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# Skeleton key

How glass opens the door for new implantable devices

## Light touch

Creating new possibilities with flexible photonics

## Go digital

The FDA regulation changing the future of the industry

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***Medical Device Developments***
Vol. 1 2019



*Medical Device Developments* is published by Compelo,

Registered in England No. 09901510.

John Carpenter House,
John Carpenter Street London, EC4Y 0AN, UK
Tel: +44 207 936 6400
www.compelo.com
www.medicaldevice-developments.com

ISSN 1747-9610 © 2019 Compelo.



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| Single issue price: | UK £31 | EU €49 | US $65 | RoW $65 |
| One year: | UK £48 | EU €76 | US $99 | RoW $100 |
| Two year: | UK £77 | EU €120 | US $158 | RoW $159 |

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Printed by Stephens & George Print Group

# On reflection

There is a famous scene in the 1967 film *The Graduate*, where a family friend takes aside Benjamin Braddock, played by Dustin Hoffman, and whispers to him, "Plastics… There's a great future in plastics." This seems odd today, particularly in light of increasing concerns about sustainability, but at the time this material was new and exciting.

If film-makers had been able to see into the future, they would have inevitably made a reference to the digital age in which we find ourselves today. An age where new technologies are transforming a number of industries, not least medical devices, where there is an ever-increasing number of possibilities to improve efficiencies in manufacturing, create more advanced devices and address unmet health needs, all of which we explore in this issue.

We investigate the use of new materials, such as using glass for implantables, which we dive into with Professor Julian Jones from Imperial College London on page 102. We also find out about potential medical devices made through the use of flexible photonics that are capable of bending and stretching in a discussion with MIT associate professor Juejun Hu on page 57.

In addition to widening opportunities for devices, the definition of what constitutes a device is also expanding. This has resulted in more companies entering the market, with unique offerings and new ways of working. The means with which consumers are interacting with devices is also shifting, where they can now be active agents, rather than passive patients, with regard to their care. We discuss these issues with Sundeep Karnik and Matt Singer from ZS in light of the new FDA regulation on 'software as a medical device' on page 12.

These advances all demand greater engagement between humans and technology, both inside and outside the body. It's an exciting time for the industry and I am thrilled to be able to provide a platform for stimulating discussions and debates on these topics.

**Emma Green, editor**

Glass is demonstrating potential in healing everything from wounds to broken bones.

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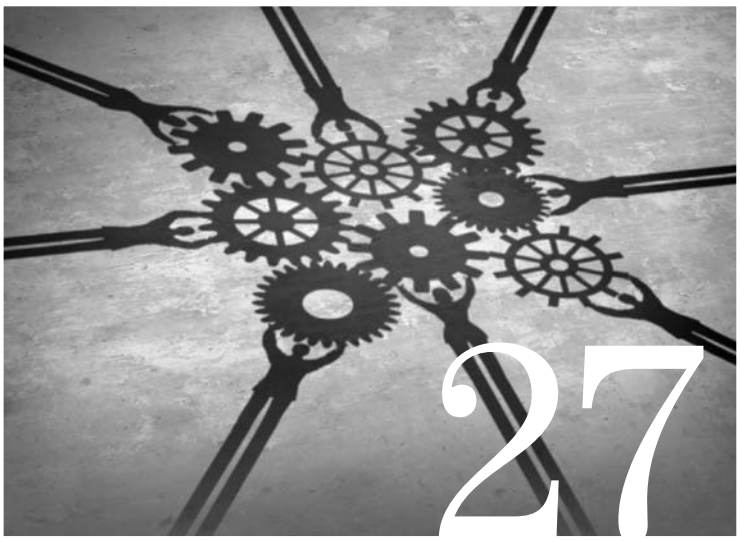
# In this issue

**Cover story**





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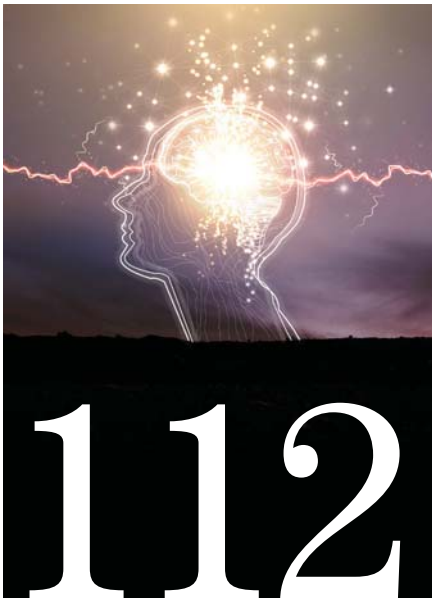


**80,396**

Number of citizens from 27 European countries that contributed to the 2012—17 Eurobarometer data on robots.

**Gnambs and Appel**

# Barriers to AI in healthcare systems

Given the effectiveness of artificial intelligence-enabled software in other domains, AI has been introduced into many areas of medicine. According to Becker's Healthcare, these tools will save the healthcare industry $52 billion by 2021.

One such application is clinical decision support software, which falls into the category of software as a medical device. In light of the prevalence of diagnostic errors and the potential impact on patients, there is an increasing drive for technologies that can support these decisions. It is estimated that these mistakes account for almost 60% of all medical errors and result in an estimated 40,000–80,000 deaths each year. AI offers huge potential to reduce this error rate by quickly scanning patient data and delivering diagnoses efficiently and more accurately than humans. The Duke Margolis Centre for Health Policy published a white paper identifying some of the challenges facing the integration of AI. The first of these is the need for more evidence demonstrating the effectiveness of these technologies, including the impact of the software on patient outcomes, care quality, costs of care, workflow, the usability of the software, its accuracy and the potential reimbursement by payers. The second barrier is the requirement of more data about the risk to patients of such technologies. The degree to which a software product comes with information that explains how it works and the types of populations used to train the software will have significant impact on regulators' and clinicians' assessment of the risk to patients.

The final challenge identified in the report concerns the ethical implications of using AI. It is essential that these technologies are ethically trained and flexible. Developers must assess the ability to apply data inputs to other settings different to the original o assess the scalability of these technologies.

**$52 billion**

Projected amount saved by AI by 2021.

**Becker's Healthcare**

## Soft-bodied robots as a novel method of drug delivery

Researchers at City University Hong Kong (CityU) have just created a tiny, soft robot with caterpillar-like legs that can be directed using magnets to deliver drugs around the body. The robot can carry a therapeutic payload of more than 100 times its own weight and has been specifically designed to carry drugs to areas like the stomach.

The robot's body thickness measures approximately 0.15mm, with each conical leg measuring 0.65mm long and the gap between the legs measuring approximately 0.6mm. This makes the leg-length-to-gap ratio around 1:1.

When an external magnetic field is applied, the soft body of the robot will locate and experience a torque and a force proportional to the strength of the field. The torque aligns the millirobot with the magnetisation field, raising the body. Meanwhile, the magnetic force provides a driving force and drags the millirobot towards the local maximum magnetic field. The robot deforms under the magnetic field, which is controlled precisely during the accurate permanent magnet motion. This allows the robot to move fluidly in the body.

The robot will be used as a prototype as the team works towards creating a fully biodegradable robot that will naturally decompose after drug delivery.

# Increasing scepticism about robots

The use of robotics is becoming more common in a number of different industries, with many researchers suggesting that we are on the brink of a robotic era. Despite their widespread use, public perceptions of robotics have rarely been investigated.

Timo Gnambs from Johannes Kepler Universität Linz and Markus Appel from Julius-Maximilians-Universität Würzburg addressed this gap in the literature and published their findings in *Computers in Human Behaviour*. According to their cross-European data analysis, robots are more negatively evaluated than five years ago. Gnambs and Appel analysed the 2012, 2014 and 2017 Eurobarometer data, which included 80,396 citizens from 27 European countries. In their research, participants first saw a general description of robots as machines that could assist people with daily activities, such as cleaning robots, or as machines working in environments that were too dangerous for humans, such as rescue missions. Responses were very different when presented with specific applications, such as self-driving cars.

From these results, it appears as though Europeans are relatively positive about robots. However, they are critical when the robot is specified and personalised.

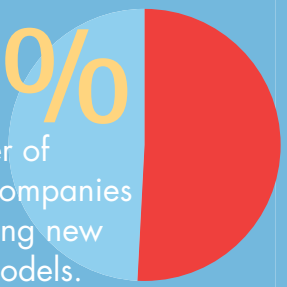
# FDA releases draft guidance for brain-computer interface devices

The FDA has recently issued draft guidance to drive the development of brain-computer interface (BCI) devices, a new generation of implants that could provide users with direct control.

BCI devices are often used to regulate limb prosthesis. These can significantly improve mobility and independence for patients. The FDA added that the devices also have the potential to help people living with severe disabilities by improving their ability to interact with their environment.

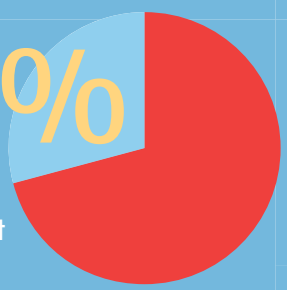
The document outlines recommendations for developers on non-clinical and clinical study design to create BCI devices for patients with paralysis or amputation.

# Internet of medical things

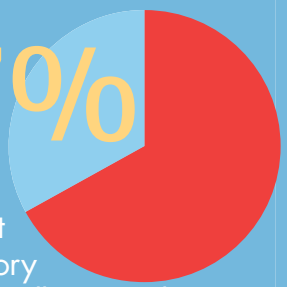
**51%**

The number of med-tech companies implementing new business models.



**71%**

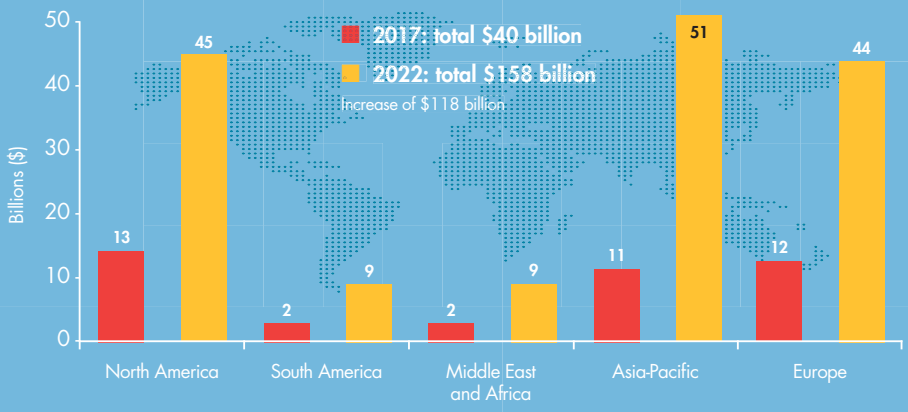
Those who believe that healthcare providers and clinicians are not ready to use data generated from connected medical devices.



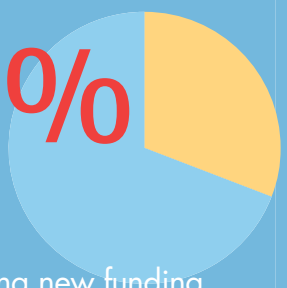
**67%**

Those who believe that the regulatory framework will not catch up with what is possible today for another five years.

## The estimated increase in value of the internet of medical things market, by region between 2017–22

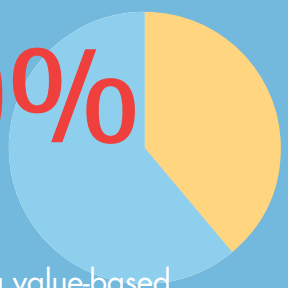



## Med-tech companies are transforming from innovative product suppliers to insightful partners



**31%**

Implementing new funding models for data as a service.



**39%**

Adopting a value-based approach to pricing.

**43%**

Using real-world evidence to drive business decisions.

**Source: Medtech and the Internet of Medical Things, Deloitte.**

# Your own devices

The US FDA plans to develop a new regulatory framework for reviewing 'software as a medical device' and has also issued guidance regarding the FDA's regulatory process for digital tools. Aiming for a more 'streamlined' review, the FDA has updated the software pre-certification pilot programme and a working model of this will soon be released. Stephanie Webster speaks to **Sundeep Karnik** and **Matt Singer** from ZS about the implications of this new regulation for the industry.

As technology continues to advance all facets of healthcare, software has become an important part of products and is now integrated widely into digital platforms serving a range of purposes. Software as a medical device (SaMD) is one of three types of software related to medical devices. The other two types include software that is integral to a device, and software used in the manufacture or maintenance of a medical device. It is the former that is associated with the most uncertainty, as it's a relatively new technology and has less clearly defined boundaries than the other types.

Use of SaMD is continuing to increase. It can be used across a broad range of platforms, including medical device platforms, commercial off-the-shelf platforms and virtual networks, to name a few. Such software was previously referred to by the industry, international regulators and healthcare providers as 'stand-alone software', 'medical device software' or 'health software', causing considerable confusion.

Due to the rapid evolution of devices based on this technology, the FDA has recently taken action to modernise its approach to regulation. It released a 'digital health innovation action plan', involving piloting a new digital health recertification programme to

ensure that patients are able to have access to safe and effective devices as quickly as possible.

These changes by the FDA have been a long time coming, with the former 510(k) process having been in place since 1976. This was heavily based upon the concept of substantive equivalence, the idea of a new device being sufficiently similar to an existing one – a predicate device. If this could be supported by data, this provided manufacturers with a fast-track to market. "While that worked for a lot of medical devices, over the past few years, as innovations have been coming to market, especially around software and digital services, this has pushed the limits of what the original intent was," explains Sundeep Karnik, a consultant at ZS.

## The rule of three

The new regulations bring about three key changes for manufacturers. The first one relates to the selection of the predicate device. "You have to be much more careful when making your selection," says Karnik. "If you choose a predicate device that was approved for particular patents, you cannot add on new features that are software and digital that are over and above what it originally had."

The second aspect centres on the concept of 'substantive'. "Before, you could get around this and say 'look, my device is substantively equivalent to this device, just give it approval,'" says Karnik. "Now, you can't simply introduce new software features that are unproven or untested."

The third element of the new FDA regulations pertains to the data being used in support of a device. "The FDA wants more data than just that of the device performance that you could measure in some animal studies," explains Karnik. "When there are new software features, these need to be tested in a different way, and the data presented to the FDA also has to be a different kind of data."

Although these are significant changes, they don't necessarily mean a longer time to market. "Part of the intent here is to actually make it faster by saying, 'before you even come here, be careful about what predicates you choose, be strategic about what differences you're going to try and argue, and be very intentional about what data you're going to use to support this,'" says Karnick. "If you have thought about it carefully, done all that homework and brought the right information to the FDA, the process should, technically, go faster."

*"Companies will be forced to think more deeply about how either a physician or a patient lives with a particular device."*

**Sundeep Karnik**

These new regulations mean that manufacturers need to think differently about the products that they want to bring to market. "I think something the

industry should think about now is whether they have products that they would have brought to market in the past because it was easier, even though they didn't really bring much value to customers or the company because it was just the red version of the blue and green one that they already have," says Matt Singer, also a consultant at ZS.

