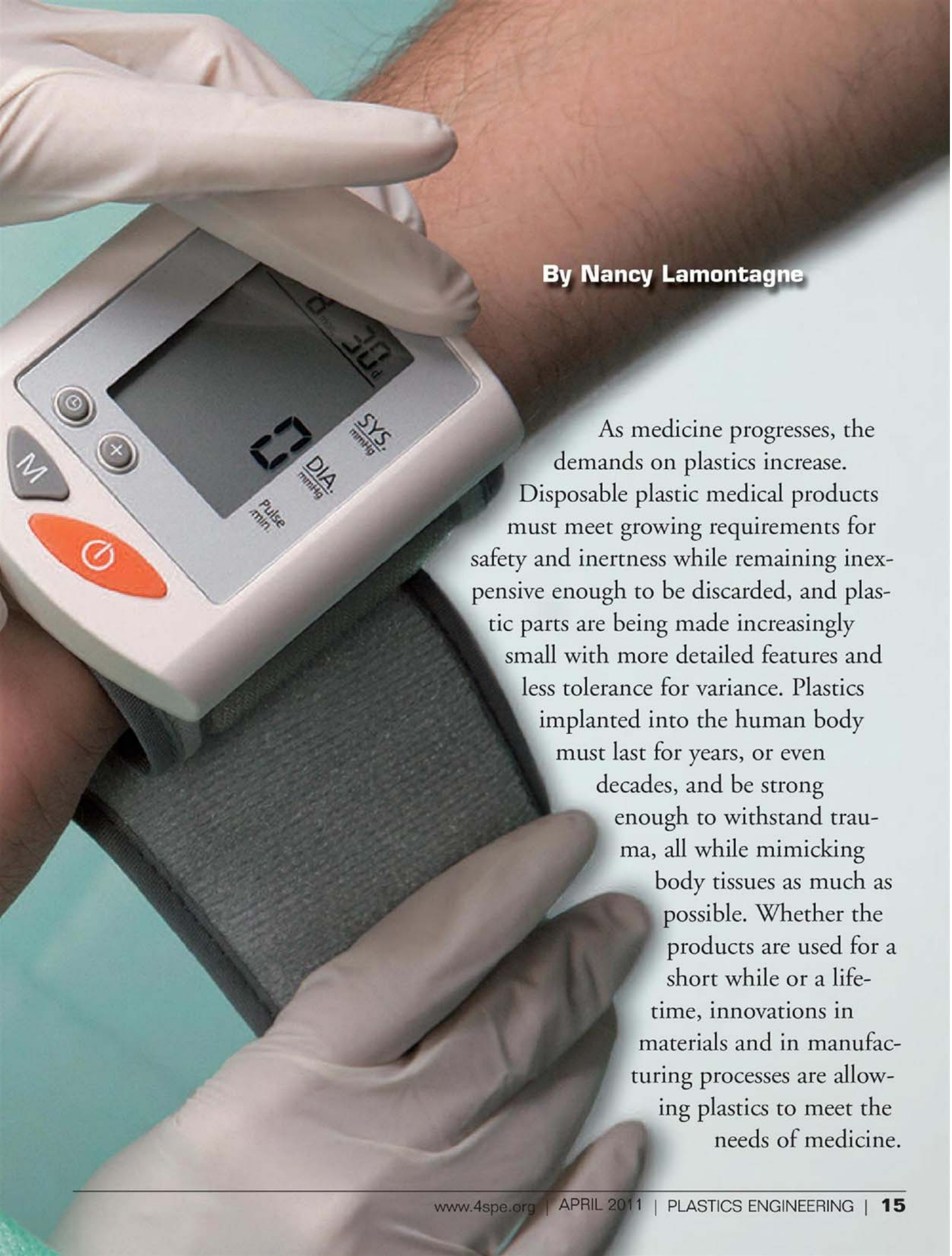
Medical Plastics:

The Innovative Beat Goes On



By Nancy Lamontagne

As medicine progresses, the demands on plastics increase. Disposable plastic medical products must meet growing requirements for safety and inertness while remaining inexpensive enough to be discarded, and plastic parts are being made increasingly small with more detailed features and less tolerance for variance. Plastics implanted into the human body must last for years, or even decades, and be strong enough to withstand trauma, all while mimicking body tissues as much as possible. Whether the products are used for a short while or a lifetime, innovations in materials and in manufacturing processes are allowing plastics to meet the needs of medicine.

