APPLICATION REPORT

Solutions for Your TOUGHEST
MIXING Applications in

PHARMACEUTICALS

Mixing of Sterile Ingredients

SILVERSON®
HIGH SHEAR MIXERS/EMULSIFIERS

PHARMACEUTICALS

Mixing of Sterile Ingredients

To respond to legislative and customer requirements, the pharmaceutical industry is having to demand ever increasing standards of hygienic construction in process equipment. This is applicable to all forms of pharmaceutical products - ointments, suspensions, syrups etc. Products manufactured under sterile or cleanroom conditions - for example injectables and vaccines - present different challenges, especially regarding product sterilization. For these products, mixing would normally take place before sterilization but there are instances where post-production sterilization is impossible for technical reasons, placing further restrictions on the mixing process. Often products will be subject to a combination of these factors:

- When the finished product is temperature sensitive and cannot be heat sterilized
- Where irradiation, often used to sterilize heat sensitive products, can damage the product
- Where the product is a suspension and cannot be sterilized by filtration

The Process

In addition to the demands of the actual mixing task, process equipment must meet a number of requirements, in terms of both design and construction:

- Equipment must obviously be designed to be cleaned-in-place (CIP) and sterilized-in-place (SIP)
- Any mixing device must have as near to zero retention as possible
- Dead areas and crevices ("bug traps") must be eliminated
- Materials of construction, including all product contact parts, must be from product compatible and traceable sources
- Equipment may be required to conform to standards such as FDA, EHEDG and cGMP
- Detailed documentation -for example packages to comply with FDA regulations - may also be required

The Problem

Conventional agitators which are modified to be hygienic, and magnetic stirrers have limitations. These are regarded as process aids and are suitable for optimizing heat transfer and simple liquid/liquid mixing.

- These low shear devices are not suitable where more complex mixing duties are involved, e.g. creating emulsions or modifying rheology/viscosity
- Magnetic stirrers are less appropriate for viscous materials and suspensions due to their design

The Solution

Silverson has developed a range of Ultra Hygienic mixers suitable for pharmaceutical and biotechnology applications, including processing of sterile ingredients. This technology is detailed in the following section. Silverson can also assist in the preparation of Installation Qualification/ Operational Qualification protocols for process equipment (IQ/OQs) and other documentation including data dossiers for FDA and other regulatory body validation.

UHLS Ultra Hygienic In-Line Mixer

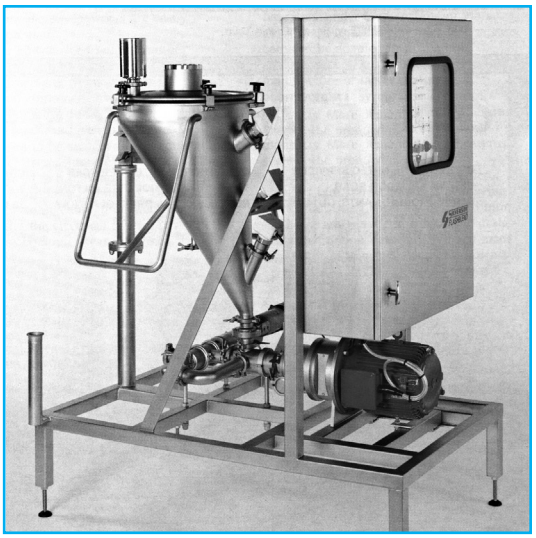
All the qualities and flexibility of standard In-Line mixers plus additional hygienic features:

- Designed to GMP and EHEDG standards
- Constructed from materials on the FDA master list
- Designed for clean-in-place (CIP) and sterilize-in-place (SIP) operation
- Self-draining tangential outlet
- Single piece inlet plate and stator optional
- Ultra Hygienic shaft sealing
- All product contact parts in 316 stainless steel
- Electropolished finish to <0.5µm Ra
- Crevice-free construction

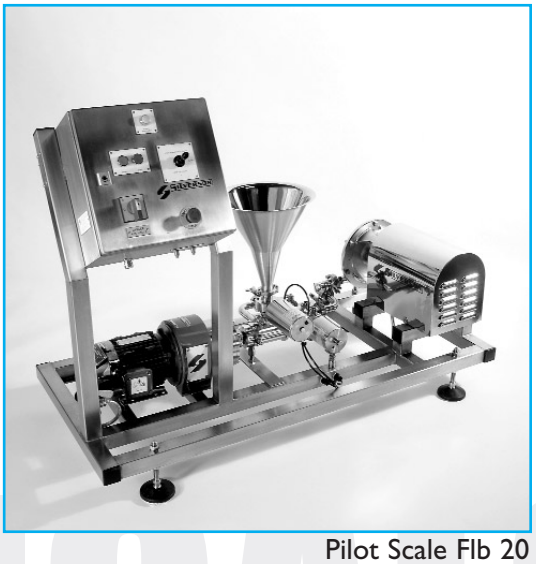
Flashblend Powder/Liquid Mixing System

A number of modifications can be made to the standard model:

- The powder injector unit, associated pipework and other product contact parts constructed in 316L stainless steel electro-polished to <0.5µm Ra
- High specification electropolished diaphragm valves can be used for the powder feed and CIP (powerflush)
- A hygienic design centrifugal pump conforming to the same standard as the In-Line mixer can be used
- A Silverson UHLS In-Line mixer can be used
- Various measures for dust filters or extraction can be incorporated
- The system can be self-draining throughout
- The hopper can be supplied with a hygienic lid, and can be modified to accommodate various conveyors and bulk powder dispensing systems such as “bulk bags” and FIBCs
- Where low volume, high cost or hazardous ingredients are being handled, several small detachable hoppers can be supplied. This allows loading of the powder outside the cleanroom or in a dispensary, minimizing powder handling in the clean area
- The hopper and lid can be designed for CIP/SIP or manual cleaning and autoclaving
- Control systems can be supplied to customer specifications



Ultra-Hygienic Flashblend



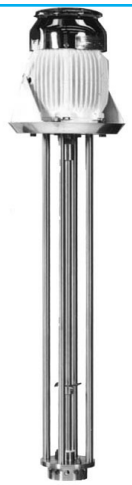
Pilot Scale Flb 20

MACEUTICALS

In-tank mixers

Silverson High shear batch mixers can be offered with hygienic features and optional modifications:

- Typically used for batch sizes of up to 400 Gallons
- Electropolished finish
- Hygienic crevice-free construction
- Quick-release of motor to permit autoclaving of vessel and mixer
- Mixers suitable for Cleaning-in-place (CIP) can be supplied
- A range of motor options including explosion proof and compressed air power
- Depending on model, seals can be product lubricated, lubricated with a product compatible liquid, or sterile gas flushed
- Mixers can be supplied for operation in sealed vessels under vacuum, atmospheric, or positive pressure; for where the vessel requires pressurizing for discharge to filling lines
- Units can be supplied for use in vessels with relatively small openings



High Shear Batch Mixer

High Shear Bottom Entry mixers

- Can be designed for Ultra Hygienic applications, incorporating features as the UHLS In-Line range
- Ideal for hydrating large quantities of powder
- Ideal for products such as creams that increase in viscosity on cooling, and where heat sensitive ingredients may only be added at low temperatures
- Normally used in conjunction with a scraper unit

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