*"The new regulations cause you to rethink some of that less innovative life-cycle management and focus more time on where you can actually differentiate or bring value."*

**Matt Singer**

"The new regulations cause you to rethink some of that less innovative life-cycle management and focus more time on where you can actually differentiate or bring value."

This doesn't automatically mean less revenue, however. "Maybe at the end of the day, it costs the company less money because it's spread across fewer products than before and is instead focused on the ones that are really going to bring value to the marketplace," says Singer.

The regulation has a number of implications, particularly for SaMD. "It legitimises that software has reached a majority, and that there is data that supports that it can, and should, be regarded as a medical device," explains Karnick. "These kind of approvals from the FDA impact the physicians to perceive something approved by the FDA as being 'real' and something they need to take action on. It also gives the same message to patients who will be more trusting about using it because the government has looked at it."

However, the perception of these changes is likely to be substantially different between companies. "If you're a newer healthcare player, you might look at this and see it as a huge move forward for you, because now the solutions developed have a clearer and faster path to market," says Singer. "If you are a classical med-tech company, and used to bringing new products to market that typically take three to five years or longer to develop, you might view this as the stakes having been raised a little bit."

The new regulations also have important implications for patient-centricity, a concept gaining traction throughout the industry. "Most med-tech companies have the product at the centre," says Singer. "They're very innovative; they have amazing engineers, and research and development departments, which can create incredible products that move medicine forward and make a substantial impact on the health of patients worldwide. The customer at the centre, whether that's a patient, doctor or hospital, is more cutting-edge thinking, which these changes could accelerate."

This means thinking in a more holistic way than has been necessary in the

past. “Companies will be forced to think more deeply about how either a physician or a patient lives with a particular device,” says Karnick. “Digital and software-based solutions imply a fundamentally different engagement model, one which is integral to the effectiveness of the device.”

## Time to get engaged

Historically, most devices have been relatively passive, and those that have been interactive have been limited in their scope. In contrast, newer technologies facilitate a much higher level of engagement with the patient. “If we take a more interactive device, let’s say you have a high-glucose problem, or diabetes, and you have a device that tells you when your blood glucose is high – you would pop a drop of blood on there, it would say your blood glucose was high and then it was up to you what you did with that information,” says Karnick. “But when you start to add software services, now that device is going to provide you with suggestions in real time on how to manage your health or glucose better.”

This influences the approach needed for the entire product development process. “In order for us to be able to provide those kind of suggestions and nudges to people, it means we have to think carefully about what patients need, how we articulate those needs, and create software and features that serve them and measure the impact to inform the value proposition of the device,” explains Karnick.

Although it has been over 40 years since the 510(k) pathway has been updated, it likely won’t be much longer. Being prepared for potential future changes is therefore key. “If you’re focused on solving important customer problems and demonstrating how you do that better than alternatives, you’re going to be a winner,” says Singer. “That is the sustainable advantage that you can have in any market.”

Central to remaining competitive is transitioning away from the traditional way of working towards a newer, more agile approach. “We have to move from the ‘build it and they’ll come’ model to becoming a lot more thoughtful and intentional about what you are going to build and why,” says Karnick. “Once we’ve decided, we then have to move a lot faster than we did in the past, because if we don’t, someone is going to bring it to the market faster – and we’ll be left behind.” ●

### A new approach

The FDA’s Total Product Life-cycle (TPLC) approach enables the evaluation and monitoring of a software product from its pre-market development to post-market performance, along with continued demonstration of the organisation’s excellence.

#### Excellence appraisal

Identifying the objective criteria and methodology that the FDA will use to pre-certify a company and decide whether a company can keep its pre-certification status.

The FDA is currently basing the pilot programme’s criteria on five excellence principles: patient safety, product quality, clinical responsibility, cybersecurity responsibility and proactive culture. The FDA is currently considering two levels of pre-certification based on how a company meets the excellence principles and whether it has demonstrated a track record in delivering safe and effective software products.

#### Review determination

Developing a risk-based framework so that a pre-certified company can determine the pre-market review pathway for their products. Potentially pre-certified companies could market their lower-risk devices without FDA pre-market review, or only a streamlined pre-market review, based on the company’s pre-certification level and international medical device regulators forum (IMDRF) risk categorisation.

The FDA is planning to leverage the IMDRF framework to help determine the risk categorisation of an SaMD product, incorporating information about the medical purpose of the SaMD and the seriousness of the medical condition that the SaMD is intended to treat.

The FDA is also considering appropriate means to educate patients and providers about the pre-market review and post-market monitoring obligations for each SaMD risk category.

#### Streamlined review

This involves identifying the type of information that a pre-certified company would include in its pre-market submission for the FDA to review software products for safety and effectiveness before patients access them.

The FDA is exploring using an interactive streamlined review of a SaMD with information the agency has already gained from the process to pre-certify a company, and additional information the company would share about the SaMD’s product performance, clinical association between the SaMD output and a clinical condition, and safety measures.

#### Real-world performance

Identifying the type of information that a pre-certified company may have access to about how its software product is performing with patients to support the regulatory status of the product, and new and evolving product functions.

The FDA is considering how best to work with a company to collect and interpret real-world information about an SaMD, and evolve the product’s safety and effectiveness to address any emerging risks. The sources of real-world performance data may include information about a user’s experience, software performance data and clinical outcomes.

Source: FDA

**Above left: Newer technologies facilitate a much higher level of engagement with patients – for example, in blood-glucose testing for diabetes patients.**

# Navigate the regulations for in vitro devices

In vitro diagnostic devices (IVDs) are subject to stringent regulation across the EU. Robyn Meurant, executive director for the IVD and medical devices regulatory team at **NSF International**, talks to *Medical Device Developments* about the full import of these rules, and how the product-testing company can help original equipment manufacturers deliver fully compliant IVDs.

### What are the main points for in vitro device (IVD) manufacturers to be aware of with regard to IVD Regulation 2017/746?

**Robyn Meurant:** Under the IVD Directive 98/79/EC (IVDD) a majority of IVDs (as many as 80%) were exempt from the requirement to submit to a notified body to obtain CE marking. This did not mean that they were exempt from the regulatory requirements, but rather that they could self-declare that a product was in conformity. With the introduction of a risk-based classification scheme in the IVD Regulation 2017/746 (IVDR), all medium to high-risk IVDs must have assessment of conformity by a notified body. It is now believed that at least 80% of IVDs will need notified body intervention. This requirement will impact not only new products to the market, but also those already CE marked.

Up to 80% of IVDs will now need notified body intervention.

*"Many IVD manufacturers think that because they have an FDA 510(k) for their IVD then they will not have many gaps to fill. Worryingly, this is not the case. Equivalence of IVDs is much harder to demonstrate."*

Product manufacturers should also be aware that, under the new system, there will be no grand-fathering.

The concept of risk management is strengthened in the new regulations, especially its implementation throughout the life cycle of the IVD. Of note are the requirements to continuously review the risk assessment, as well as the need to eliminate or reduce the risk as far as possible. This later requirement is not new, but a common approach that does not apply is to reduce risk to as far as reasonably possible. Manufacturers who have taken this approach must revisit their risk assessments and associated solutions.

There are also a lot of new requirements for labelling, including the addition of a unique device identification (UDI), as well as additional roles and responsibilities for economic operators within the pre and post-market arena, whether that be the authorised representative, legal manufacturer, importer or distributor. As a result, the performance of the IVD will come under much greater scrutiny than under the previous regime.

### What are the clinical evidence requirements for the IVDR?

Manufacturers must demonstrate clinical evidence based on a continuous process of performance evaluation. It means that manufacturers must now include evidence of scientific validity, a term used to describe clinical association of a marker with a disease state. For established IVDs, evidence in peer-reviewed literature can be used to support scientific validity and clinical performance; analytical performance must always be demonstrated by actual studies using the IVD. When evaluating the performance of an IVD, the process must take into consideration favourable and unfavourable data.

### What is Eudamed?

Eudamed is an acronym for the European electronic database on medical devices, and is the tool designed for competent authorities primarily to strengthen market surveillance and transparency of IVDs and

other medical devices by providing the authorities with fast access to information. It consists of the electronic systems for the registration of devices, the UDI database; the electronic systems for registration of economic operators, notified bodies and certificates; performance studies; vigilance and post-market surveillance; and electronic systems on market surveillance. Manufacturers, or their authorised representatives, have a number of obligations under the IVDR with respect to registration and data input with Eudamed.

Contrary to popular belief, equivalence of IVDs is hard to demonstrate.

### What is a PRRC?

A PRRC is a 'person responsible for regulatory compliance'. This is a new role that must be fulfilled for all manufacturers and is similar to that of a qualified person in pharma. Each manufacturer shall have at least one person responsible for regulatory compliance who possess the requisite expertise in the field of IVD and medical devices.

Small and micro enterprises do not have to have this person within their organisation but must have one permanently at their disposal. This person, as the name infers, is responsible for regulatory compliance, including ensuring reporting obligations are fulfilled. Authorised representatives are also required to have a PRRC permanently and continuously at their disposal.

*"The main deadline for the EU IVDR is May 2022. Manufacturers are allowed to maintain their current certifications until they expire but there are a number of new post-market activities they are obliged to incorporate after May 2022."*

### What are the time frames for the EU IVDR and how can manufacturers prepare?

The main deadline for the EU IVDR is May 2022. Manufacturers are allowed to maintain their current certifications until they expire but there are a number of new post-market activities they are obliged to incorporate after May 2022 and the end of the certificate.

However, if a manufacturer makes a 'significant change' after May 2022, they have to switch to the new regulation. It goes without saying, therefore, that they have to be prepared. As most IVDs do not have certificates of conformity issued by a notified body, these products will need to meet the new requirements by May 2022.

Preparations among manufacturers should typically start with a gap analysis, which compares the current processes and procedures with what the new regulation requires. From there, they need to march though a very methodical, project-managed time line to start handling some of those gaps.

Many IVD manufacturers think that because they have an FDA 510(k) for their IVD that they will not have many gaps to fill. Worryingly, this is not the case. Equivalence of IVDs is much harder to demonstrate, especially with the emphasis in European law on demonstrating state-of-the-art capabilities in the product.

Indeed, the IVDR impacts on almost all functions of a manufacturing company, not just the regulatory affairs and quality assurance departments. It is imperative that senior management are aware of the extent of the impact and support the transition. Companies may need to rationalise their product range as well as decide whether they are going to hire additional resources to keep manufacturing in-house or if they will use third parties for some of these functions.

### How does NSF International help companies implement these procedures?

An impressive offering at NSF International is its regulatory and quality training. We are continually producing e-learning resources and face-to-face training because regulations are constantly changing. If people haven't thought of some of these things, there is a fantastic e-learning module on the new regulation. Our staff includes ex-regulators from the EU, ex-notified body staff and internationally recognised IVD experts. NSF International goes beyond traditional consulting. There are people involved in clinical evaluation reports, technical file remediation and performance evaluation reports. They are now helping companies remediate those files and keep them updated. A call to action is the biggest message. Companies cannot wait for more guidance – they need to act now. ●

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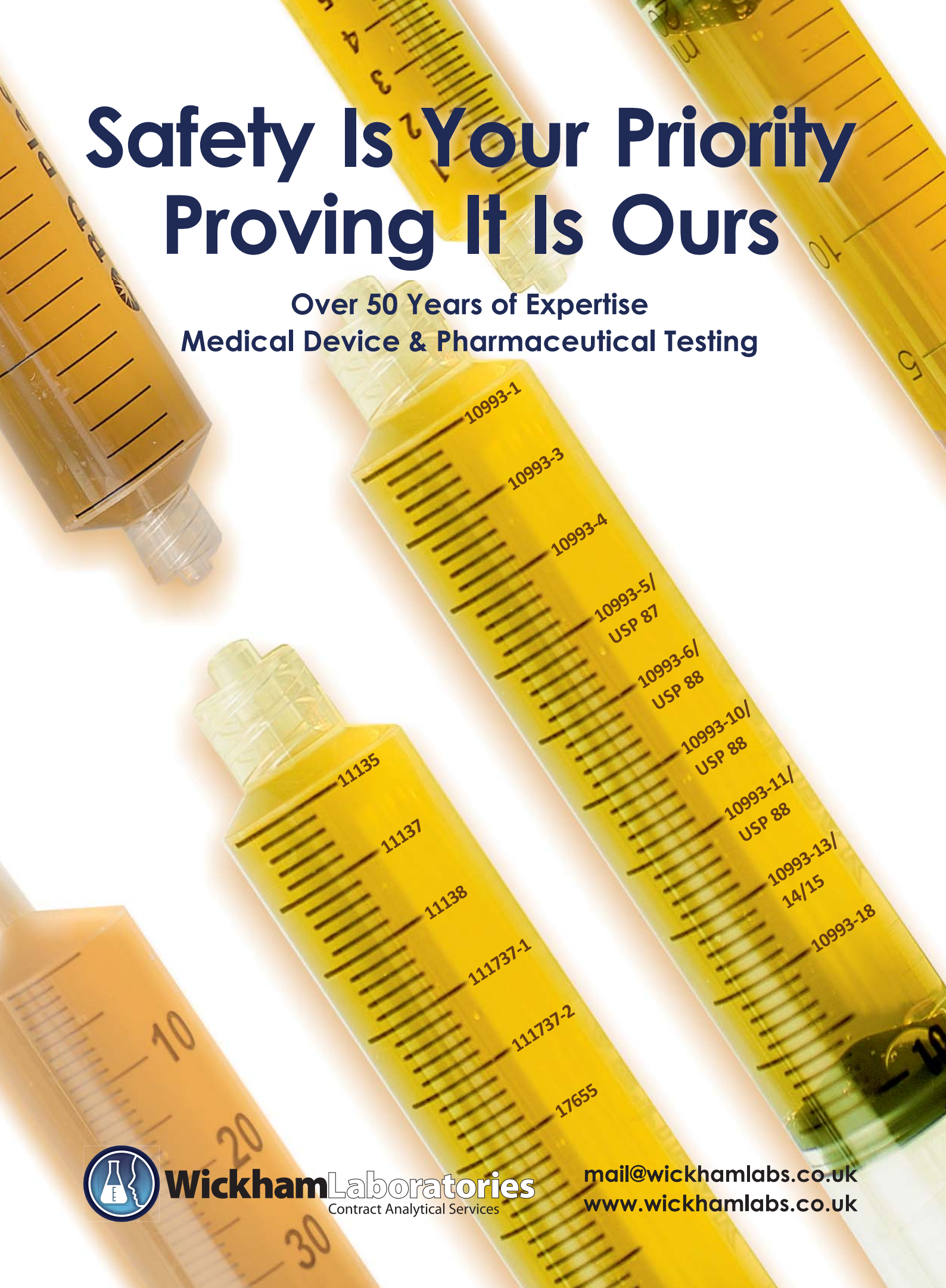



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# A test of character

**Wickham Laboratories** carries out biological assessment reports (ISO 10993-1) on a range of medical devices, working with clients to determine the appropriate regulatory pathway, saving them money and reducing unnecessary testing.