But even if new technology is developed, introducing new materials or processes for medical products isn't an easy process, says Len Czuba, president of Czuba Enterprises Inc. and Chair of the Society of Plastics Engineers' Medical Plastics Division. "Medical devices are highly regulated, and a lot of time and cost are put into developing them and getting them cleared for use by the FDA (U.S. Food & Drug Administration). Once the materials of construction of a device are selected, tested, and shown to be safe, it is unlikely that alternative materials will be considered for that device. For this reason, new materials are more likely to be used for new products, not ones that have already gone through the approval process."

He explains that even a new supplier selling a product line or even a change in the name of a material will mean that new labels and documentation for a medical device will be required. Similarly, new manufacturing processes have to be tested to ensure the plastic products are consistent and not contaminated in any way. Even with these challenges, the industry continues progressing with new materials and technology.

PVC Alternatives

PVC is one of the most widely used materials for disposable medical products such as tubing, but lately much attention has focused on health and environmental concerns regarding the plasticizers added to make PVC flexible.

The European Union banned several types of phthalate softeners, including DEHP (diethylhexyl phthalate), from use in toys or items that children can place in their mouths. "In the U.S., the FDA listened to the science on the subject, which showed that there was no reason to ban these plasticizers. Most exposures are so small that they are not to be concerned about," says Czuba. At a recent conference, he organized a roundtable discussion on the topic of extractables; he recounts that the participating experts agreed that there was not enough scientific evidence that plasticizers or other so-called "dangerous chemicals," such as bisphenol A (BPA), in the extremely low levels extracted from medical-device plastics caused health problems.

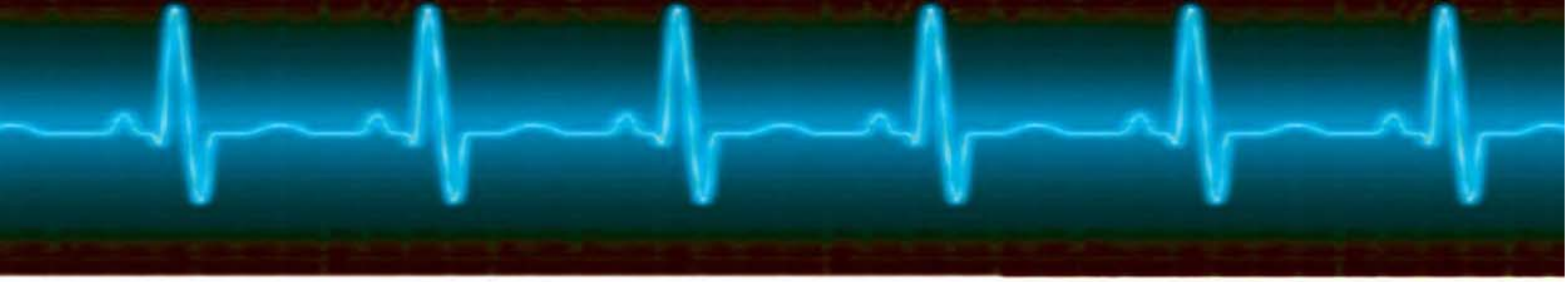
However, the negative attention given to PVC has led to an increasing market demand for alternatives. "The pressure to eliminate PVC from medical devices is constantly increasing, due to legislation against plasticizers, environmental concerns, and specific company policies," says Nick Sandland, senior market manager—medical products, at Teknor Apex Company.

Teknor Apex, a compounder of flexible PVC for the medical market, has offered DEHP-free and phthalate-free PVC compounds for several years. Recently, the company set out to develop a non-PVC offering. The development process began by bench-

Teknor Apex's Medalist® MD-500 series of medical-grade elastomers offer an alternative for medical tubing made of PVC.

