SOLVENTS AND PROCESSES

CENTER FOR ENVIRONMENTALLY RESPONSIBLE SOLVENTS AND PROCESSES CERSP

SOLVENT-FREE METHODS OF CHEMICAL SYNTHESIS LEAD TO CANCER THERAPIES, NCI CENTER

"Once you get scientists and engineers working in an interdisciplinary manner, you can't contain it," laughs Joseph DeSimone, director of the Center for Environmentally Responsible Solvents and Processes (CERSP) and the William R. Kenan, Jr. Distinguished Professor of Chemistry and Chemical Engineering at the University of North Carolina, at Chapel Hill (UNC-CH).

CERSP director Joseph DeSimone

CERSP co-director Ruben Carbonell

"Things have evolved certainly beyond the original scope of our center. Starting off with a focus on sustainability and green chemistry has led us into new cancer therapies and imaging agents," says DeSimone.

CERSP's initial goal was to establish the scientific fundamentals necessary to enable liquid and supercritical CO_2 and solvent-free processes to replace aqueous and organic solvents in a large number of key processes in our nation's manufacturing sector.

More than 30 billion pounds of organic and halogenated solvents are used worldwide each year as manufacturing process aids, cleaning agents, and dispersants.

In the future, manufacturing and service industries must work to avoid the production, use, and subsequent release into the environment of contaminated water, volatile organic solvents, chlorofluorocarbons, and other noxious pollutants.

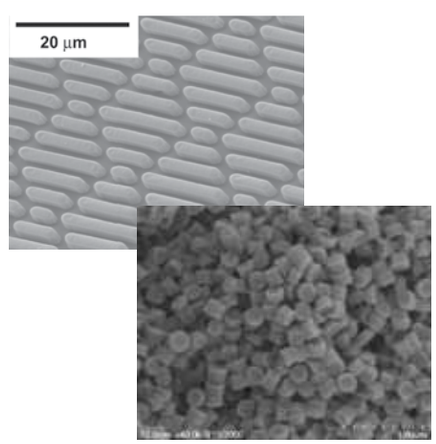
CERSP began as a multi-disciplinary effort with participants from five academic centers and two national laboratories: UNC-CH, North Carolina State University, North Carolina A&T University, University of Texas at Austin and the Georgia Institute of Technology.

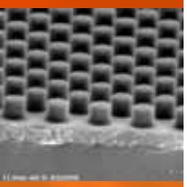
CERSP codirector Ruben Carbonell points out that many companies are focusing today on finding alternatives to fluorinated surfactants that break down into a compound called perfluorooctanoic acid, or C8, which accumulates in the body and may pose a health threat. Center researcher Keith Johnston and colleagues are looking at alternative surfactants that have different chemical structures that won't bio-accumulate and have good surfactant properties.

The manufacture of Teflon™ is a case in point. The conventional process uses a C8 surfactant to make an emulsion. An alternate synthesis, developed in the center, doesn't require any surfactants, says Carbonell. It's done completely in CO_2.

The process has been commercialized. "There's a DuPont plant in Fayetteville, North Carolina that makes Teflon™ in carbon dioxide. The technology, developed in DeSimone's lab, was licensed by DuPont several years ago," says Carbonell. One of the advantages is a smaller environmental footprint.

"There are no surfactants at all—it's just the monomer reacting in the presence of carbon dioxide. The particles grow, and when you reduce the pressure, the particles fall out of solution, completely dry and with no surfactant," says Carbonell. "And the process should be cheaper because there's no need to evaporate water at the end of the process. One of the major energy consumption points in making any polymer, but particularly Teflon-based materials, is that they're made in aqueous solvents or aqueous-organic emulsions. If you make it in CO_2 and depressurize, the polymer powder comes out completely dry. And the CO_2 is recycled for use."





Green Chemistry Pays Dividends for Research on Cancer Therapy

"What's curious—what has evolved—is that research on solvent-free methods has led to a new technology for making cancer therapeutics that we didn't anticipate," says DeSimone. It has led to us landing one of the eight centers of nanotechnology excellence funded by the National Cancer Institute, a $24-million center. It just shows the unbounded opportunities that happen when you get a bunch of good people together from different disciplines that are open-minded."

Initially, CERSP researchers were using carbon dioxide as a solvent-free method for making new fluoropolymers. They made some new materials that turned out to be excellent molding materials. The method called PRINT™—Particle Replication in Non-wetting Templates, was published in July 2005 issue of the *Journal of the American Chemical Society.*

The process begins with a liquid fluoropolymer that can wet surfaces very well. It is poured into a master and irradiated to make an array of tiny molds, not unlike a little ice cube tray, which can be used subsequently for mass production of particles of uniform size and shape, creating features of nanometer size.

The breakthrough came when they realized these particles could be used in medicine. "We use these particles as basically a 'delivery truck' for therapeutics and imaging contrast agents," says DeSimone. "Because it's such a gentle technique—we're just molding—we can easily paint the particles with targeting ligands, like monoclonal antibodies. And so now we have particles that can have on the surface an antibody and in the interior have a therapeutic. We're beginning to develop the tools and methods for scale-up and we've now molded particles and done our first pharmacokinetic studies in mice to see the biodistribution of these organic carriers," says DeSimone. □

STARTUP COMPANY

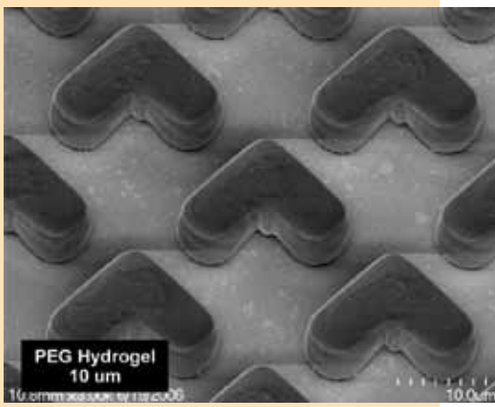
LIQUIDIA MAKES NANO-ENGINEERED PRODUCTS FOR LIFE SCIENCES, ENERGY, AND MATERIALS SECTORS

Joseph DeSimone and his colleagues from CERSP at the University of North Carolina at Chapel Hill have created a startup company called Liquidia Technologies based upon the PRINT™ nanoscale molding process, targeting applications in the life sciences, energy, and materials sectors.

Founded in 2004, Liquidia is working to precisely design and manufacture micro- and nano-structures in bulk, with particle sizes ranging from tens of nanometers to tens of microns. These structures may take multiple forms, including particles and patterned films.

Liquidia has partnerships with several major corporations to provide gram quantities of material for prototyping and feasibility studies. Examples include supplying particles that might become part of a medical device or an active layer in a display, and making fuel cell membranes or active layers in photovoltaic devices.

The company had grown to 24 people as of spring 2007 and raised a total of $25 million, says co-founder and senior scientist Ginger Denison Rothrock, a former graduate student at CERSP. Located in Research Triangle Park and formerly squeezed into 4,000 sq ft—"quite cramped but loving it"—the company was scheduled to move into a 17,000-sq-ft facility in August 2007.



In the life sciences, Liquidia is using the PRINT™ process to make particles containing therapeutic drugs that may be used to deliver medicine to a target site and gradually release it. The PRINT process gives precise control over particle size, shape, composition, modulus, and surface properties. According to the company, "Liquidia is the only company in the world that can independently tailor these variables simultaneously in the creation of engineered drug therapies." Rothrock notes that discussions are underway with three major pharmaceutical companies for prototyping projects.