Medical device testing is one of the more complex services offered in the life sciences sector, both in terms of the diversity of the products tested and the different levels of safety or biocompatibility required prior to approval for use in patients.

There is a high demand for reliable testing services for medical devices as it is one of the fastest-growing industries in healthcare. The European medical device industry, constituting a third of the global market, is thought to be worth approximately €100 billion.

Within the US, the FDA's Center for Devices and Radiological Health (CDRH) is responsible for ensuring the safety and effectiveness of medical devices. The FDA was given authority to begin regulating all medical devices in 1976, when President Ford signed the Medical Device Amendments Act.

The EU's rules relating to performance and safety of medical devices were harmonised during the 1990s and recently updated in 2017 with two applicable regulations: the medical device regulations (MDR) and the in vitro diagnostic device regulations (IVDR).

Wickham Laboratories is committed to determining the appropriate regulatory pathway for clients.

## Medical device testing overview

The classification of a medical device covers a wide range of device types, each requiring various levels of safety or biocompatibility testing before market release.

All biocompatibility testing carried out should adopt a tiered approach in order to minimise the amount of in vivo testing required. This means that before any testing takes place, it is essential to have both the device and materials used for manufacturing assessed to ensure the correct route of testing or evaluation is taken.

ISO 14971, the application of risk management to medical devices, is a standard that specifies a process for the manufacturer to identify any hazards associated with the device. These specifications should always be adhered to and the standard is applicable to all stages of the medical device life cycle.

In addition, pharmaceutical and medical device manufacturers should always consider environmental monitoring before manufacturing, as this can lower the risk of contamination and help them to understand the levels of microorganisms within their environments.

## In the lab

Before considering testing, Wickham Laboratories works with clients to determine the appropriate regulatory pathway for their situation, keeping its ethical obligations at the forefront. It recommends biological assessment reports (ISO 10993-1) instead of testing, ultimately saving the client money and reducing unnecessary testing.

Biocompatibility testing, or 'Biological Evaluation of Medical Devices' (as set out in ISO standard series 10993), is a set of guidelines and testing parameters for assessment of medical device safety before any medical device comes to market. The required tests are generally referred to as the ISO 10993 or USP Plastic Class I-VI series; they include:

- 10993-3: Genotoxicity
- 10993-4: Haemocompatibility
- 10993-5/USP 87: Cytotoxicity
- 10993-6/USP 88: Implantation
- 10993-10/USP 88: Sensitisation and skin irritation
- 10993-11/USP 88: Acute, sub-acute, chronic systemic toxicity and pyrogenicity
- 10993-13: Identification and quantification of degradation products from polymers
- 10993-14: Identification and quantification of degradation products from ceramics
- 10993-15: Identification and quantification of degradation products from coated and uncoated metals and alloys
- 10993-18: Chemical characterisation of materials.

There are a variety of other tests that may also be required, including 11135-1 and 11737-2: Sterility testing, and 11737-1: Bioburden determination. ●

**For further information**

www.wickhamlabs.co.uk

# Change on the horizon

With uncertainty around Brexit and what it means for the NHS, along with news about the government's 10-year plan, it is easy to have missed some important signals that support the greater use of structured data within the health service. The Global Medical Device Nomenclature Agency's chief executive, **Mark Wasmuth**, gives some insight into how medical devices can be more accurately identified to optimise patient safety.

NHS medical device suppliers have been told to prepare product data to comply with procurement contract standards introduced by the 2014 NHS e-procurement strategy.

Despite challenges around new IT systems introduced to the health service, the policy is still intact. In fact, the latest initiative from the Department of Health and Social Care, NHSX, takes the digital transformation to a new level, promising "a new joint organisation for digital, data and technology" for the NHS.

The NHS e-procurement strategy directs trusts to ensure that the medical devices they purchase are barcoded and their relevant product data is collected in a central database.

Most people are familiar with barcodes in the supermarket, and they also appear on medicine packets, but, surprisingly to many, they are only starting to appear on medical devices.

Barcode numbers are individual to each product from each manufacturer and often also contain additional information, such as the batch number or

expiry date. They are especially useful for managing the stock level of individual items, whether that is baked beans or syringes.

Putting aside the odd problem at the self-service checkout, they are a powerful aid to helping retailers know exactly what they have in stock, planning future demand and knowing when extra supplies need to be ordered or when to cut back.

The use of barcodes on products is particularly helpful when you need to locate a batch that needs to be returned to the manufacturer or has exceeded its expiry date. For instance, supermarkets use barcodes to instantly identify and remove specific packs of food that have been identified by the manufacturer as having a safety issue.

Hospitals are also starting to make use of this technology to help them better manage their supplies and capital equipment.

Examples of how barcodes can bring dramatic healthcare benefits include the use of barcoded wristbands to improve the identification of patients, enabling the reduction of errors in their care. For instance, the medical implants used to treat a patient can be scanned before an operation and linked to a specific patient, making them easier to monitor after the operation.

But barcodes are not so useful when you need to compare similar devices made by several manufacturers; invariably, the codes they use will be different, because the barcode relates just to the specific product from one specific manufacturer.

## Device categorisations

The need for a standardised system for naming and grouping medical devices has led to the creation of the Global Medical Device Nomenclature (GMDN) international categorisation of medical devices by those responsible for medical device safety.

This categorisation system is important for several reasons, ranging from improving hospital efficiency and patient protection, to helping long-term medical studies find out what devices are most effective.

For instance, at a basic level, a hospital may well want to know how many 50ml syringes or bedside scanners it has. The GMDN enables them to quickly answer this as it helps hospitals measure and control inventories where they have similar devices by different manufacturers.

The GMDN can also be used to improve efficiency. It allows easy comparison when an improved or more cost-effective device comes on the market while older versions are still in use – whether it's beds, operating tables, syringe pumps or respirators. Another example of how the GMDN is used is in long-term medical studies, which often need to compare the use of similar medical devices from a range of providers. The GMDN groups medical devices that have the same use, which is also vital when it is discovered that the problem with a medical device is not limited to one manufacturer but may also be shared by other products that use the same technology or materials.

A good example of this is metal-on-metal hip joints, which were found to cause problems and were produced by several different manufacturers. The GMDN would enable this systematic problem to be identified early, whereas the barcode is only useful for identifying an issue with a specific device from one manufacturer.

*"The GMDN groups medical devices that have the same use, which is also vital when it is discovered that the problem with a medical device is not limited to one manufacturer but may also be shared by other products that use the same technology or materials."*

The GMDN can be used to identify all the different products in the market that might have the same problem, so hospitals can quickly be alerted to remove the faulty products, thereby reducing risks to patients.

The key to the success of using the barcode and the related product information, including the GMDN, is that the database lists all the products to form a catalogue. This is used to retrieve data when the barcode is scanned.

## Data mining

A central catalogue of products is being created for the NHS, primarily using the existing GS1 data pool network, which borrows its specifications from the requirements used by the US FDA in its UDI Rule. The US FDA has been collecting product data from manufacturers as part of a continuous programme to ensure it has a complete list of medical devices on the US market.

The programme started in 2014 with higher-risk devices, and is being phased in to include all devices by 2022. It has been a considerable challenge for manufacturers to consolidate the large amounts of data necessary to identify all the devices on the US FDA database system, called GUDID.

The NHS catalogue is being built as part of new contractual arrangements between trusts and suppliers. The new NHS pre-acquisition questionnaire (PAQ Form) is already being seen, which may also form part of a new contract. The PAQ Form uses the GMDN code to identify the general description of the medical device. ▶

### Agency for change

The GMDN Agency is a non-profit organisation responsible for the ongoing maintenance of the GMDN, a system of internationally agreed descriptors used to identify medical device products that will meet a global need for identification purposes. It is a registered UK charity, subject to an independent audit each year and regulated by the UK Charites Commission. The agency's objectives are to preserve and protect health, and to relieve sickness for the public benefit by developing and maintaining the GMDN.

Source: Global Medical Device Nomenclature Agency

It is taking some time to get trusts to implement the new catalogue and barcoding systems into general use. Soon, new regulation will reinforce the work started by the NHS across several demonstrator sites.

The planned introduction of the new European regulations for medical devices (MDR/IVDR) will mandate the barcoding and collection of data elements, including the use of the GMDN. The data will be included in the central European database, called EUDAMED. The new regulations are planned to be introduced in 2020, and deadlines for providing data for different risk groups of products are planned until 2027.

But what about Brexit – what happens if the UK leaves the single market?

## The 'B' word

In its latest guidance on a no-deal Brexit, the UK regulator (MHRA) is planning "the expansion of the MHRA's registration system to all classes of medical device". The MHRA is fully committed to using the GMDN following its recent introduction, in early 2018, of requiring the GMDN code for all registrations for low-risk devices. The most recent evidence has been the publication of the draft regulation 'The Medical Devices (amendment etc.) (EU exit) Regulations 2019', which borrows heavily from the EU regulations.

So, there will be no getting away from the need to organise and provide large amounts of product information, and manufacturers unfamiliar with the requirements should get a hold of the new European regulation and see what is needed. This may require bringing together product data from different parts of an organisation and assembling it in a new database.

The GMDN Agency is a charity that works closely with manufacturers to make sure the GMDN represents all medical device products on the market, as well as keeping it up to date with the latest innovations. It provides the GMDN to hospitals and helps them improve their barcode systems for managing the products they use – thereby supporting patient safety.

Each hospital uses thousands of different medical devices daily to treat patients. Trying to keep track of all these items is difficult even when their names are clear and succinct. But often names are far from clear, with many manufacturers using widely different terminology for the same type of device.

For example, a carotid artery stent, used to treat the narrowing of arteries and thereby decrease the risk of strokes, is named by three different manufacturers as a 'closed cell self-expanding stent', 'carotid stent system' and 'nitinol stent system'.

These devices are medically the same yet sound completely different to anyone other than a specialist. Imagine this problem across each of the complex products a hospital needs to treat patients in a modern health system.

On top of the sheer amount of extra time and effort needed for sourcing the right devices and comparing alternatives, such confusion creates further complications that may lead to wrong devices being ordered and better alternatives overlooked.

The GMDN standardises the name by providing an official term for each medical device on the market.

This also includes a five-digit code and a full definition, to further clarify important differences and similarities between products.

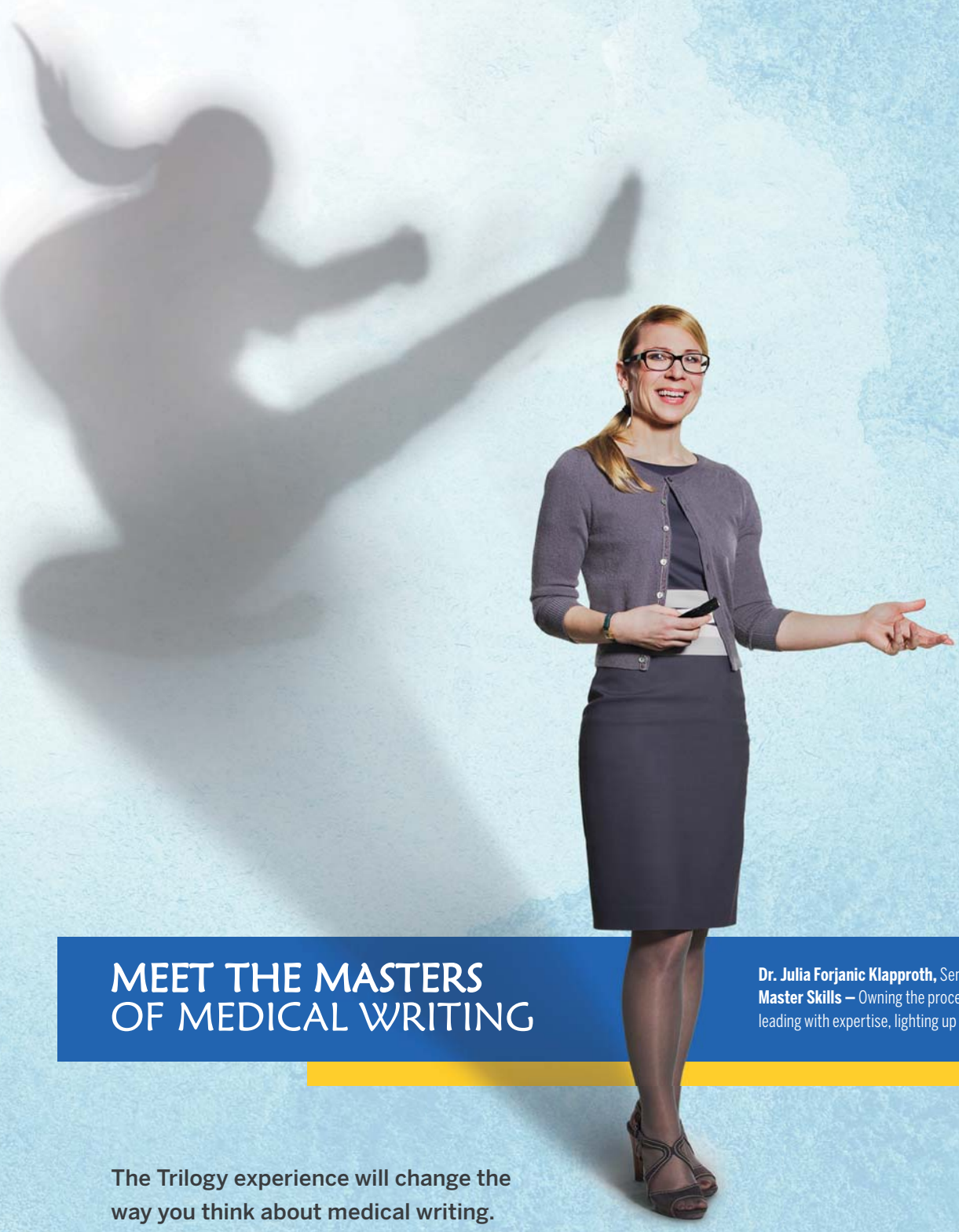
A simple example of this is a scalpel, which can be either single or multiple use. Anyone seeking a single-use scalpel can go to suppliers and request items with the GMDN number 47569 to confidently ensure they have the right item, regardless of how it is described by the manufacturer or distributor. For other types of scalpel there are different codes to avoid any confusion.

The GMDN system, and online database, provide device manufacturers and hospital staff with the information they need to determine the standard name for each device, so every item of stock within a hospital's vast inventory can be clearly identified and organised using the GMDN, efficiently and accurately.

The global importance of the GMDN is obvious when you consider that the database is translated into over 25 languages. In many countries, the GMDN is required by the national regulator, and therefore it is growing in popularity with manufacturers and healthcare providers.

