Critical Cleaning

Ultrasonic Cleaning of Medical/Pharmaceutical Devices and Equipment

While many ultrasonic applications in the medical and biological fields are already well established, an interest is growing in new applications in noninvasive medical treatment as an alternative for invasive surgery. Dispersion of biological cells and diagnostic medical imaging are two applications where the nature of ultrasonics is substantially different. A low, high powered ultrasonics (20-40 kHz) is used for cell dispersion and a much safer, extremely low powered megasonics (3-7 MHz) is used in diagnostic imaging.

Ultrasonic applications in the pharmaceutical area include the cleaning of certain tools and equipment such as pill punches and dies and general maintenance of drug making vessels. Another important application is the use of sonochemistry to enhance drug manufacturing.

This article will focus on ultrasonic technology and processes in relation to precision cleaning applications.

Critical Cleaning

Critical cleaning of components or substrates is the complete removal of undesirable contaminants to a desired present level, without introducing new contaminants into the process.1 “Present level” is normally the minimum level at which no adverse effects take place in a subsequent operation or final application. To achieve the desired cleanliness level, it is critical to not introduce new contaminant(s) into the cleaning process. In an aqueous cleaning process, for example, it is important to have high quality rinse water and a minimum of two rinse steps. Otherwise, residual detergent and/or ionics from the rinsing water become the new contaminants.
Another source of re-contamination of cleaned parts is out-gassed residues from packaging or storing materials.\textsuperscript{1,2} Improper cleaning methods can often be blamed for rejected parts, the curse of the assembly line. To meet production and quality demands, selecting the appropriate cleaning method, chemistry, and process is essential. Additional requirements to consider for high yield processes:

- Proper ultrasonic frequencies must be selected and tested per application.
- Cleaning chemistry must be effective and safe on components and the environment.
- Parts must be properly fixtured and oriented for optimum results.
- Effective filtration of the cleaning solution and rinses, if needed, is required.
- Same criteria above are applied if solvent is selected.
- Automation and process controls are essential in having a validated high yield consistent process.\textsuperscript{3}

### Ultrasonic Cleaning Technology

**Transducers.** Ultrasonic cleaning uses high frequency sound waves (higher than 18 kHz and as high as 1 MHz) transmitted into a cleaning solution/liquid. Ultrasonic waves are mechanical pressure waves formed by actuating ultrasonic transducers with high frequency, high voltage/current generated by electronic oscillators (power generators). A typical generator produces ultrasonic frequencies greater than 20 kHz (Figure 1).

Transducers commonly used for generating ultrasonic vibrations are piezoelectric, magnetostrictive, electromagnetic, or pneumatic. The piezoelectric transducer (PZT) is the most widely used technology in cleaning and welding applications. It offers wide range of various frequencies from about 20 kHz to the megasonic range.

A recent transducer invention discloses a greater sound energy transmission at very low acoustic impedance for various high frequencies. Numerous benefits are realized from this invention, including high quality surface cleanliness and efficient submicron particle removal.

Typically, PZTs are mounted on the bottom and/or the sides of the cleaning tanks. The transducers can be mounted in various designs and sizes of sealed stainless steel containers, and can be immersed in the cleaning solution/liquid (immersibles).

The push-pull transducer rod is a recently patented immersible titanium transducer.\textsuperscript{4} The immersible is made of two PZTs mounted on the ends of a titanium rod. The generated ultrasonic waves propagate perpendicularly to the resonating surface. The waves interact with liquid media to generate cavitation implosion.

**Cavitations.** When a solution is subjected to the rapid oscillation from the high frequency sound waves, minute vacuum bubbles are generated. These bubbles grow to a certain critical size based on number of variables and then implode. This phenomenon is known as cavitations.

When using ultrasonics, the cleaning action relies on cavitations or microimplosions. The micromechanical scrubbing action of ultrasonic cavitations is directionless and can reach minute crevices, blind holes, intricate or irregular surfaces or internal passages, and other hard to reach areas. When cavitations occur in the vicinity of contaminated surface, mechanically held contamination is released from the surface, soluble materials rapidly dissolve, and oils and other similar contaminants are easily displaced with the cleaning chemicals. The released energies can reach areas that are inaccessible to other cleaning methods such as high velocity spray or contact brush (Figure 2).\textsuperscript{5}

**Frequencies.** At a frequency of 68 kHz, the total time (in microseconds) from nucleation incipient to implosion is estimated to be about one third of that at 25 kHz. The energy released from an implosion in close vicinity to the surface collides with and fragments, or disintegrates, the contami-
nants, allowing the detergent or the cleaning solvent to displace it at a fast rate. The implosion also produces dynamic pressure waves, which carry the fragments away from the surface being cleaned. High-speed microstreaming currents of the liquid molecules accompany the implosion.

The abundance of cavities generated in a solution increases with frequency but the energy released by individual cavities decreases and becomes milder, thus ideal for small particle removal.

