phasex corporation
...the Supercritical Fluids People

Supercritical Fluids for Cleaning & Extraction of Medical Components

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Sept '09

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1. INTRODUCTION – Need for a Superior Cleaning Process

During the past fifteen years, there has been increasing attention directed to the development of improved cleaning processes for medical devices, both metal/ceramic and polymeric based. With the advent of next generation microporous metal and ceramic components (for example, for hip and knee replacements) current vapor degreasing or liquid fill-and-flush procedures do not satisfactorily penetrate pores and extract machining /grinding oils used in component manufacturing. Polymeric components such as hydrocephalus shunts, aorta grafts, urinary and endotracheal catheters, etc., represent an especially, demanding class of materials. They cannot be cleaned or extracted with traditional methods because of the absorption of solvent by the parts; organic liquid solvent residues could, in fact, be removed by heating, but the heating process, although it removes the solvent, can be deleterious to the properties and performance of the part.

Phasex Corporation recognized the opportunity to apply its supercritical fluid technology for alternative cleaning processes in 1990. Responsing to a Department of Defense need to replace ozone-depleting solvents used widely for cleaning precision parts in military operations Phasex developed a supercritical carbon dioxide (CO_2) process for oils removal. This process was proven to be superior for cleaning missile gyroscopes, accelerometers, and other critical precision parts. (Other companies were working on different CO_2 processes at this time, viz., CO_2 "snow" and CO_2 pellets; when shot through a small tube, the snow and pellets abrade particulates from flat surfaces but the process cannot remove interstitial oils.)

Because CO_2 is a gas, it has no surface tension limitations; as was shown on the DOD program, supercritical CO_2 could clean oils and lubricants from porous and metal parts and metal-polymer parting planes with dimensions of 10(!) nanometers in hours, rather than the weeks that was required for chlorinated liquid-based cleaning processes. In Phase II of the program, the supercritical CO_2 cleaning process was refined, and extraction equipment was designed, constructed, and installed at the US Air Force Metrology Center.

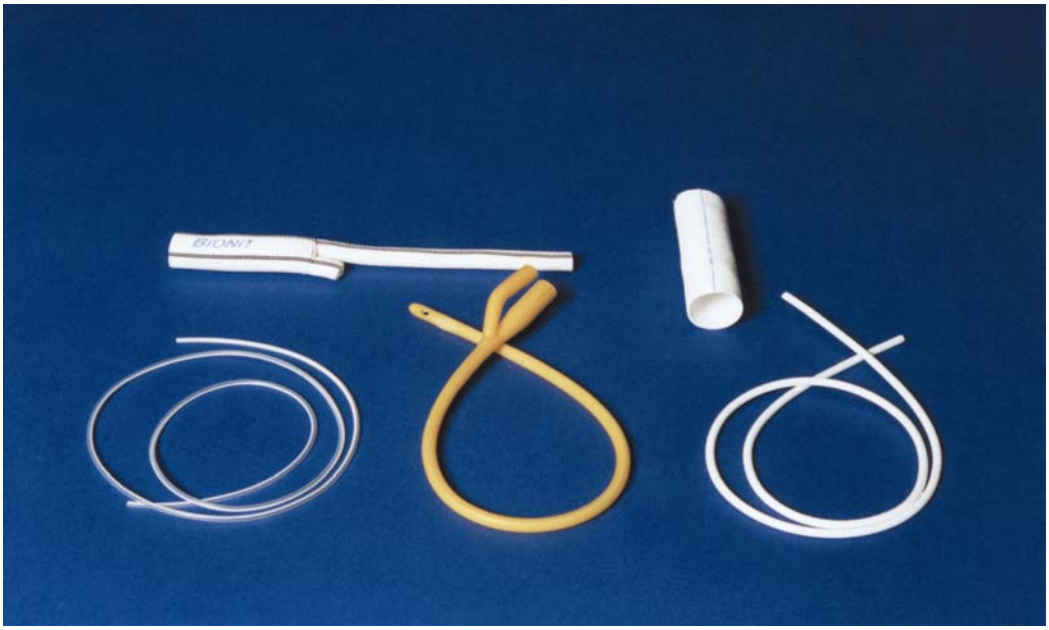
In the mid 1990s the expertise and knowledge base developed by Phasex on the government-funded programs was developed further and extended to the industrial sector, which was facing increasing scrutiny (by EPA, OSHA) of volatile organic solvents (VOCs) and ozone-depleting chlorinated solvents (ODCs) used in standard cleaning operations. Although many "drop in" replacements, i.e., liquid solvents such as IPA, n-propyl bromide (NPB) and others, have found wide application in industrial sector bulk metal degreasing operations, they were inadequate for meeting the more stringent requirements of cleaning precision components. Thus, Phasex focused its supercritical fluids expertise to the development of a superior cleaning process for precision parts, and today a variety of precision parts, multi-component assemblies, metal powders, and in-body medical products are increasingly being cleaned with supercritical CO_2.