This supports communication between hospitals and international suppliers, and helps reduce the dangerous misuse of medical equipment due to misidentification. It is also intended that regulators use the new larger data sets to quickly identify the signals that would single out problem devices, such as those that might be counterfeit or substandard, and remove them from the market before they do any harm.

Hospitals worldwide now benefit from the GMDN's consistent naming – useful when your phrase book does not stretch to 'carotid artery stent'. ●



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# Strategic medical writing for device submissions

Julia Forjanic Klapproth of **Trilogy Writing & Consulting** explains why it is time to start using strategic medical writing in the world of device submissions.

Until recently, the documents needed for device evaluations were not well defined and were generally written by one person (often a medical writer), essentially on their own. Now, with the increased regulatory requirements brought on by the EU medical device regulations from 2017, more people are getting involved in preparing the clinical evaluation reports (CERs) and the writing game is changing.

Input is needed from a team of CER contributors and reviewers, including a clinical specialist who understands the environment the device is to be applied in; a regulatory expert who has knowledge of the regulatory background for the class of device and who can inform the medical writer about the assessor's expectations based on prior discussions with the CER regulatory assessor; the safety surveillance group to provide details of post-marketing surveillance; and someone who can provide depth of knowledge on the technical development and characteristics of the product.

Many of these newly formed teams do not have experience in preparing regulatory documents and are unsure of how to make these documents do what they need to. More than ever, the medical writer is there as an advisor to provide knowledge gleaned from writing many regulatory documents in the arena of drug development and understanding the needs of regulatory guidelines. With larger teams, the role of the medical writer becomes more strategic, as they serve to ensure all functions on a CER team (medical affairs, clinical, safety surveillance and research and development) provide necessary input while helping mediate cross-functional differences of opinion on what messages there are to tell.

Writing scientific documents as a collaborative process, instead of as a single author, does not come naturally to many contributors. Experienced medical writers often serve as a kind of glue for the different functions on the CER team. They pull team members together by focusing them on telling a cohesive narrative – this is achieved by effective interpersonal skills. Strong argumentation and leadership skills are needed to challenge and guide a team to find the best way of presenting complex data sets, and telling the story consistently and clearly.


The strategic medical writer is a 'glue' to hold the CER team together.

Furthermore, although scientists understand the principles and ideas behind the science of what they are working on, many are not skilled at communicating those ideas in the written form. For device documentation, the science behind the product is an important part of the story to be told. There is a lot of non-medical data to be described in addition to the clinical data. The scope of scientific knowledge that medical writers bring to these documents is very relevant in order to effectively tell the whole story of the device. Experienced medical writers have the skills to interpret scientific data and present it in a way that meets the regulatory goals, ensuring that agency reviewers will clearly understand the messages to be told.

## Well-honed tricks for new sectors

In the world of drug development, this role of strategic medical writing to assist dossier writing teams in pulling ideas together has been applied for decades. Now that the world of devices has become more regulated, this role of the medical writer has become important to efficiently produce CERs that aid the clinical evaluation of devices. Medical writers experienced in writing submission dossiers for drug applications are well versed in applying the evidence-based principles required by the new EU medical device regulations.

By tapping into this experience, device manufacturers have access to a well-developed skill set that will make producing and updating CERs less of a burden, and ensure these documents are truly fit for purpose. ●

*References available on request.*

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# Act together

There has been ongoing debate about the relative merits and disadvantages of insourcing versus outsourcing in manufacturing. However, recently, companies have become more interested in new ways of working. Within the UK, this has taken the form of partnerships with Academic Health Science Networks (AHSNs) in order to capitalise on the expertise of academia and industry. Louise Thomas takes a look at these developments.

It is an exciting time for the industry. Fresh opportunities are increasing each day, driven by the needs of healthcare systems to improve patient diagnosis, treatment and experience. This has not only led to greater demand for innovative devices, but also the potential to work in a new, more collaborative way, breaking down the traditional silos between industry and academia, as well as interacting with healthcare professionals throughout the development process.

A model that has begun to be more heavily used in the UK is the partnering of industry with Academic Health Science Networks (AHSNs). These are UK organisations, first licensed in 2013, which are pioneering new ways of developing and implementing innovations for use within the UK's NHS in the disease areas defined as being the highest priorities. AHSNs have established a med-tech innovation national network to accelerate this process for medical devices, which includes

physical devices and in vitro diagnostics. This remit therefore excludes software as a medical device and large devices, such as MRI scanners. The Eastern Academic Science Network (Eastern AHSN) has reported that the NHS currently spends £6 billion a year on medical devices, highlighting the huge potential for manufacturers.

The medical device landscape is shifting and faces challenges in the form of new regulatory requirements, as well as the strong market forces demanding competitively priced products for a complex and diverse healthcare procurement environment. In their 2019 report, the Eastern AHSN proposed an innovation pathway aimed at manufacturers seeking to tap into this market, which aimed to ensure that the resulting products meet patients' needs as well as being commercially successful. Throughout this process there are a number of areas for collaboration with academics and healthcare professionals.

"The health and science infrastructure in the UK is uniquely positioned to take advantage of the opportunities for economic growth and improved patient outcomes created by med-tech," says Piers Ricketts, vice-chairman of the AHSN and CEO of the Eastern AHSN. "However, there is a risk of companies getting lost as they navigate the innovation maze."



## Take the stages

The first of the stages outlined in the report is 'creation'. As the name suggests, this involves identifying the market value of the concept, the impact on health outcomes and identifying market access barriers. To assist in this stage, AHSNs offer Innovation Exchanges, funded by the UK's Office for Life Sciences, where potential medical devices can be linked with existing local healthcare system challenges. This stage might also involve patient and public involvement, including direct interaction with NHS trusts, AHSNs and medical charities, as well as the National Institute for Health Research (NIHR)'s national advisory group, INVOLVE.

Development is the second stage, where the product is refined for regulatory assessment and clinical evaluation. The first step in this process is prototyping, in which there are a number of opportunities for collaboration. For example, through catapult centre, which are non-profits that facilitate UK businesses, scientists and engineers to work together on late-stage research and development. There are 11 of these centres in the UK, spanning a diverse range of areas, including cell and gene therapy, digital, high-value manufacturing and precision medicine. There is also the NHS Innovation Accelerator, an NHS England initiative delivered in partnership with AHSNs. It was launched in July 2015 to support delivery of the NHS 'five year forward view'. It supports the uptake and

spread of high-impact, evidence-based innovations across the NHS.

The second step in the development process is testing through clinical trials. This will, of course, vary significantly, depending on whether the device is in vitro or not, and its perceived level of risk. Collaboration in this stage may involve interaction with the newly formed NIHR med-tech and in vitro diagnostics co-operatives (MICs), which act as centres of expertise, bringing together patients, clinicians, researchers, commissioners, and industry to support the development and evaluation of medical devices within clinical settings. There are a number of MICs in the UK, each with a different theme and led by a specific NHS organisation.

It is also in this stage that contract research organisations might be used for the clinical testing of the product. With the increasing demand from regulators for real-world patient data, use of Health Data UK's digital innovation hubs can be useful to obtain health-related data at scale for research and innovation. The HealthTech Connect horizon scanning database can also be valuable, as it provides a record of medical devices at all different stages of development. This aims to reduce duplication and provide a smoother route to market in the UK.

Regulation is the following stage, which is invariably complex with the huge amount of legislation to navigate. To help with this process, there are med-tech innovation briefings, commissioned by NHS England, which provide evidence-based advice to those considering the implementation of new medical devices or diagnostics. These aim to be fast, flexible and responsive to the need for timely advice about novel technologies. The National Institute of Clinical Excellence (NICE) organises these to avoid local NHS organisations having to produce similar information for local use.

**£6 billion**

The amount spent each year by the NHS on medical devices.

**Eastern Academic Science Network**

*"The health and science infrastructure in the UK is uniquely positioned to take advantage of the opportunities for economic growth and improved patient outcomes created by med-tech."*

**Piers Ricketts, AHSN**

NICE plays a large role in reviewing the evidence for a specific technology once it has received a CE mark. The NHIR, hosted by the University of Newcastle, undertakes horizon scanning to inform NICE of any products early in their development, to help ensure that guidance can be published as close as possible to the launch date. ▶

### Case study: CMR Surgical

CMR Surgical, from Cambridge, has developed a next-generation surgical robotic system that aims to transform minimal access surgery (MAS) over the next few years. The system, named Versius, is designed to be more portable, versatile and cost-effective than existing systems. The CMR vision is to make MAS universally accessible, thereby improving healthcare outcomes at lower cost. The Versius system is specifically designed to meet this vision. The medical robotic market is highly competitive, with an established global leader and emerging competition from several companies the backing of which includes the likes of Google and Johnson & Johnson. Global annual revenues for robot-assisted MAS are presently approximately $4 billion and anticipated to reach $20 billion by 2025. The Versius system takes up a smaller footprint, is portable and flexible, and is intended to come to market at a significantly lower cost. CMR recently attracted $100 million in the largest ever series B investment deal raised by a European medical device company.

"Typically, medical device development, from idea or design through to commercialisation, is normally a 10-year journey, and we will have done that in around five," says ECO Martin Frost. "You can only do that by having clear focus on what you want to deliver and why, recruiting excellent people and creating a culture that facilitates creative, responsive thinking.

"We identified an unmet need – 95% of minimal access procedures are not yet done robotically," he continues. "We then looked at why this was the case and what we could do to address that need. From the beginning, we had a plan of how we would get our product to market and our commercial advantage."

Source: 'The MedTech Landscape Review' by the AHSN Office for Life Sciences and the NHS

Commissioning and adoption is the next stage. The NHS supply chain has a new operating model that aims to deliver improved procurement and logistics support to the NHS. This will be achieved in three ways: increasing uptake of products published via the national route to market, increasing the use of a standard range of products by the NHS, and using enhanced buying power to influence purchasing behaviours and ensure that the best products are provided in a cost-effective way to the NHS.

*"The potential of cutting-edge technologies to support preventative, predictive and personalised care is huge, and the UK has the chance to lead the world."*

**Richard Phillips, Association of British HealthTech Industries**

There are six main routes to market for companies interested in supplying their products to the NHS. These are direct to trusts or primary care organisations, through the NHS supply chain, through collaborative purchasing arrangements, national framework contracts, government tenders and contracts, as well as selling to companies that use the product to deliver their service in the NHS. AHSNs play a key role in supporting adoption of new devices into the NHS, which has been supported by a recent study by the King's Fund. Findings highlighted the need for new technologies to be incorporated into a wider service redesign in order to positively impact health outcomes.

## Relationships of convenience

Working more collaboratively with academia can also take the form of 'clustering', when companies concentrate efforts in a particular geographical location. The NIHR has designated 11 MICs to build expertise and capacity in the NHS to develop new medical technologies and provide evidence on commercially supplied diagnostics. These bring together patients, clinicians, researchers commissioners and industry.

There is growing interest in these clusters, with a current network of more than 100 science and technology parks in England. Although there is no single formula for a cluster, the Eastern AHSN has identified a number of key success factors.

The first of these is academic strengths, as facilities can provide world-leading expertise from researchers in physical sciences and engineering. The interdisciplinary way of working also allows areas of convergence to be capitalised upon. In addition, clusters facilitate access to leading research clinicians, patient populations and real-world data.

Effective business networking can also take place within these clusters, as they bring together small and large companies in a structured way. Regional sponsorship is another potential advantage. These environments are attractive in terms of schools, housing and transport. There are also opportunities for funding of relocation and supportive business rates. Furthermore, the ecosystem also includes legal advice, specialist design consultancy and manufacturing, and access to investors. The infrastructure not only provides specialist facilitates and equipment but also local capabilities such as advanced manufacturing.

"The potential of cutting-edge technologies to support preventative, predictive and personalised care is huge, and the UK has the chance to lead the world," says Richard Phillips, director of healthcare policy at the Association of British HealthTech Industries, who co-authored the report. "We have the opportunity to build an ecosystem that continually creates the best technology that can be exported, alongside new methods and insights that can contribute to health outcomes globally."

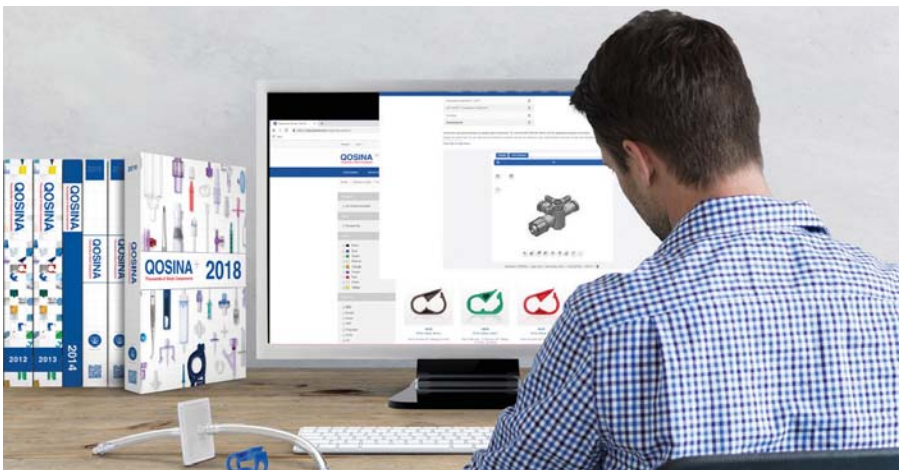
The AHSN's work remains in an early stage but offers huge potential for OEMs to work in a more collaborative way – in manufacturing and the other aspects of the product development process. The AHSNs have outlined the next steps of their work. This includes rigorously assessing and prioritising technologies for national support in the UK, facilitating access to cutting-edge research and development, connecting companies to high-tech manufacturing advice, partnering with NHS providers seeking to adopt novel technologies and supporting OEMs in market access activities. ●

# Using stock components can reduce time to market

As one of the leading medical device component suppliers of OEM components to medical and pharmaceutical industries, **Qosina** is there every step of the way, from prototyping, through sourcing and customising components, to providing material and technical specifications.

Getting your product to market is rarely an easy task. In fact, it can be quite daunting. As engineers, you may feel that you spend much more time searching for and developing parts than actually creating products. Qosina hopes to alleviate this stress by providing medical OEM components and innovative solutions to make your device concept a reality.

Here's how Qosina helps to eliminate your go-to-market challenges.




Qosina provides 3D CAD models and material specifications that allow the easy implementation of components into designs.

### Prototyping – easier and cheaper

If you're still in the prototyping phase of research and development, you don't want to order a bulk quantity of a part that might not work for you. Sampling is key early in the process, and Qosina's selection of over 5,000 in-stock SKUs is perfect for building out your prototypes without committing to large orders. Qosina offers complimentary samples on most of its products, so you can explore a wide range of materials, colours and configurations. This allows you to evaluate and test in advance of purchase, removing technical risk from the product development process.