Property	Test Method	Three Medical-Grade Compounds for Tubing: Standard PVC	Gamma-Stable PVC	Medalist® MD-575
Specific gravity	ASTM D792	1.20	1.20	0.88
Shore A hardness (15 sec. delay)	ASTM D2240	75	75	72
Tensile strength, psi (mPa)	ASTM D412	2,150 (14.8)	2,150 (14.8)	1,961 (13.5)
Tensile stress, psi (mPa)	ASTM D412	900 (6.2)	900 (6.2)	623 (4.30)
Tensile elongation, %	ASTM D412	420	420	722
Color shift, post-gamma[1], ΔE	CIELab	2.55	1.42	1.91
Color shift, post-gamma, heat aged[2], ΔE	CIELab	10.52	7.01	2.02

1. Dosage at 30 kGy. 2. Accelerated aging at 50 °C for 48 hours to simulate field performance.



marking PVC materials and then focusing on the attributes that device-makers identified as most important. "The most difficult functional attributes to match were related to properties that are not typically on a data sheet. For example, the kink resistance, clarity, and drape were attributes considered to be very important for success; however, they can only be truly determined on the finished product," Sandland says.

The company's Medalist® MD-500 series of compounds resulted directly from this work. These medical-grade elastomers offer a PVC alternative for medical tubing with the same haptics (feel), crystal clarity, kink resistance, clamp resilience, and performance characteristics of PVC, plus enhanced gamma stability and flexibility at a reduced density. "Based on customer feedback to date, we are confident that this hard work was worthwhile," Sandland says.

During one of the last stages before product launch, the company challenged industry experts to distinguish between PVC and Medalist tubes. Some could not tell the difference, and for those that could, it took some time. "The unique aspect of this project was the way in which we utilized both our in-house knowledge of PVC and end-use applications to ensure that we produced a material that looks, feels, and behaves like PVC," Sandland says.

Fighting Infection

As hospital-acquired infections are still a major problem, Czuba says that adding antimicrobial properties to plastics is something everyone is considering lately. "Cutting down on microbial growth sounds good, but we have to be sure it is not giving doctors and nurses a false sense of security that keeps them from following safe practices leading to even more problems going forward," he says.

PolyOne Corp. makes WithStand™ inorganic and organic antimicrobial additives that can give antimicrobial characteristics to Class I, II, and III medical devices and to medical packaging. "Since 2008, when Medicare stated it would no longer cover hospital-acquired infections, the need for antimicrobials has increased significantly," says Larry Johnson, global healthcare marketing director at PolyOne. Antimicrobials are now used in medical applications that include CVC catheters, IV tubing, infusion tubing, drainage tubing, blood transfusion bags, needle ports/injection sites, urinary tract access devices, airway management, hospital durables, and wound care.

PolyOne's WithStand antimicrobial technology can be used across a variety of resins from specialty engineered thermoplastics to vinyl compounds and thermoplastic elastomers. "We offer inert base materials that are chemically resistant to

PolyOne's WithStand antimicrobial technology is being used on products as varied as toothbrushes and devices that monitor vital signs.

disinfectants and that maintain physical properties after sterilization procedures. Our WithStand antimicrobial technology provides inherent infection control, and our collaborative approach to application development includes recommendations on part design, such as minimum texturing, elimination of crevices, and other preventative measures."

While antimicrobial additives can't replace good safety practices, their use can be part of an overall strategy to control hospital infection. "A combined infection-control strategy should include base material selection, infection-control technology, and part-design considerations," Johnson says. The company continues to seek ways to improve the performance of its offerings. "We're actively looking for new raw materials that can provide improved antimicrobial properties. In general, we are looking for faster-acting materials that kill bacteria more effectively, with higher kill rates," he says.

New Drugs, New Challenges

New drugs such as advanced cancer medicines and biologics are creating new challenges for IVs, containers, syringes, and the fittings and plungers associated with these drug-delivery devices. The plastics traditionally used for these applications can react with more aggressive drugs currently being developed, causing changes that may reduce their effectiveness. This reactivity could also cause changes in DNA or kill living organisms that are the basis of the new generation of biologic medicines.