Several medical components are currently being cleaned via supercritical CO_2 at Phasex Corporation in GMP operations; some examples are described in this paper.

2. EXTRACTION OF RESIDUALS FROM POLYMERIC PARTS

Medical components, such as hydrocephalus shunts, defibrillator leads, intraocular lenses, aorta grafts, and catheters contain reaction byproducts or residual raw materials that can be detrimental to the performance of the device or pose potential health risks in the body. For example, all silicone tubing and valves, parts which have been lightly cross-linked to provide tenacity, contain up to 5% migrateable cyclic siloxanes; even “low cyclic” content products that are cross-linked with platinum catalysts contain ~ 2% of the cyclic migrateable species that can leach into the body over time.

The figure below shows some surgically implanted devices that Phasex is currently processing with supercritical CO_2, providing superior cleanliness and maintaining physical and mechanical integrity of the devices.



Medical components: Upper left and right, polyester aorta graphs; lower left, silicone hydrocephalus shunt; middle, silicone urinary catheter; right, barium-filled hydrocephalus shunt

Organic solvents, such as hexane and methylene chloride, could, in fact, be used to extract residual materials from silicone medical components, but remnants of these solvents can themselves be difficult to remove without degrading or altering the characteristics of the part. Leaving no solvent residues after extraction, supercritical CO_2 is extremely attractive for purifying these medical components. After the cyclics are extracted from a structure any absorbed CO_2 diffuses away when the pressure is reduced, and the component retains its original shape and integrity.

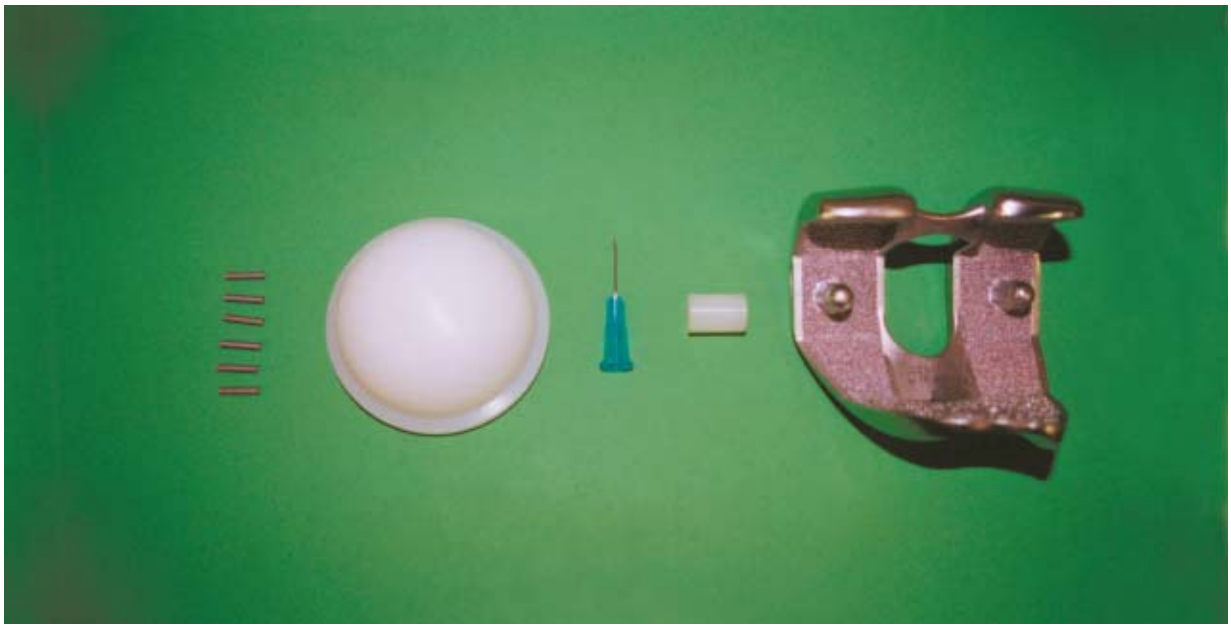
3. CLEANING OF METAL AND CERAMIC COMPONENTS

As was demonstrated during R&D on the DOD program to clean gyroscope parts, supercritical CO_2 could extract gyroscope oils from nanopores and planar contact surfaces of much less than 1μ in dimensions. Phasex successfully extended its findings to medical components having close-tolerances, minute pores, and intricate design.