### Sourcing and customising components

Using stock components can significantly lower the cost and time of creating a mould, since one may already exist. However, if the item you require is not in Qosina's inventory, it will work to develop the part to your exact specifications. A slight alteration of an existing mould can be a cost-effective way to create a new part to meet your requirements. Qosina's knowledgeable product development team can easily adjust stock design, size, colour and material for your purposes.

### Easy access to required documentation

With the ever-increasing demands on engineers, a certified, technically proficient component distributor should offer additional value propositions to reduce any supply-chain-related burdens. Qosina provides 3D CAD models and material specifications that allow you to easily implement components into your designs, while staying up to date with government and safety regulations. Qosina offers CAD files in a variety of formats, which can be helpful for everything from adapting engineering drawings to sharing visuals with non-technical team members.

Qosina also provides comprehensive technical specifications, such as material safety and data sheets, technical data sheets, material certification and compatibility information on all of its products. You can easily access these resources on the company's website.

### Streamline your vendors

Using one supplier for everything, from running materials through tooling to quoting secondary operations for secure supply chains, will streamline your vendor list and prevent complicated outsourcing. Consolidating purchases and suppliers with one order can also significantly reduce overheads.

### Education on relevant industry topics

Qosina keeps you in the loop regarding complex and pressing subject matter in the medical device industry. Download white papers and case studies, and read the company's latest blog posts for information, guidance and solutions on hot-button issues.

Qosina's number one priority is to offer the best solutions to fit its customers' needs and adapt as the development process continues. The company is constantly adding new products to its line, and providing cost-effective solutions to help you get your project off the ground and into production. ●

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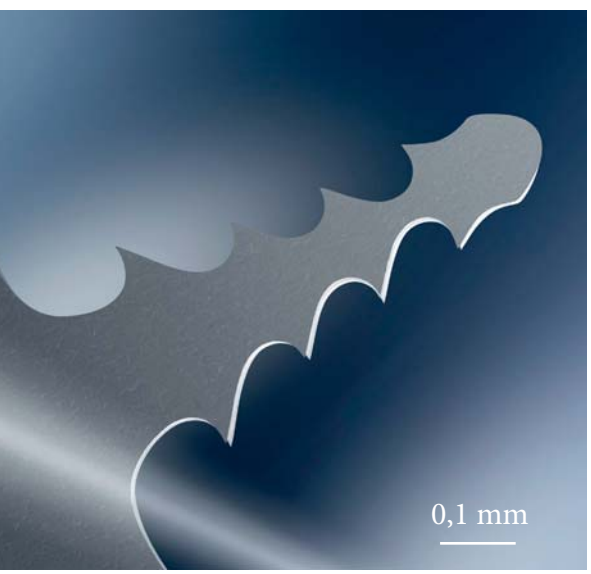


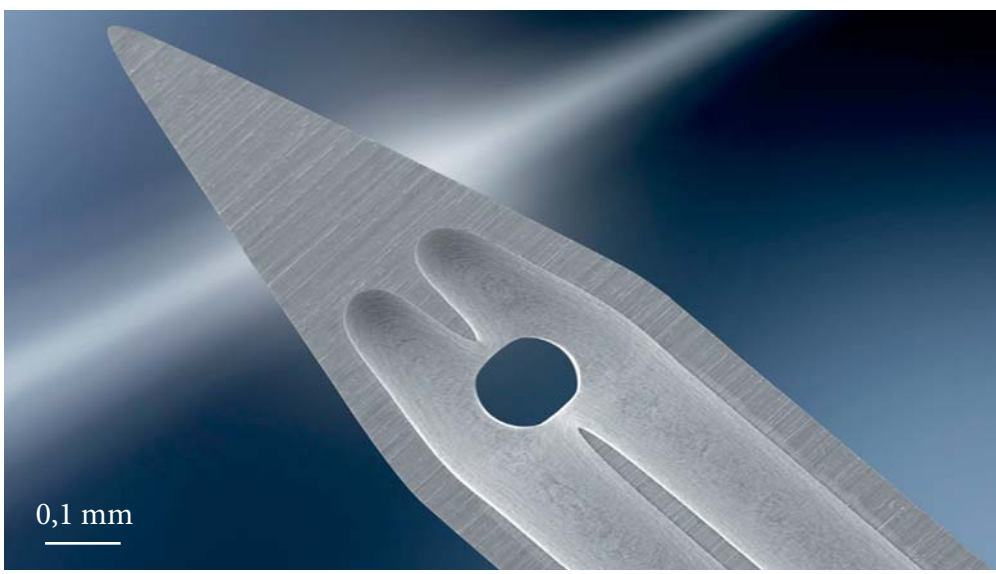


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# Advanced photochemical etching solutions

Karl Martinson, **Micrometal**'s North American sales director, looks at the challenges involved in the design and manufacture of photochemically etched metal components for the medical industry, and the advancements in technology and increased levels of precision achieved to address them.

Many medical devices and applications require small metal components that demand very specific characteristics. These can include:

- ultra-high precision
- very thin material
- unique physical features
- unique surface textures
- identification features
- extreme consistency part-to-part
- ease of integration into the final device
- competitive cost.

Also, different medical applications require components made from a variety of different metals including stainless steel, copper, alloys and clad materials. It is a significant challenge to balance the combination of the above characteristics with the desired material, while maintaining cost and production requirements.

While numerous manufacturing technologies exist to create precision metal components, one technology in particular offers the capability to incorporate all of these characteristics in one seamless manufacturing process. Photochemical etching – also referred to as photochemical machining or chemical milling – possesses the unique ability to meet all of the above demands when compared with technologies such as stamping or laser machining.

Photochemical etching also eliminates the need for certain post-processing, such as removal of burrs and thermal stresses, sharpening of blades, for example. The development of continuous 'reel-to-reel' etching production has dramatically improved production capacity while reducing cost and improving consistency in quality.

Common examples of etched components are surgical blades, surgical needles and lancets, micro-separation filters, screens, implants, springs and electrical contacts.

Etched parts can be manufactured in thicknesses as low as 0.025mm (0.001in), up to 0.500mm (0.020in).

Parts can be manufactured in thicknesses as low as 0.025mm (0.001in), up to 0.500mm (0.020in) with hole/feature sizes smaller than the material thickness.

Advancements in etching technology allow levels of precision, both in physical feature size and in dimensional tolerances, that were previously considered unachievable for volume production components. Micron-level precision is common for many applications.

## A focus on precision

The precision in physical feature size comes from a combination of technology developments. Thinner photoresist layers and high-resolution photomask tools, such as those used by Micrometal, provide exceptionally tight tolerances.

These, combined with extremely precise monitoring and control of the chemical etching rate, allow features and precision that cannot be achieved in production with other manufacturing technologies such as stamping or laser cutting.

Most importantly, etching offers exceptional design freedom; features are not limited to two dimensions. Blade edges, capillary grooves, conical holes and textures can be included in the design. Etching allows medical component designers to 'think outside the box' with regard to component size, shape and features.

Because the process is non-mechanical, there are no residual artefacts such as burrs or material stresses that must be removed. A non-mechanical process also ensures that there is no wear or degradation of tooling over time, providing the ultimate consistency from part to part. Production capacity from a single set of photomask tooling is essentially limitless; the first component will be identical to the 10 millionth component. Also, because the process generates very little heat, there are no thermal stresses and no localised hardening of the material (as would result from a process like laser machining).

In summary, photochemical etching provides a compelling solution to many of the medical industry's demands for high-precision metal components. The technology has evolved and improved dramatically in recent years. By offering a distinct combination of precision, unique physical features and competitive cost, etching may be the ideal manufacturing technology for many applications. Component designers have new options for designs that they may have considered to be impossible in the past.

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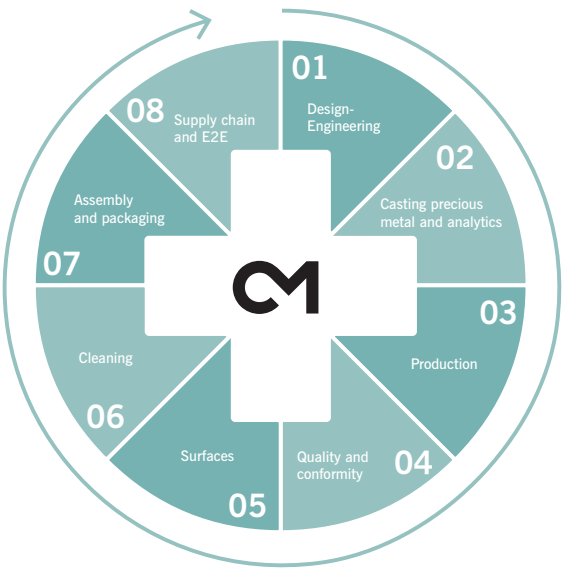


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# The art of science

Developing a metal medical device requires balancing a budget, deadlines, design considerations and more. In light of rapid technological advances, deciding upon the best process to maximise manufacturing efficiencies can be challenging. Louise Thomas explores the important factors to consider when making this selection.

Manufacturing all the components for tools and devices in the industry is an ongoing effort involving balancing precision and quality. With the growing needs of life sciences, metal components have become an integral part of building medical devices for the treatment of a range of diseases.

Biocompatibility is a constant challenge as devices need to be used internally and externally within a range of medical applications. For this reason, designs are continually changing and require rapid prototyping to ensure that they are fit for purpose. The ability to meet these demands in an efficient and effective way is the result of rapid advancements in metals and alloys for components that are small or complex.

When manufacturing a device that involves metal, a key decision lies between machining and stamping. These choices are determined by the fit, form and function of a particular component, along with the geometry of the part and material used.

If a medical device is designed for a large number of uses, then machining works best, as it produces complex parts that support durability. For products that are meant to be used just once, stamping is more suitable as it produces precision parts that tend to be less durable. Volume is another key driver in the decision-making process.

When millions of components are needed on a weekly basis, this can be easily achieved with stamping. Machining these quantities could require over 100 machining centres, making it unfeasible for this purpose.

Tooling costs are another important consideration. As machining is more versatile and precise, it is preferable for devices requiring tight tolerances that need to be produced in high volumes. As long as a suitable machining centre is available, it can be relatively easily programmed to accommodate the part geometry. In contrast, a progressive stamping die takes much longer to design and build, and is much more costly.

Part geometry is also an important variable to bear in mind as there are some components that are not able to be stamped. Certain diameters cannot be pierced using stamping. In such cases, machining is a better option, which can be combined with laser technology.

Material selection factors are also significant in making a decision between stamping and machining, particularly thickness and hardness. For example, stamping can be limiting because thickness must be uniform throughout the part and hardness needs to be carefully considered because of the potential for cracking during forming. In contrast, almost any hardness can be machined. ▶

Most red metals, stainless steels, titanium and cold-rolled steel can be stamped. Titanium and stainless steel are the most commonly used materials for stamping. Both are popular for implantable medical devices due to their biocompatibility. However, titanium is often only available in wire, rod and sheet forms, rather than in continuous strips, the latter of which tends to be needed for the majority of stamping operations. The heavier the gauge and higher the hardness, the more difficult it is to use stamping.

There is also less room for error with stamping than with machining; it is thus hugely important that the designs are reviewed and approved by the manufacturer early in the design process. With machining, it is difficult to re-engineer the part using stamping to reduce costs without making fundamental design changes.

*"Metal injection moulding can be a useful middle ground to minimise costs while gaining the benefits of machining. MIM has been increasingly used in recent years by manufacturers to expand their design capabilities."*

## Meet in the middle

Metal injection moulding (MIM), or metal injection moulding plus machining, can be a useful middle ground to minimise costs while gaining the benefits of machining. MIM has been increasingly used in recent years by manufacturers to expand their design capabilities.

Increasingly complex applications mean that sometimes MIM is the only suitable process. With the inclusion of biocompatible and implantable materials, components that were routinely machined can now be 'MIMed' for a fraction of the cost. Some OEMs have brought this process in-house, but as it demands specialised skills and equipment, contract manufacturing can be an attractive alternative.

Orthoscopics was one of the first fields to adopt MIM. Graspers, blades, staplers and cauterising cutters are small, geometrically complex and must be manufactured in a biocompatible material. Early designs were machined, which meant each component was expensive. However, as MIM become more established, suppliers became more consistent, and more companies began using the process.

Today, MIM applications are broad, including bone drills, robotic arms for surgery, bone rasps, cutting jaws, biopsy jaws, needle guides, saw guides and hundreds of endoscopic instruments. Over time, moulding has become much more sophisticated, with pressure sensors in each cavity, as well as in runner systems.

MIM is essentially a four-step process, consisting of compounding, moulding, debind and sintering. The biggest disadvantage with MIM is the lead time. However, the choice of materials makes it a popular choice for OEMs. It is best suited to shaping complex components in high volumes and when higher material properties, or implantable materials, are needed.

Many OEMs have considered bringing MIM manufacturing in-house, but this has been met with mixed success. Start-up costs can be several million dollars for the equipment alone, which includes compounding, moulding, debind, sintering and secondary apparatus.

MIM has been proposed to be 85% science and 15% art. Understanding the dynamics of sintering, and how to minimise the effect of gravity and friction, is essential, and developing a consistent process often takes years of experience.

This can be minimised with the hiring of experienced personnel, but they are in high demand and thus can be hard to find. A further issue is how to design for the MIM process. Most specialists will help with redesigning components, but this can take time, as most also serve as programme managers.

In recent years, some companies have started to help OEMs design components to optimise the advantages of MIM. This can save time and money, as they can go directly into production without any expensive redesigns during the production process. Such organisations are also able to manage the entire journey from design, through production, and can teach the OEM about the process throughout.

## A big decision

Finding the right supplier can be difficult, with hundreds of qualified contractors worldwide. Often newer suppliers will underestimate the amount of work needed to get a medical component into production. An established facility with substantial experience is thus likely to better meet required timelines and have a comprehensive understanding of the procedures required to meet medical specifications. However, the additional work created by increased quality requirements, along with the required documentation, means that established MIM facilities will be more expensive than newer suppliers.

Companies unfamiliar with requirements may initially be cheaper, but will soon discover they need additional resources or training to meet the needs of a particular device, so may not be cheaper over the long term. It is therefore essential for OEMs to do their homework and prequalify any potential supplier well in advance of making a decision. This can be assisted by a visit to a potential supplier's manufacturing facility to

discuss the device requirements and learn more about the processes that would be implemented.

## Contractor considerations

There are a number of considerations once a supplier has been selected, whether for stamping, machining or MIM, to ensure that the process runs smoothly. Instigating a dialogue right from the start is key. An OEM cannot assume that the current contractor will work in an identical way to their previous contractor. Each organisation is different and has its own specific, potentially idiosyncratic, working practices. Communication might therefore involve confronting the contract manufacturer directly if there are any concerns or suspicions.

In situations where there is a clear mismatch between OEM and supplier, it can be tempting to finish what has been started to avoid unnecessary delays. However, in most cases, it is better to accept a setback and find a contractor who will be a more favourable fit over the long term. As in all outsourcing situations, cultural affinity is crucial, and both parties need to feel that they're aligned in working towards a common goal.