Fluoropolymers such as fluorinated ethylene propylene (FEP) and perfluoroalkoxy (PFA) are alternatives that can overcome many of these challenges. They are highly inert and compatible with most organic compounds, have good barrier properties and high continuous-use temperatures, and can withstand steam sterilization. The non-stick properties of these polymers can also be useful to reduce liquid, gel, and powder adhesion and stick slip, which can all affect dosing consistency. Avoiding the need for silicone coatings traditionally used to reduce friction also addresses growing concerns about silicone buildup in the body resulting from long-term use of drug-storage and drug-delivery devices.

However, fluoropolymers are difficult to injection-mold, and the perception persists that it can't be done. "We've been surprised at the lack of awareness and understanding about fluoropolymer injection molding for medical applications," says Ken Kelly, general manager of Performance Plastics Ltd. Since 1999, the company has produced 50 million parts by injection molding fluoropolymers. "We've spent the last 12 years developing and refining this technology."

The expense of fluoropolymer resins has often made the cost associated with waste the limiting factor in producing parts inexpensive enough for high-volume manufacturing. "By eliminating the runner system associated with conventional techniques, we can significantly reduce material usage and provide tremendous cost savings," says Kelly.

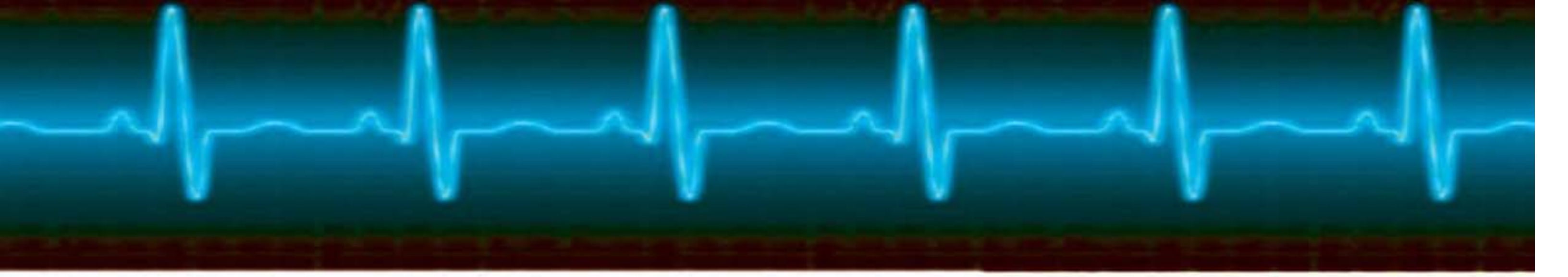
The company's injection-molding system uses direct gating, proprietary methods, and mold materials that allow the plastic to be injected at high pressures without melt fracture or loss of mechanical properties. The system uses special hard metals that are resistant to the hydrofluoric acid by-product of molding. These metals don't become corroded or misshapen under high pressures like traditional steels. The result is the capability to produce small, high-quality parts that can have complex geometry features and thin walls. "We've consistently produced a thin-walled webbing with critically high pressure of 36,000 psi and speeds of 12 inches per second," says Kelly.

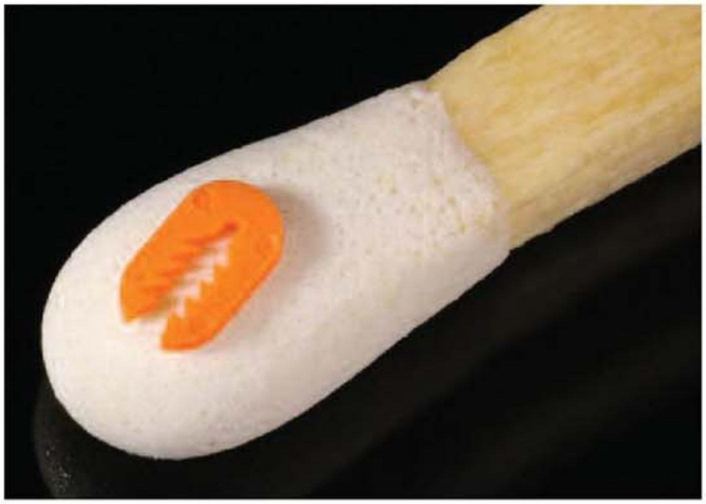
Although some companies are using injection molding with fluoropolymers for the semiconductor or chemical processing markets, most are not dealing in high volumes to make disposable medical products, according to Kelly. "More large OEMs have been coming to us because of the new drugs being developed," he says. "We want to make OEMs aware that they can use fluoropolymers rather than having to compromise on performance or use a lot of coatings with other materials."