At low frequencies (20-30 kHz), for example, a relatively small number of high energy powerful cavitations are generated (Figure 3). Low frequencies are appropriate for cleaning heavy and large-size components, while mid-range frequency ultrasonics (40-80 kHz) is recommended for cleaning a variety of surfaces.

At higher frequencies (68-200 kHz), more cavitations with moderate or lower energies are generated, which are good for cleaning delicate components such as stents. This feature also makes it effective in the rinse step. For example, at 68 kHz and 132 kHz the cavitation abundance are high enough and mild enough to completely remove detergent films and small particles, without inflicting surface erosion. Selecting the proper frequency for a particular application is an extremely important step and must be carefully investigated.

**Ultrasonic Cleaning Equipment**

Ultrasonic aqueous batch cleaning equipment typically consists of four components: an ultrasonic wash unit, a minimum of two ultrasonic separate (or reverse cascading) water rinse tanks, and a heated re-circulated clean air unit for drying. The drying step is not included if the post cleaning operation includes an aqueous bath, such as in electro- or electroless plating.

Ultrasonic transducers are bonded to the outside bottom surface or outside of the sidewalls or provided as immersibles inside the tanks. Two types of immersibles are commercially available in various sizes and frequencies. The traditional sealed metal box contains a multi-transducer system. The cylindrical immersible is powered by two main transducers, which are located at both ends and are known as push-pull immersibles.

An effective cleaning process must first be developed and then the number and the size of the stations are subsequently determined based on the required cleanliness level, yield, total process time, and space limitation.

Automation of the ultrasonic cleaning system is a well-established feature, which includes a computerized transport system, able to run different processes for various parts simultaneously, and data acquisition and monitoring capabilities. Advantages of automation are numerous, including consistency, achieving desired throughputs, and full control on all process parameters.

Typical industrial tank sizes range from 10 to 2500 L; selection is based on the size of the parts, production throughput, and required drying time. The entire machine can be enclosed to provide a cleanroom environment meeting Class 10,000 down to Class 100 cleanroom specifications. Process control and monitoring equipment consist of flow-controls, chemical feed-pumps, and in-line particle counters as well as equipment for TOC measurement, pH, turbidity, conductivity, and refractive index. Tanks are typically constructed from corrosion resistant stainless steel or electropolished stainless steel. Titanium nitride or similar coating is used to extend the lifetime of the radiating surface in the tanks or the immersible transducers.

**Cleaning and Chemistry**

The use of ultrasonics does not eliminate the need for proper cleaning chemicals and implementing and maintaining proper process parameters.
The chemical composition of the cleaning medium (for aqueous or solvent cleaning) is a critical factor in achieving the complete removal of various contaminants without inflicting any damage to the components.

Ultrasonic cleaning using only plain water is workable, but only for a very short time. Redeposition of contaminants will occur shortly after a buildup of these contaminants takes place. Evidently, some reactive contaminants must be catalytically hydrolyzed to break the chemical bonds with some metallic surfaces. Furthermore, cleaning is more complex in nature than simply extracting the contaminants from the surface. Soil loading and encapsulation/dispersion of contaminants are important determining factors for the effective lifetime of the cleaning medium and the cleaning results.

Reproducibility and consistency of the cleaning results are essential requirements for all successful cleaning processes. Cleaning chemistry, as part of the overall cleaning process, is an essential element in achieving such consistency. The following factors must be addressed when deciding on the appropriate chemistry:

- The ability to cavitate well with ultrasonics
- Its compatibility with components to be cleaned
- Its wettability, stability, soil loading, oil separation, effectiveness, dispersion, or encapsulation of solid residues
- Its ability to rinse freely
- The ability to be disposable at low cost

Both aqueous and solvent cleaning have advantages and disadvantages. Aqueous cleaning is universal and achieves better cleaning results. Solvents perform well when removing organic contaminants, but fall short on removing inorganic salts. With aqueous cleaning, for example, the drying and protection of steel components are valid concerns. The current available aqueous cleaning technologies, however, offer effective ways to alleviate these concerns.

The chemistry’s role is a multi-tasked one in order to displace oils, solubilize or emulsify organic contaminants, encapsulate particles, and disperse and prevent re-deposition of contaminants after cleaning. Special additives in the cleaning chemistries are used to assist in the process of breaking chemical bonding, removing oxides, preventing corrosion, or enhancing the physical properties of the surfactants or the surface finish. Ultrasonic rinsing with water for injection (WFI), deionized (DI) water, or reverse osmosis (RO) water is important in order to achieve spot-free surfaces. A minimum of two rinse steps is recommended.

**Parts Handling and Orientation**

To maximize the use of ultrasonic cavitations in cleaning, parts must be racked on a fixture or arranged in one layer and placed on an open mesh (preferably wire screen) basket and immersed in the ultrasonic tank. Stacking the components in layers is not recommended since the lower layers partially mask the ultrasonic waves. For optimum results, parts must be placed 1½-2 in. away from the ultrasonic radiating surface. To achieve cleaning with constant rotation, if needed, special requirements must be considered such as surface characters and basket loading.