Dialogue is of course a two-way street. It is crucial that the OEM understands the contractor's manufacturing processes and capabilities, and allows its designers and engineers to provide recommendations about where those capabilities would be better served. In addition, the contract manufacturer should also feel able to provide suggestions and take a degree of ownership as part of the process. First and foremost, the OEM must pay close attention to its own design first, and there needs to be a balance between complete prescriptivism and an overly lax approach. When relying on multiple contract manufacturers, it remains absolutely crucial that all parties are on the same page throughout the process. ●

### The MIM process

MIM brings together the shape-making capabilities of plastic injection moulding with the strength of metal. The four-step process begins with compounding, where a fine metal powder is mixed with a plastic binder.

This compounded material is then placed in a modified plastic-injection-moulding machine and injected into a mould. The component is called a 'green' part. This is then put into a chemical bath and most of the plastic binder is removed. Some binder remains in order to keep the metal powder in the moulded form. The process can take up to five hours, dependent on thickness and size.

The green part is subsequently put into an oven where the plastic binder is removed through evaporation. This process can last between hours and days, based on the part size. However, Most MIM companies are moving away from this process.

After debind, the green part becomes 'brown', and goes into a furnace, either vacuum or continuous, where any remaining binder is removed and the temperature increased to close to the metal's melting point. The component then shrinks by around 20% to reach its final size.

Source: *Powder Technology*

# Myopic medicine

In order to achieve sustainability in manufacturing operations, it needs to be incorporated in all stages of the supply chain. One key aspect is obtaining sustainable components from eligible suppliers. Recently, this topic has gained greater attention from industry and academia. **Ben Wicks** from Team Consulting speaks to Emma Green about the status of sustainability within medical device manufacturing.

Discussion of sustainability is increasing in all sectors. Loosely defined as the ability to meet the present needs of an industry without compromising those of future generations, its principles have not been readily adopted by most OEMs. This is largely because in relation to the wealth and gravity of other factors to consider within medical device manufacturing, it pales into insignificance.

This is certainly the view of Ben Wicks, a med-tech consultant with over 20 years' experience in the industry. With a background in microbiology, immunology and virology, as well as a PhD in clinical biochemistry, he certainly isn't short of credentials. He also isn't afraid of holding back in a discussion about sustainability within medical device manufacturing.

"For much of the industry, I don't think sustainability is very important," he says. "We've got a ton of other regulation to worry about, everyone is concerned with FDA and the European notifying bodies because they hold the key to you having a product on sale or not. Sustainability is not in their world or in their remit."

Although legislation on sustainability is currently lacking, this may change in the near future.

Wicks remains unconcerned about this possibility, however. "I suspect it will start becoming something you're asked to think about, and we are seeing and hearing patient groups and industry start to get it on the table for discussion," he admits. "But it's still often an almost inconsequential issue."

In light of this context, it is thus unsurprising that, unlike other sectors, the industry has been reluctant to embrace sustainability. The responsibility to ensure patient safety has also been a large contributor. "We are focused on trying to save people's lives –right here, right now," Wicks says. "Rightly or wrongly as an industry, we think that we have a higher calling.

That allows us to think that we don't have to care about it."

Sustainability is not uniformly rejected but it remains low on the agenda for most companies, especially when developing novel products, where time and money are particularly pertinent factors. "It's just very far down on the list, particularly if you're developing something new and clever," says Wicks. "Bringing it successfully to market is the most important thing, whether it slightly damages the planet or not, or some of the parts could be recycled but aren't at the moment, just doesn't come into your thinking."

For more established devices, there is greater openness to exploring sustainability. "If your product is mature and the risks are low and well understood, then you can turn your attention to sustainability," explains Wicks. "And why wouldn't I think about reducing its carbon footprint? I benefit, I'll save some money and the user will be happier."

## Fix the flaws of perception

It's not just the perception of sustainability that hinders its implementation; there are also a number of practical considerations when attempting to integrate its principles into the manufacturing process. "For many people in the industry, we're sweating bringing the product to market, and once we have brought it to market, it's difficult to make changes to the product without doing a ton of reverification," Wicks explains. "If it's just the secondary packaging, I might be able to cope with that. But if I've got a complex medical device and want to change its primary packaging, I might have to reverify my sterilisation or my stability trials, and that might cost several million pounds." This means that any benefit to sustainability is likely outweighed by the hassle of successfully achieving it.

Ben Wicks

*"For much of the industry, I don't think sustainability is very important. We've got a ton of other regulation to worry about, everyone is concerned with FDA and the European notifying bodies because they hold the key to you having a product on sale or not."*

This is in stark contrast with direct-to-consumer products where sustainability is not only high on the priority list but also much more feasible to implement. "For a consumer product, you think 'Well, if I can just save 20% of the packaging by a bit of a change here and there... bish, bash, bosh, off you go and do it. You get the product out there, everything continues and you're happy, but you just can't often do that in the medical device industry."

For Wicks, and many others in the industry, sustainability is perceived as a luxury, an expensive indulgence that often isn't deemed worthy of consideration. "Sustainability is in everyone's thinking in the developed world, and during design and development, you'd give it a thought," says Wicks. "In a sense, it's in people's minds but it's always down the priority list, certainly with complex devices."

If sustainability was on the agenda, selecting a sustainable supplier would be an important step in the process. However, for Wicks, as with manufacturing in general, it remains a relative footnote when making a decision. "I think about if they've got a high-quality system, if they're reliable, if they'll continue to give me parts that work and

**0.85°C**

The average global temperature increased during 1880–2012.

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The rise in sea levels 1901–2010.

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can ensure that the end device means that patients get better and don't get worse," says Wicks. "Sustainability hardly makes it onto that checklist for supplier selection."

### The status sphere

The low status of sustainability within the industry is also driven by the relative lack of consequences if its principles are not adhered to. "You screwing it up, if that product fails and people die, lawsuits fly around, products come off the market, companies go bust," says Wicks. "Nobody loses their job or dies if I use a printed circuit board that wasn't as recyclable as another one."

*"If a product fails and people die, lawsuits fly around, products come off the market, companies go bust. Nobody loses their job or dies if I use a printed circuit board that wasn't as recyclable as another one."*

It's clear that from a purely business perspective, sustainability just does not come into the equation. "It's not like someone running off with a commercial advantage saying 'look at our devices, they're all biodegradable,'" says Wicks. "That just isn't a thing."

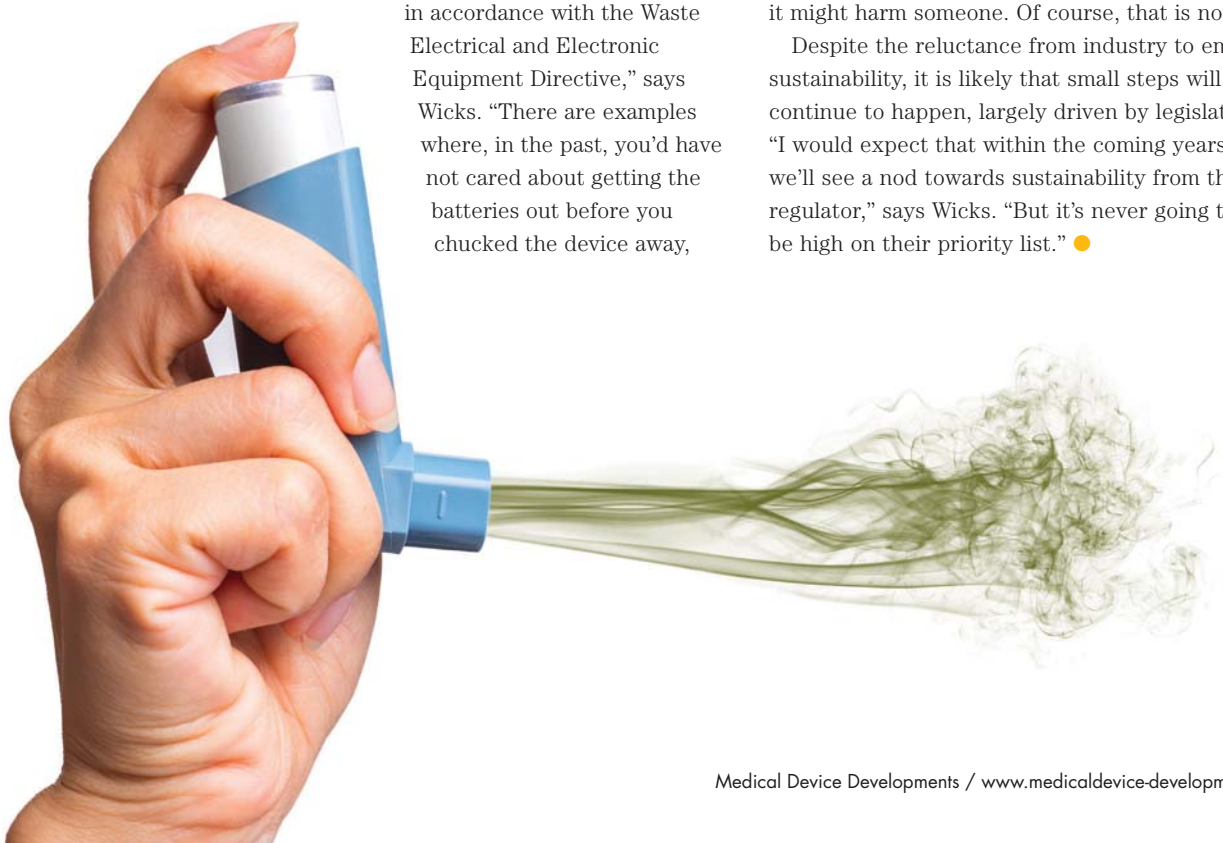
Nevertheless, there are small indicators of change in the industry, such as batteries in disposable goods. "Nowadays you would expect a disposable medical device that has a battery in it for you to be able to take the battery out in accordance with the Waste Electrical and Electronic Equipment Directive," says Wicks. "There are examples where, in the past, you'd have not cared about getting the batteries out before you chucked the device away, but now you have to because that's standard practice." One rare case where sustainability did become more important was the use of propellant in metered-dose inhalers (MDIs). "They originally used chlorofluorocarbons as propellants, which have a serious ozone-depleting effect," explains Wicks. These were discontinued in January 1996, except in a few rare cases.

A new class of propellant, called hydrofluoroalkanes took over, which was much more environmentally friendly. However, they are certainly not carbon-neutral. "These are way better but they are still a serious greenhouse gas contributor," says Wicks. For large companies, the use of these propellants contributes a significant amount to their overall carbon footprint.

There are currently discussions about moving to an alternative propellant, but manufactures are reluctant to make any changes unless it becomes mandatory. "The industry doesn't want to make the switch if it can help it because it will be a pain to do all the reverification and revalidation," says Wicks. "Nobody wants to spend the time or money, or cause potential risk to their patients."

Although clearly unlikely to immediately jump to the top of the priority list for OEMs, public perception looks set to be a future driver of sustainability within the industry. "We are seeing patients and users, such as healthcare professionals, starting to recognise these issues," admits Wicks. "But even though they say that, as a device developer, it's a secondary or tertiary issue. Ultimately, if this device doesn't work safely, it might not be commercially viable or, worse still, it might harm someone. Of course, that is not okay."

Despite the reluctance from industry to embrace sustainability, it is likely that small steps will continue to happen, largely driven by legislation. "I would expect that within the coming years, we'll see a nod towards sustainability from the regulator," says Wicks. "But it's never going to be high on their priority list." ●



**The search is on for a propellant with minimal environmental effects.**

# Your perfect moulding partner

Maintaining an efficient micromoulding project is a delicate balancing act. Having a clear plan, understanding the risks and, not least, choosing the correct partner are all crucial to success. Aaron Johnson, vice-president of marketing and customer strategy at **Accumold**, talks about the challenges involved in the moulding process.

As minimally invasive procedures have become more prevalent, demand for smaller, more complex medical devices has increased. This has put more pressure on original equipment manufacturers (OEMs) to design specialised components with thinner walls and more intricate features.

One of the technologies used to support this ever-shrinking world is micromoulding, a highly specialised manufacturing process that produces small, high-precision thermoplastic components that are used in a variety of medical tools.

With over 30 years of industry experience, Accumold is one of the leaders in this field, producing plastic components for microelectronics, micro-optics and sensors in a range of medical devices. These include surgical tools, hearing aids, handheld devices and micro-connectors.

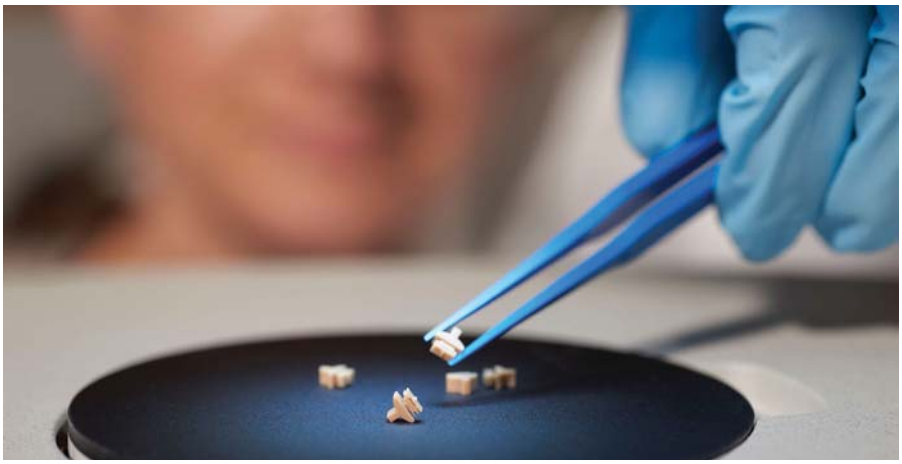
As a vice-president for marketing at Accumold, Aaron Johnson is acutely aware of the steps required in overseeing a successful micromoulding project. For Johnson, ensuring design for manufacturability (DFM) is the single most important part of the process.

"We always say, start with your ideal design in mind," he says. "And then let's have a conversation about where you can push the limits, or what is capable with microplastics."

## Pick a partner

For Johnson, a good moulding partner needs to provide three things: capability, scalability and sustainability.

When it comes to the former, precisely the right equipment is required to ensure that specific micro-level features or tolerances can be made in a detailed and efficient manner.



Accumold is one of the leaders in the field of micromoulding and has over 30 years of experience.

Given that these tolerances can be down to a few microns – a fifth the size of a human hair – there is precious room for error here.

"There has to be a clear and efficient infrastructure dedicated to micromoulding," Johnson says.

Because of the nature of the business, partners also need to make extremely small and sophisticated parts a million times over.

"If you are making a disposable, you need to know the system can provide, not only from the prototype, but all the way through to production," says Johnson.

And the final requirement is concerned with sustainability.

"Once they get approved, medical devices don't tend to like change, so you need to find a partner that can be with you for the life of that product," says Johnson. "Sometimes that can be for a very long time."