Making Small Parts

Some medical applications require parts such as plugs or clamps that are smaller than a match head. Small parts still need to have high quality and high precision even when made in large quantities. The MicroPower family of injection-molding machines from Wittmann Battenfeld GmbH is designed to meet these challenges.

Making tiny parts on a machine designed to make large parts produces a large amount of waste and expends a lot of energy. By using minimum shot volumes as low as 0.05 cm^3, shorter cycle times, and lower material and energy consumption, the MicroPower machines can





Miniature medical clamp—shown resting on a match head—was made on a Wittmann Battenfeld MicroPower injection-molding machine using a mold from Microsystems UK.

reduce costs by 30%–50% compared with standard machines, according to the company.

The high-quality micro-parts are achieved thanks to a unique two-stage injection system that combines a 14-mm diagonally angled screw with an injection piston. Smaller sprues and parallel movement via a rotary table reduce cycle time, and the machine is electric, which improves the precision and uses less energy.

Gimac Microextruders also specializes in small parts. The company makes machines that extrude biopolymers to form devices with microsized dimensions. These devices are meeting the needs of new and challenging medical applications such as targeted drug delivery, tissue engineering, and biodegradability. Gimac's systems have been used to produce microcatheters for brain and cardiac surgery, for example.

Microextruders are designed to deliver optimum molecular weight, crystallinity, processing volume, and system cleanability. The extruded biopolymers are produced in small volumes but must have precisely controlled properties even on a microscopic scale. This is accomplished through an accurate design of ducts and flow-channels, and with the right polymer and flow-rate it is possible to produce a device with the desired microstructure.

Simone Maccagnan, sales manager at the company, says that microextrusion is particularly useful for parts where there cannot be any variation in molecular weight. These include drug-eluting devices, scaffolds, and biodegradable devices. A case study performed using a Gimac machine to extrude polylactic acid (PLA), a biodegradable material used for surgical sutures, showed that the extrusion procedure did not substantially modify the material's molecular-weight distribution.

There are still some hurdles to overcome as the technology matures. For example, Maccagnan points out, there aren't many inspection devices that operate in the range of microns to find surface defects and layer-to-layer discrimination, and the company is continuing to look for ways to reduce the prices of the systems as the technology becomes more established. "Gimac continues to extend the number of features that allow a reduction in the costs of the final product, higher speeds, more automation, online inspection and selection, and intermittent extrusion, which can avoid post-process steps. The company is also improving on functions that allow higher performances such as direct variation of elongational properties," Maccagnan says.

Strong and Flexible Implants

In the late 1990s, polyetheretherketone (PEEK) was first used for implants. PEEK-based spinal spacers were used to hold vertebrae upright after disk removal. Unlike titanium, PEEK parts didn't eventually subside into bone, and they allowed visualization of the bone surrounding the implant in X-ray or CT images.

These advantages and others have led to many more PEEK-based implants. Marcus Jarman-Smith is a technology leader at Invibio Ltd., which has been making PEEK-Optima® polymer for over a decade. He says that in addition to spinal implants, the material holds clear benefits for knee-replacement and hip-replacement parts. PEEK parts don't produce the health concerns associated with the metal against metal wearing of traditional hip replacements. The strength of Invibio's bearing grade, Motis®, means it can be used alone to make hip-replacement cups instead of combining a metal cup with a polymer liner. The resulting thinner cup requires the removal of less bone. In addition, polymer parts flex and pass on stress to the bone rather than focusing the stress on the implant. This transfer of stress helps bone

Acetabular liners manufactured using Motis® polymer from Invibio Biomaterial Solutions offer the benefits of excellent wear properties and eliminate the concerns of metal-on-metal debris.

maintain strength and means that damage is less likely to occur.