Next generation hip joints are being designed with porous surfaces (that promote enhanced cell adhesion), but the porosity presents a problem during cleaning operations:

Liquid solvents (such as NPB, IPA, and aqueous surfactants), because of their high surface tensions, cannot readily penetrate the pores to dissolve/extract the machining oils. Because supercritical CO_2 is, strictly speaking, a gas, it suffers no surface limitations, and thus, can penetrate into the smallest of pores and crevices and dissolve/extract the oils from orthopedic implants.

The figure below shows several medical components.



The right hand object is a porous-surface titanium knee joint and the dome shaped piece, a polymeric (UHMWPE) hip socket. Supercritical CO_2 proved to be a successful means of extracting the machining oils. Supercritical CO_2 cleans the titanium knee joint to a lower residual oil content than the standard multiple-flush process with aqueous surfactants. The tests carried out on the HDPE socket were directed to a different goal: the elimination of free radicals generated in the structure during the radiation cross-linking step to produce a more stable material. Exposure of UHMWPE to supercritical fluids resulted in a significant reduction in free radical concentration compared to using heat alone (which can contribute to the oxidation of UHMWPE and influence the mechanical properties of the final device).

4. PURIFICATION OF POLYMER RAW MATERIALS

In some cases a polymer can be purified before it is manufactured into a device, and Phasex has exploited the properties of supercritical fluids for “front-end” cleaning of polymeric materials. The photograph below shows a 1kg sample of a ground polyester polymer, the raw material that is used to form a membrane that separates blood plasma from red blood cells. The extracted impurities, shown spilling from a beaker on the right, could not be removed by traditional means in an economical fashion (and without solvent residues).

Although the polymer possesses superior technical characteristics for the intended medical application, it contains about 0.1% of a byproduct that can be deleterious to red blood cells. Supercritical CO_2 was successfully applied to the polyester purification problem. The deleterious by/product, the yellow liquid shown spilling from the beaker, was extracted from the polymer at 99.8% efficiency. The polymer is purified at Phasex in the Tolling Processing plant in campaigns of 1000s of kg.

In this case, as with the silicone shunts, an organic solvent such as heptane, could be used to extract the interfering byproduct, but the resultant fused mass would be an intractable raw material which itself would contain many percent heptane.

5. ABOUT PHASEX

Phasex Corporation, founded in 1981, is internationally recognized for its development of improved products and separations processes using supercritical fluid technology. The company is staffed with a team of problem-solving chemical engineers, chemists, and manufacturing specialists. Phasex offers laboratory feasibility testing and process optimization, improved and new product development, toll processing, and licensing for all sectors of industry.

Phasex applies the attributes of supercritical fluids to the solution of difficult processing problems for the pharmaceuticals, polymers, natural products, and fine chemicals industries, especially in applications that cannot be carried out by industry's traditional processes. For the medical industry Phasex employs supercritical fluids to remove machining oils from titanium and ceramic medical parts and to extract residual raw materials and solvents from medical polymers, volatile materials from high vacuum adhesives, and low molecular weight oligomers from synthetic lubricants. Supercritical fluids are attractive for the purification of very reactive monomers, especially when high vac or wiped film evaporation cannot achieve the requisite specifications.

It is the unique combination of the physical properties of supercritical fluids, viz., low viscosity, high diffusivity, liquid-like density, and the absence of surface tension limitations that afford these fluids unparalleled qualities and capabilities compared to traditional liquid solvents. The complete absence of solvent residues in medical products is critical, and

supercritical fluids can not only extract residual solvent to the level, but can replace most common extraction solvents thereby eliminating even the threat of solvent contamination.

Phasex has state-of-the-art facilities for developing supercritical fluid processes starting at laboratory scale and progressing in size to manufacturing campaigns of 1,000 to 10,000kg. The company's equipment includes bench scale systems for R&D and for processing materials from the grams to kilograms level. Several intermediate-scale, product-dedicated systems for processing at 100kg, and a Class 1, Division 2 production plant capable of processing liquid and solid feedstocks in multi-ton campaigns. Several products are processed under GMP guidelines in the Toll Processing plant or in product-dedicated equipment in a Class 10,000 clean room.

6. CLOSING REMARKS

Supercritical fluids offer technical advantages for processing medical devices and medical and biopolymers. Interfering components are extracted with a gas, thus leaving no solvent residues in the parts. Additionally, supercritical CO_2 possesses attractive health, environmental, and work place characteristics: It is non-toxic, non-hazardous, Generally Recognized as Safe (GRAS), and Organic. Because of its ability to penetrate porous structures, supercritical CO_2 provides a superior means of cleaning machining oils from porous titanium components and other intricate assemblies implanted in the body.

Increasing performance demands and increasingly stringent regulatory constraints being placed on medical polymers and implantable devices are being satisfied with supercritical fluid-based processes. Phasex possesses the experience and expertise to meet the ever-changing demands of the medical polymer/medical device industry.

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