Over the course of its 30-year history, Accumold has consistently focused on sustainability, endeavouring to make smaller components more efficiently, with less waste. The company continues to endorse that mantra by committing to the ISO 14001 environmental standard. It is also championing a zero waste manufacturing initiative, collaborating with Mega Recycling to ensure that all of its components are reused.

"We feel like we have made a great accomplishment by being as productive with our resources as we possibly can," Johnson says. "Of course, it doesn't hurt that our products that we make are very tiny."

Asked about the future, Johnson is adamant that things are going to get smaller.

"We are amazed at the innovation and ingenuity in the industry, whether we are making wearable devices for diagnostics or delivery, or a transcatheter that is delivering a new way to treat patients inside the body," he says. "The more creative the industry becomes, the more it pushes limits and the more we can provide. We will continue to help customers do more in the same space or do more in less space – and that trend isn't going to stop." ●

**For further information**

www.accu-mold.com

# Break the fourth wall

Since we entered the fourth age of the industrial revolution, known as industry 4.0, manufacturers have begun to explore a wide range of new technologies. **Karen Taylor**, director of the Centre for Health Solutions at Deloitte, speaks to Stephanie Webster about how to best implement these technologies into manufacturing processes to maximise efficiency while minimising cost.

We are all aware of the rapid pace of change across multiple industries due to significant technological developments and the reduced costs of using them. These trends are distinct from the greater level of process automation, driven by advances in electronics and information technology, since the 1970s. The greater adoption of industry 4.0 is paving the way for disruptive approaches in a number of areas, including medical device manufacturing.

It's important to note that these technologies are not new. "What's changed is the cost, and the fact that the connectivity, miniaturisation, computer speeds and infrastructure has all changed to make it a reality to apply it at scale," says Karen Taylor, director of the Centre for Health Solutions at Deloitte. This is in line with Moore's Law, which predicts that the capacity of microchips, bandwidth and computers doubles every 18 months, representing exponential growth.

## Humans and robots

In light of the highly regulated nature of the medical device industry, it is imperative that a strategic approach to implementation is taken. However, there remain huge opportunities for industry 4.0 to enhance manufacturing processes.

One such technology is factory automation, which makes production lines more efficient, enhances resource effectiveness and improves productivity. Although seemingly simple to integrate, they can be complex to manage on a daily basis. "Factory automation is probably the simplest application of robotic process automation," says Taylor. "But these technologies, especially if they're going to have connected sensors embedded in them, are very sensitive to change and need to be highly monitored."

Cobots, or collaborative robots, are expected to be used increasingly within manufacturing. Recent research has predicted this market will grow from $710 million in 2018 to $12.3 billion by 2025. This is largely due to the technology being safer, more adaptable and compact than ever before. However, such technologies are not yet able to replace humans. "There is a need for human-in-the-loop, but you

### Define industry 4.0

Although the term industry 4.0 is widely used, it is rarely defined. Deloitte has described it as involving a move from traditional linear data and communication towards real-time access to data and intelligence. As part of this shift, there is a need for the integration of digital information from many different sources.

Throughout this process, real-time access to data and intelligence is driven by the continuous and cyclical flow of informationn and actions between the physical and digital worlds, known as the physical-to-digital-to-physical loop. This consists of three stages:

1. **Physical to digital:** information is used from the physical world to create a digital record.
2. **Digital to digital:** information is shared to create insights using advanced analytics, scenario analysis and artificial intelligence.
3. **Digital to physical:** algorithms are applied to translate digital-world decisions to effective data, to spur action and change in the physical world.

In order to achieve this, industry 4.0 combines a variety of technologies, including analytics, additive manufacturing, robotics, high-performance computing, natural language processing, artificial intelligence and cognitive technologies, advanced materials and augmented reality.

Source: Deloitte

probably won't need as many humans," explains Taylor. "You are already seeing this in the car industry and in other industries where you've got highly automated processes."

Such technologies might not result in a reduction of workers, due to increased demand in other aspects of manufacturing. "You will also need new types of staff to make sense of all the information that is being generated, so you'll need data scientists and analytical skills and talents, which haven't been something that has traditionally been needed," explains Taylor.

A 2018 Deloitte report indicated that, while companies are increasing their expenditure on their operational and IT budgets, they are reducing their research and development budgets. On average, they are spending 30% of their operational/IT budget on digital transformation but only 11% of their research and development budgets on this area.

One cost-effective solution to this issue might be to outsource, rather than recruiting or training in-house. "These individuals are in short supply and that's where maybe the best solution is – to partner with people and companies who have those skills," says Taylor.

There are also a number of emerging technologies that are likely to become increasingly implemented, such as digital twins. These are exact virtual replicas of physical products or processes, which can be updated in real time. They could be used to run simulations, and machine-learning technologies could be implemented to predict breakdowns and schedule maintenance.

Virtual, augmented and mixed reality is another valuable tool for the industry. This can be integrated into manufacturing in a number of different ways. For example, this technology can be used to design a new product, which can be refined in the virtual world before developing a prototype to test further. It could also be used to get support from an engineer remotely, who could use mixed reality to be able to see what the problem is in the manufacturing process and quickly rectify it.

Industry 4.0 also brings challenges, of course, including dealing with compatibility issues and ensuring systems are secure. Overcoming these challenges is possible, though, presenting considerable opportunities for manufacturers.

## Risky business

Despite the opportunity for these technologies to improve manufacturing processes, they do raise new issues. "With all of these, you get new challenges, like data security, privacy cybersecurity – all of those are, as a result of the innovation on the one hand, raising challenges on the other side," says Taylor.

A 2015 Deloitte report found that the level of cybersecurity risk could increase strongly (35%) or very strongly (48%) among respondents across a number of industries as a result of industry 4.0. Cyberattacks and viruses could be hugely problematic, bringing networked and smart production systems to a halt, creating substantial costs.

However, such difficulties are not insurmountable, but they do require tailored risk management and security strategies to be put in place. It is also important to note that as technologies continue to develop, this will also bring an improvement in cybersecurity systems. The limiting factor will largely come down to implementation, rather than technological capability. When integrating these systems, it is important that they can prevent and treat cyberattacks effectively.

Although there is increasing discussion about the challenges and opportunities for industry 4.0, implementation is still at an early stage. "There are a number of global surveys, which my colleagues have done, that show that in terms of digital maturity and the adoption of technology, life sciences are lagging behind some of the other industries," says Taylor. "However, we cannot underestimate the impact that the regulatory environment has. It is an enabler for innovation but at the same time also stymies it because of concerns about meeting the requirements."

## Four paradoxes

In light of the increasing technologies available, as well as the opportunities and challenges they bring, many companies remain in inertia. A Deloitte report, 'The industry 4.0 paradox', marks the discrepancy between the enthusiasm for these technologies and their implementation in a survey of 361 executives across 11 countries. While results show a strong will, balancing current operations with the opportunities

of industry 4.0 remains difficult, manifesting in four paradoxes.

The first is the strategy paradox. Nearly 94% of respondents identified digital transformation as a top priority but this didn't correspond with exploration within their organisation. Interestingly, only 68% believed industry 4.0 was an avenue for profitability, which likely is part responsible for this incongruity.

The supply chain paradox was also prevalent. Although this was an area indicated to be fruitful for current and future investment by executives, those outside the C-suite who were more involved with the daily management of the supply chain did not have a voice in decisions about digital transformation investments.

Another paradox was present with regard to talent. Despite respondents asserting confidence that they had sufficient capabilities within their organisation to implement industry 4.0, with only 15% admitting that any changes to skill sets of workers was necessary, they also acknowledged that obtaining, training and retaining the right people was an ongoing challenge.

Innovation was the subject of the fourth paradox identified. Executives reported that their strategies for industry 4.0 largely revolved around improving existing operations, rather than using them in a more transformative way. In light of the huge potential for innovation of manufacturing processes, such opportunities should not be overlooked.

## Make the most of it

In order to close the gap between conceptualisation and implementation, it is clear that action is needed. In the report 'Forces of change: Industry 4.0', Deloitte identifies five steps that are needed in order to optimise the use of these technologies.

It is imperative that companies immerse themselves in innovation, exploring the potential of industry to transform manufacturing processes, rather than merely improving them.

Building an ecosystem is key to ensure that these technologies can be successfully integrated. This might involve leveraging existing resources, as well as attaining new ones, either internally or externally.

Although there is a tendency to want to make dramatic and rapid changes, it is better to start with smaller stakes, testing and refining, before scaling up where the consequences are more significant. This can help to gain confidence in the capabilities of these technologies, ultimately leading to greater innovation.

And above all, it is important that companies do not expect perfection from industry 4.0. It is still evolving, and it is important to learn from previous experiences to inform future initiatives and priorities.

**$12.3 billion**

The predicted value of the collaborative robots market in 2025, up from $710 million in 2018.

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# Connect the bots

Collaborative robots, or cobots, are a new class of robots that are bridging the gap between fully manual assemblies and fully automated manufacturing lines. Lightweight, flexible, easily programmable and safe to implement, cobots can meet some of the challenges associated with these processes in an efficient and effective way. **Astrid Weiss**, senior researcher at Vienna University of Technology, speaks to Emma Green about how best to integrate these cobots into manufacturing processes.

Robots have long fascinated authors, scientists and the general public. Despite the high levels of interest, not all predictions about robot capabilities have materialised. It is notable that *Blade Runner*, a world of humans and human-like robotic replicates, was set in the year 2019. Nevertheless, the momentum of these technologies is stronger than ever. The International Federation of Robotics has predicted the sale of industrial robots, as well as of service robots, to grow with double-digit margins over the next few years. Researchers have suggested that many societies are currently on the verge of a robotic era, which will result in robots soon being commonplace in people's daily lives worldwide.

The perception of robotics is not uniformly positive, however. A 2019 study by scientists at the University of Würzburg reported increasing

scepticism to their use, particularly within the workplace. This is likely to be in large part down to the ongoing concern of robots replacing people, resulting in job losses. However, interestingly, the use of robots in this setting was rated more favourably by participants than in surgeries or autonomous cars.

It is clear when discussing the applications of robotics that humans are a major consideration and play a much more significant role than the technology itself. This is particularly true within a new class of collaborative robots, known as cobots.

Astrid Weiss, a senior researcher at Vienna University of Technology, knows a lot about cobots. With a background in sociology, social psychology and human-computer interaction, the focus of her work is how humans interact with new technology. As developments in this area are progressing at a rapid pace, it is essential to not only explore the capabilities of the technologies themselves but also the way in which to best integrate these with current working practices.

Cobots offer a number of benefits compared with traditional robots, if used mindfully. "Collaborative robots may reduce some of the environmental and spatial dangers traditional robots may cause, allowing them to work alongside humans," explains Weiss. "However, this is only true if the robots are very easily reprogrammed, ideally by naive operators, and if safety is ensured."

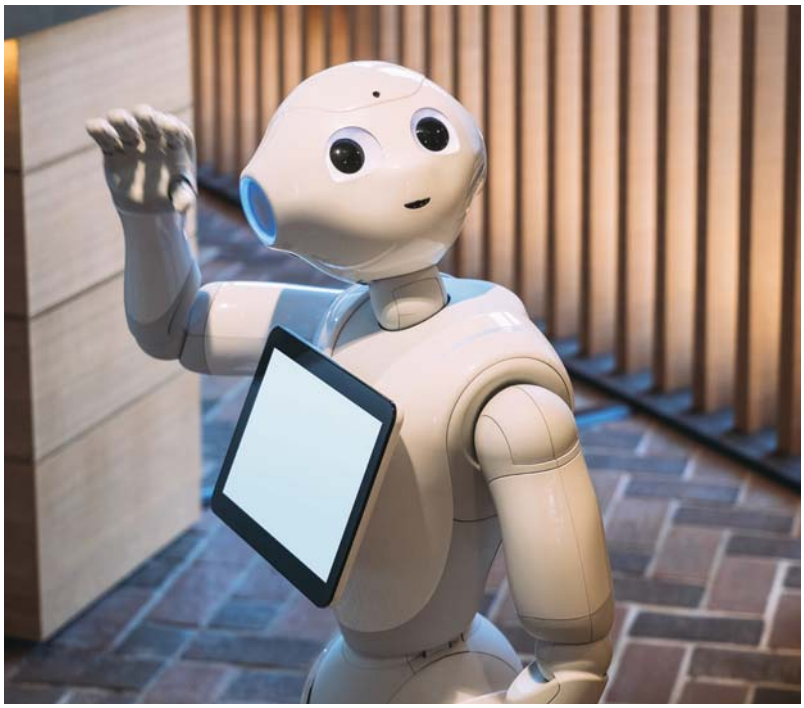
It's important to bear in mind that, although possessing a wide range of abilities, these cobots are not suitable for all manufacturing activities.

"In cases where very precise manufacturing tasks are done, such as polishing small metal parts, collaborative robots could not achieve satisfying results," admits Weiss. "For other domains, such as screwing or gluing parts together, they are much more effective."

## Question to consider

When considering whether cobots offer an advantage to a particular manufacturing application, Weiss suggests considering three key questions: can safe human-robot collaboration without a fence be guaranteed? Do I have a use case in which the robot increases productivity? Do I have a use case in which the robot performs equally well or better than the human in its specific task?

Cobots are best suited to small and mid-sized production applications, where they are much more likely to represent a good return on investment. When using this technology in such situations, Weiss highlights two key success factors that must be met. The first of these relates to cost, an important consideration when the average cobot costs around $24,000. "They must be able to be implemented safely without expensive safety hardware, like dedicated workspace or fences," explains Weiss.



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**Designed by Softbank Robotics, Pepper is a semi-humanoid robot that is able to read emotions.**

The second relates to the amount and nature of human input needed for a particular task. "Cobots offer most benefit to smaller production volumes and lot sizes that require frequent reprogramming – ideally without expensive software tools or robot and computer vision specialists."

*"Collaborative robots may reduce some of the environmental and spatial dangers traditional robots may cause, allowing them to work alongside humans."*

There are also a number of challenges that come with using cobots. "Traditional robot systems are mostly programmed offline, with text-based programming languages or by complex CAD/CAM-based simulation tools," explains Weiss. "That is only suitable for specialised situations such as optimised and fenced working environments, which only exist within the context of high production volumes."

In response to such concerns, robot manufacturers have already begun to optimise their safety and ease of use. Work in this area has included "limiting system power and implementing safe control system structures and functionalities, such as restricting speed or the workspace they can operate in". This ensures that use meets the DIN ISO 10218, a piece of regulation specifically

**$24,000**
Average cost of a cobot.
**Barclays**

### The AssistMe project

Astrid Weiss was involved in a two-year, collaborative project involving a number of parties, including Acin, Vienna University of Technology, Profactor, BMW and GPN. The research focused on user experiences of novel robotic assistance systems.

AssistMe used haptic (force feedback) interaction technology, which recreates the sense of touch by applying forces, vibrations or motions to the user, by means of machine vision. This was combined with methods from the field of spatial augmented reality.