"Because of the polymer's high strength and bearing properties, it is starting to be looked at more for trauma applications," says Jarman-Smith. He says that PEEK has a high strength-to-weight ratio and allows more flexing than metal plates and nails used to repair a broken arm or leg. If the patient is a child, or if the patient develops an infection, plates or nails may have to be need removed, which is difficult with metal because it tends to bind to the bone, whereas PEEK doesn't. The Quantum™ Humeral Composite Nailing System from N.M.B. Medical Applications Ltd. was the first PEEK intramedullary nail to gain FDA approval (March 2010). The nail is made of Invibio's Endolign®, a composite of continuous carbon fibers in a PEEK-Optima polymer matrix.

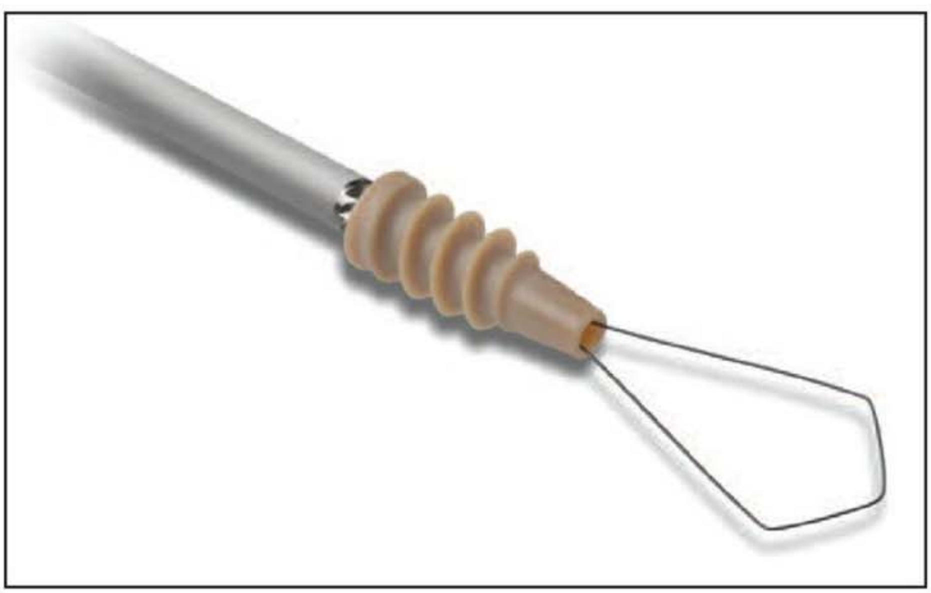
For future developments and applications, the company is considering options such as combining PEEK with additives that help it bind better with bone or encourage bone growth. "We also want to see if we can use it to make scaffolds or porous PEEK parts that can support tissue and allow tissue to grow inside and regenerate," says Jarman-Smith.

Although PEEK has many advantages for medical implants, it can be difficult to mold in a clean-room environment because of its high melt temperature. PMC Smart Solutions has been implementing new ways to handle this challenge. The company, founded in 1929, entered the medical molding market four years ago. It specifically focused on long-term surgical implants made of materials such as PEEK because of the potential growth in this market.