For best results, it is recommended that parts to be positioned so that all surfaces receive equal exposure of ultrasonic energy. Parts should be oriented to maximize drainage as well. Vertical oscillation of parts may be essential to have in the wash and the rinse steps in certain applications.

**Examples of Ultrasons Applications**

Successful ultrasonic cleaning processes developed for medical and pharmaceutical applications include hip and knee metal replacements, metal stents, pacemakers, polymer intraocular lenses, CR-39, and polycarbonate lenses. Scopes used in surgery such as endoscopes and laproscopes have also been successfully cleaned using ultrasonics. Additional ultrasonics applications include the cleaning of various components for diagnostic X-ray and CAT scan machines, microcatheters, hearing aids, regular and electro-surgical blades, cannulas, disposable syringes and needles, tools, and implants. Cleanliness levels were measured and verified with Fourier transform infrared spectroscopy (FTIR) analysis, optical microscopy, and a liquid particle counter (LPC). The following are several examples with more details on ultrasonic processes.

**Cleaning Tablet Punches and Dies**

These devices are frequently cleaned, particularly with every new batch or on switching from making one type of medicine to another. A solvent vapor degreaser was used with mixed results. Some components of certain drugs are not solvent sol-
ubable and the instrument had to be manually re-cleaned afterward. Switching from using solvent to aqueous ultrasonic cleaning was not an easy task. The punches are made of special hard steel that is susceptible to flash rusting.

Aqueous cleaning processes for cleaning ferrous and non-ferrous metals together in the same aqueous cleaner, using properly formulated chemistries, was met with complete success. For example, aluminum, copper, brass, steel, and stainless steel can all be cleaned in the same cleaning chemistry without interactions.

An aqueous ultrasonic process was specially designed utilizing 25 kHz in the wash and 40 kHz in the DI water rinses. A proprietary proprietary inhibitor was developed and used in the rinses to protect the parts in the rinse and drying steps. The analysis of the cleaned parts performed by the user had clearly shown thoroughly cleaned surfaces with no sign of flash rust.

Cleaning Stents
Stents are important medical cylindrical metal devices designed to support the interiors of blood vessels and urinary tracts to keep them from collapsing after catheterization.

These devices are made of special fine mesh, are cylindrical in shape, and have different lengths and diameters. An ultrasonic cleaning process was developed to remove the lubricants and metal fines residues. Following a comparison of the FTIR analysis performed on the ultrasonically cleaned stents with the results from their manual cleaning, the process clearly showed success in achieving very clean parts.

The process utilized the proper cleaning chemistry, 68 kHz ultrasonic frequency in the wash and in the pure water rinse steps, and drying under HEPA filtered high velocity hot air. To avoid any stress fatigue damage to the product’s delicate structures, the ultrasonic frequency and its total duration in the process were selected after an extensive study by the manufacturer to determine the resonant frequency of the mesh.

Cleaning of Bone Replacement Implants
Hip and knee replacement components are manufactured from titanium and other special alloys. They have different designs and surface textures to enhance tissue growth into the device. These parts are manufactured in a multi-step custom operation. The process includes utilizing lubricants, special polymers, and complex buffing compounds, which must all be completely removed in the cleaning step prior to passivation and sterilization.

Without ultrasonics, it takes a labor-intensive operation to clean such surfaces. An additional problem with the manual cleaning operation was an in-consistency in cleaning results.

The fully automated ultrasonic cleaning process for this application successfully utilized 40 kHz ultrasonics, two different cleaning chemistries, and included an acid passivation step in the machine.

Conclusion
Ultrasonic technology offers a unique means to achieve ultra clean surfaces in various fields, particularly for the medical and pharmaceutical industries (Figure 4). Aqueous or solvent ultrasonics cleaning is a value-added option that offers several advantages over mechanical or non-ultrasonic methods. Selecting the right ultrasonic frequency, the appropriate cleaning chemistry, and optimizing the cleaning process parameters are necessary elements to achieve consistency and reproducibility of the desired clean surfaces and achieving better overall yields.

FIGURE 4. Advantages of ultrasonic cleaning.

- Efficient cleaning in recessed areas and blind holes.
- Capability of cleaning assemblies or devices.
- Removal of micro- and sub-micro contaminants.
- Various scrubbing intensities with different ultrasonic frequencies.
- With proper chemistry, ultrapure, consistent cleaning.
- Shorter process time.
- Full automation and control, batch and continuous processes.

References
1. Sami B. Awad, “Ultrasonic Cavitations and Precision Cleaning,” Precision Cleaning, Nov. 1996, p. 12. (Figure 1 and Figure 2)

Contact Sami B. Awad, Ph.D., Vice President of Technology, Crest Ultrasonics Corp., at Scotch Rd., Trenton, NJ 08628; 609-883-4000, fax 609-406-7045; sawad@crest-ultrasonics.com