powder was added to the hopper manually for all three.

TEST PROTOCOL

FIGURE 6

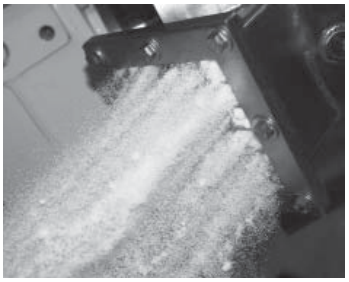


FIGURE 7

Testing followed a clearly established protocol agreed to by ILC Dover and the manufacturer, and was run on equipment provided by ILC Dover, in a facility operated by the manufacturer.

The primary purpose of the testing was to establish whether or not powder fed freely into the JetMixer system or if bridging occurred. For the glucose powder, testing was also used to establish whether or not clogging of the injector occurred due to vapor from the hot water reacting with the powder.

The test protocol specified procedures and parameters for charging the reactor vessel, monitoring and controlling process water temperature to ensure operation at target temperature, recirculation to stabilize temperature, complete injection of one drum of powder, and system cleaning (duration = 30–60 min.).

Individual trials for dextrose powder included operation with no vibration, with vibration, with bag dumped into the hopper and with bag poured into the hopper. Because of agglomeration of the feedstock, both the sodium chloride and HEPES were processed through an ILC Dover JetBreaker system before feeding to the JetMixer system. Some trials were conducted with vibration and some without, for both powder types.

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TEST RESULTS

1. For **dextrose**, the system successfully mixed 25 kg of powder into water at 65° C, in times ranging from 1 minute, 9 seconds to 2 minutes, 14 seconds, depending on method of loading hopper and whether or not vibration was used.

2. For **sodium chloride**, times to mix approximately 20 kg of powder ranged from 58 minutes at a water temperature of 33° C (no vibration) to 52 minutes at a water temperature of 28° C (with vibration).

3. Testing for the **HEPES powder** demonstrated that, even with significant delumping using the JetBreaker, time to mix 11.5 kg of powder into water at 21° C was just 35 seconds.

CONCLUSIONS

According to an assessment by the manufacturer, the combined results for all trials for all three powder types showed:

1 Performance of the JetMixer system surpassed expectations of the manufacturer's team.

2 The manufacturer affirmed that, based on test results, the system would fulfill its needs, not just for the three powders tested, but also for other powders used in its production processes.

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Innovators at our core, we develop engineered solutions for our customers' complex problems. Recognized globally for our flexible containment solutions, ILC Dover serves customers in a diverse range of industries, including pharmaceutical and biopharmaceutical manufacturing, personal care, food and beverage, chemical, aerospace, healthcare and government agencies. At ILC Dover, quality is a culture, not a measurement. Our customers will tell you that we cater to their every need and that we're highly innovative, responsive, dedicated and competitive. We have been innovating since 1947. ILC Dover's visionary solutions improve efficiency, safeguard workers and product, and prevent disasters — proof that we are on the front line of business excellence.

Engineering evolution beyond boundaries.

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