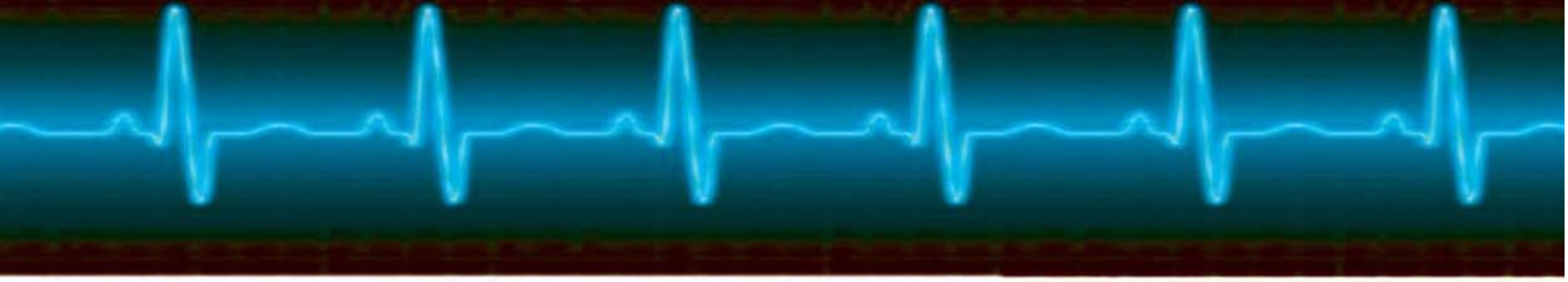
"Consistency is very important for implants," says Lisa G. Jennings, president of PMC Smart Solutions. Using heat-transfer oils for mold-temperature control can potentially cause product contamination. Electric cartridge heaters are subject to temperature problems that can affect product consistency because they cannot control the mold's surface temperature in a tight window across a part and often have hot and cold spots along their length. Cartridge heaters are also unable to remove heat from the mold if it becomes too hot.

Thus, PMC examined using pressurized water for precise mold-temperature control. Pressurized water can be heated to temperatures as high as 400°F. The company partnered with Single Temperature Controls of Charlotte, North Carolina, USA, which sells temperature-equilibrium systems that pump water through the mold at a set temperature. Heat is transferred to the mold if the water is hotter than the mold and removed from the mold if the opposite is true.

In PMC's experiments, it found a 44.2°F variance in mold temperature with electric heating and only 5.0°F



PMC Smart Solutions uses pressurized water for precise mold-temperature control. The PEEK suture anchor pictured is used in rotator cuff surgery.



variance with the water-heated system. The effects from this variance could be seen through a 0.003-inch increase in part shrinkage and average 18.5% reduction in relative crystallinity in the same parts produced using the electric-heated molds.

The pressurized water system has allowed the company to make complex parts of PEEK and other high-melt temperature plastics. For example, it has made insert-molded porous metal parts for orthopedic implants. "We were among the first to use high-pressure water to control mold temperature for making medical-device implants in a clean room," Jennings says. Since PMC shared its data showing the benefits of using water to control mold temperatures, other companies have followed its lead in using this technology. The complete white paper is available on www.pmcsmartsolutions.com.

Polymers That Imitate Biology

Implantable parts aim to imitate the flexibility of bone, but imitating biology on the scale of cells or even smaller can be more difficult.

Scientists from the University of California (Berkeley, California, USA) and the Lawrence Berkeley National Laboratory (USA) recently published work showing how they coaxed polymers to self-assemble into wispy nanoscale ropes that approach the structural complexity of biological materials. The scientists created conditions that allowed polypeptoids to self-assemble into ever-more complicated structures by first assembling into sheets, then into stacks of sheets, and finally rolling up into double helices that resemble a rope only 600 nm in diameter. Although the science is early in development, the researchers want to use the polypeptoids to build synthetic structures that behave like proteins. For example, the structures might act as drug-delivery vehicles that target disease at the molecular scale or could mimic the protein recognition capabilities of antibodies. This work was published in the *Journal of the American Chemical Society* (DOI: 10.1021/ja106340f), October 22, 2010.

Researchers at the University of North Carolina at Chapel Hill (USA) are developing synthetic blood cells, recently succeeding in producing soft hydrogel particles that mimic the size, shape, and flexibility of red blood cells and that can circulate in the body for extended periods of time. This extended circulation might allow the particles to deliver more aggressive cancer-fighting medicines. The researchers used the "particle replication in nonwetting templates" (PRINT®) technique developed in their laboratory to make the red-blood-cell mimics. As published in *PNAS* (DOI: 10.1073/pnas.1010013108), the researchers found that in mice, the more flexible particles lasted 30 times longer than stiffer ones. More rigid particles tended to lodge in the lungs, while more flexible particles did not and were removed by the spleen, the organ that typically removes old "real" red blood cells.