One of the components of the project was a case study that explored the use of an industrial robotic prototype in the context of human-robot cooperation within an automotive assembly line. Workers were interviewed about their experiences after working with the cobot for three weeks. It was found that cooperation with a robot that executes predefined working steps impeded the user in terms of flexibility and speed. This changed the working routine and has the potential to decrease productivity. The project highlighted the need to ensure that robots can better adapt to the needs of workers and to a dynamic smart factory environment.

Source: AssistMe

**Astrid Weiss**

pertaining to the implementation of cobots within manufacturing.

Unfortunately, safety and performance do not always go hand in hand, especially in terms of speed and accuracy. A promising approach in this area is the use of pressure-sensitive skins, which can be mounted onto existing factory robots, turning a normal robot into a cobot.

Recent work has also involved attempting to standardise human-robot interfaces for teaching and controlling robotic systems. This aims to allow cobots to handle more complex scenarios while also being simpler to use, so that they can be operated by non-specialised members of staff. Weiss's research in this area found that more generalised solutions weren't ideal, and that it is better to adapt interfaces for specific use cases.

*"As robots work closer with humans, there is a great need for them to be able to respond to users and adapt their behaviours. Newly introduced robotic systems allow a high level of adaptiveness towards the user's individual rhythm, speed and working steps."*

## The new guy seems nice

Progress has also been made in making these robots better able to work with humans. "As robots work closer with humans, there is a great need for them to be able to respond to users and adapt their behaviours," explains Weiss.

"Newly introduced robotic systems allow a high level of adaptiveness towards the user's individual rhythm, speed and working steps." Such capabilities could be achieved through the use of additional sensors for posture recognition, in order to measure the worker's movements and waiting positions.

Efforts within this area have also focused on the paradigm of joint/shared attention. As the name suggests, this describes the shared focus of two individuals on an object. Joint/shared attention is achieved when one individual alerts another to an object by verbal or non-verbal means through gestures such as eye-gazing or pointing. "Due to ambient noise in the manufacturing environment, gesture and touch-based interfaces are preferable compared with speech-based interfaces," says Weiss.

Enhancing these capabilities also helps with improving the perception of cobots by workers, an area of particular interest to Weiss. "A lack of flexibility can increase perceived shortcomings, such as usability aspects and general helpfulness of the novel technology." Weiss's research in this area found that direct interaction with the cobot improved opinion of its capabilities, including its helpfulness and anticipated future performance.

Conversely, collaboration could be negatively affected if individuals need to adapt their working practices to accommodate the robot. More work in this area is needed, which includes ensuring that cobot behaviour can be anticipated.

The issue of predictability is not unique to robotics. Related technologies, such as AI and automation, have often been described as a 'black box', whereby their inputs and outputs are known but there remains uncertainty about the exact process between the two.

Shared control has also been a focus of recent efforts within collaborative robotics. A well-established idea within teleoperated robotics, shared control entails the user having a level of governance over the robot. "Transferring this approach to collaborative robots will enable more-complex collaboration tasks," explains Weiss.

Although there have been a number of exciting developments within cobot technology, the realisation of their use within a smart factory paradigm has not yet been achieved. Cobots currently demand a relatively rigid production line, which is at odds with the dynamic requirements of a smart factory.

There is also a need for robots to be able to sense and respond to changes in the environment, which is essential in order to prevent slowdowns in manufacturing processes or drops in output quality.

"Clearly there is a lot of potential for more complex capabilities," Weiss admits. "It will be crucial that the robot can adapt to unexpected circumstances – like missing tools or working with humans who deviate from the plan – and adapting to the capabilities of different operators."

# 3D-printed for long-term implantation

State-of-the-art technology from **Apium** makes 3D printing of medical grade PEEK possible, without affecting its biocompatibility and sterilisation properties.

Apium, the innovative professional 3D printing company from Germany, is the pioneer and one of the world leaders in processing speciality polymers.

The company's activities focus on the key industrial 3D printing trends, high-performance polymers, metals and medical 3D printing.

Apium is a technology leader in PEEK 3D printing and the first company worldwide to make 3D printing of long-term implantable PEEK medical devices commercially available. The company's design and development activities have resulted in advanced products and improvement in time-to-market for medical devices.

### Apium M220 Series 3D printers: a game-changer technology in healthcare

Apium's engineers have developed a professional material extrusion 3D printing technology, which enables the 3D printing of medical-grade PEEK, without affecting its biocompatibility and sterilisation properties.


The processed medical-grade PEEK filament meets key biocompatibility criteria for implants and devices.

The best-in-class temperature management system of the Apium M220 3D printer enables temperature regulation in the processing of the 3D-printed medical devices for the best possible results, and together with the integrated filtration system, prevents contamination of the printed part.

The medical-grade PEEK filament processed by Apium's M220 3D printer is developed from the VESTAKEEP i4 resin by the speciality chemical producer Evonik.

The 3D printing of this medical-grade PEEK, using Apium M220 3D printers, meets the biocompatibility criteria required to produce medical implants and devices in the areas of craniomaxillofacial and hand.


The M220 3D printer from Apium features a best-in-class temperature management system.

The necessary certificates of biocompatibility for material and machine can be provided upon request and are included in the delivery of the product.

*"Apium is a technology leader in PEEK 3D printing and the first company worldwide to make 3D printing of long-term implantable PEEK medical devices commercially available."*

This new production technology is guaranteed to reduce lead times and the cost of implant manufacturing. With medical-grade 3D printing, production can now be performed on-site in hospitals, and medical devices can be supplied with shorter lead times, saving patients' lives in time-critical surgeries.

### Disclaimer for Apium M220 and Apium PEEK

The additive manufacturing device Apium M220 is not covered by the guidelines on medical devices. However, it is suitable for clean rooms and for the production of medical devices.

Some of the statements and claims in this article may be forward-looking statements or statements of future expectations based on currently available information. Such statements are naturally subject to risks and uncertainties. Actual results or developments may vary depending on changes in the operating environment.

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# Somos® materials

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# Perform at a higher level

Dutch multinational **DSM** is helping world-leading medical equipment maker GE Healthcare improve imaging equipment for patients and clinicians.

When GE Healthcare began developing a new imaging device component, it partnered with MGS Mfg. Group and chose DSM additive manufacturing materials for the application. GE Healthcare and MGS have transformed the product development process for this component, resulting in faster prototype production and cost savings of nearly 70%.

"GE Healthcare's partnership with MGS, and use of DSM materials, has resulted in streamlining new product development," says Jesse Schrimpf, senior AME – additive, GE Healthcare. "The ability to 3D print moulding inserts and then test design iterations with real materials has made product development much more robust. It also has the added benefit of making the designs more 'mouldable' as we transition towards the creation of expensive production tooling."

## Challenges to overcome

Reducing lead time and costs to make prototypes that perform like the final product is a significant challenge faced by all product development teams. GE Healthcare successfully produces 'printed' prototypes for its product development groups in-house but needed to expand its capability to include printing tooling inserts that can make 'moulded' prototypes. GE Healthcare knows that for truly effective new-product testing, it is imperative that prototype parts closely match the finished product in terms of colour, strength and chemical resistance.

Kevin Klotz, engineering manager at MGS – a DSM business partner and a US rapid prototyping specialist – says, "3D printing additive materials have been used to print tooling inserts for several years. However, optional injection moulding resins that can be processed using additive manufacturing (AM) tooling was limited to resins that process at low temperature and pressure. Typical examples include the polyolefin and elastomeric resin families. Even so, AM generated tooling rarely moulded greater than 50 parts before failure."

GE Healthcare has partnered with MGS to help refine and optimise its product design and development process, specifically targeting shorter lead times, lower costs and high-performance resins.

## Enabling manufacturability

"Early involvement by MGS and DSM in design considerations for manufacturability for customers like GE Healthcare has significantly improved the prototyping stages of product development, which leads to a seamless transition from prototype tooling to high-quality production-grade tooling," says Klotz.

Development of an imaging device component for GE Healthcare demonstrated how MGS partners with customer product design teams to identify the best 3D machine/material system to generate rapid tooling and moulded prototypes.

A key part of this is how MGS helped GE Healthcare build its injection mould design skills early in the production process. For the GE Healthcare imaging device, and many other projects, MGS had recommended DSM additive manufacturing materials.

## Solution on offer

"DSM products, like Somos PerFORM, make possible additive manufactured tooling inserts that perform exceptionally well during injection-mould processing of various resins. Somos PerFORM tool inserts withstand the pressures, temperatures and abrasive characteristics of high-performance moulding resins that other additive manufacturing materials simply cannot withstand," explains Klotz.

The GE Healthcare imaging device component needed 100 or more parts moulded of a material that demanded challenging process conditions. In one test that mirrored a metal tool, MGS used Somos PerFORM to produce printed inserts to successfully mould more than 100 parts. Several other 3D-printed materials performed admirably during similar testing, but none performed nearly as well as the DSM material.

## Benefits to be had

DSM materials are playing a key role in helping businesses reduce cost and time to manufacture, and bring new products to market. For the GE Healthcare medical instrument project, Somos PerFORM enabled MGS to produce tooling three times faster than traditional steel tooling, at a third of the cost. The tool produced using Somos PerFORM inserts cost near $6,000, compared with a steel tool that would have cost upwards of $20,000. Furthermore, the quality of the moulded parts using Somos PerFORM inserts was so good that GE Healthcare was able to use them for customer testing.

Another key benefit is being able to quickly and cost-effectively produce a tool when changes are needed. This helps make product design and development more effective. Using Somos PerFORM, designers are able to produce a realistic physical part, test it, and, if necessary, make changes and quickly produce another tool.

In addition, producing tools out of Somos PerFORM makes the moulding of prototypes possible in materials such as glass-filled nylons, polyesters and even filled polyetherimide materials.

MGS is now providing this service to several clients. Klotz says, "The ability to successfully provide prototype parts moulded of engineering-grade materials is the differentiating factor between Somos PerFORM and inserts printed in alternative SL resins." ●

**For further information**

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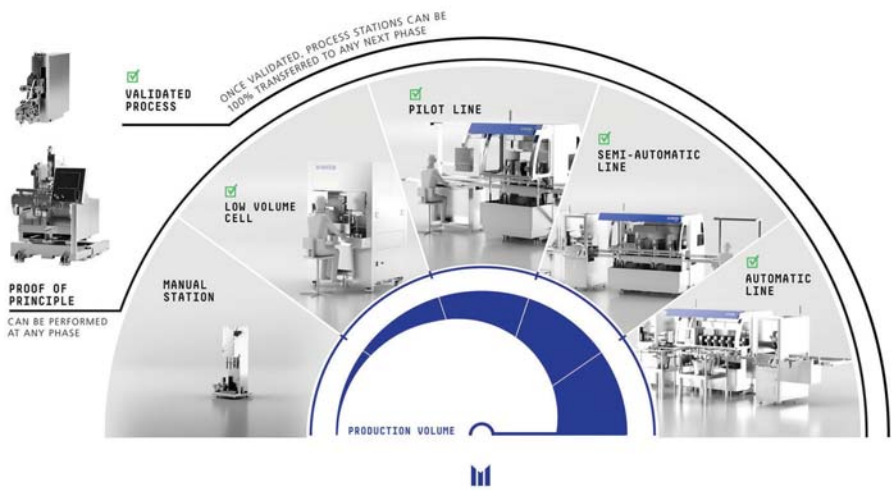
Whether in the pharmaceutical, medical technology, automotive or electrical industries, the demands from customers have risen sharply in recent years. In an extremely competitive market, pressure on performance is rising and the lead time for new products is getting ever shorter.

An assembly solution often has to be ready before all the details of the new product are even known. In many cases, assembly solutions also need to be frequently switched to another variant. So it is no wonder that demand for innovative, cost-optimised solutions has risen dramatically over the past few years. The future belongs to agile automation systems that can be expanded and enhanced easily and cost-effectively – from the development phase through to fully automatic production.




Mikron Automation scalable solutions.

*"The future belongs to agile automation systems that can be expanded and enhanced easily and cost-effectively – from the development phase through to fully automatic production."*

### From the first prototypes up to fully automatic production lines

Will production trials continue in low quantities? Or is it now time to search for a fully automated solution for large volumes? When looking for assembly solutions, manufacturers need a partner that leaves all options open to them. With its modular and scalable platforms, Mikron is always thinking and acting one step ahead.

"Customers appreciate the cooperation with Mikron because, with our many years of experience, we think beyond the horizon and advise them on how to prepare the line for the next steps," points out Félix Arrieta, general manager of Mikron SA Boudry in Switzerland. "From the design for assembly to the proof of principle, from the validation process through to the pilot line, and to the highest-performance production, our full range of G05 automation and feeding platforms serves our customers in the long term."

"A major factor in our success is that we have a close partnership with our customers in order to understand their needs, allowing us to react immediately," says Rolf Rihs, president of the Mikron Automation division. "That is why the scalability of our automation systems is so important."

Mikron's customers can count on a knowledgeable, experienced and trustworthy partner. Thanks to its standardised platform philosophy, going from the manual workplace to the fully automatic cell, Mikron offers almost unlimited layout options. Throughout the whole process, it is easy to redeploy and reconfigure whenever necessary. This considerably increases cost efficiency and greatly shortens delivery times. What is more, using the company's standard platforms, process stations are validated at an early stage and can be transferred from one automation level to the next.

### Minimum risk with flexible production starts

The key word in the brave new world of flexible automation systems is 'scalability'.

"For customers, the new approach means minimum risk, and a faster, reliable and more flexible production start – in several stages if required," says Arrieta.

For many years, Mikron Automation has enjoyed an excellent international reputation as a partner for high-performance automation solutions in the large-scale manufacture of precision products.

"For many, however, the fact that Mikron Automation is also one of the leading providers of scalable and flexible automation systems is the base for the future," adds Arrieta.

Mikron is thus strengthening its industry position as a first-choice, long-term partner. ●

**For further information**

www.mikron.com

# Everything is illuminated

Traditional photonic devices have been fabricated from rigid materials on rigid substrates, limiting their applicability in the healthcare sector. Now, researchers at the Massachusetts Institute of Technology (MIT) have developed a method for making photonic devices that can bend and stretch without damage and without compromising optical performance. Patrick Kingsland speaks to MIT associate professor **Juejun Hu** about the application of this technology for medical device manufacturing.

It is a word that is rarely used in common parlance, but over the past few decades, photonics – the science of generating, controlling and detecting light – has become an integral part of our everyday lives.

In the manufacturing sector, laser-based technologies are enabling cleaner, higher-volume and lower-cost methods of production. In the field of communications, photonic technology is driving advances in optical fibres – the backbone of today's internet.

Perhaps the most life-changing – or saving – field of photonics can be found in the medical device sector. From oil candles to electricity, light sources have been used in healthcare throughout human history. But with modern optic and photonic technologies, new possibilities are emerging in the diagnosis, treatment and prevention of disease.

"Light is an extremely important probe that people can use to investigate biomedical phenomena," says Juejun Hu, associate professor of materials science and engineering at the Massachusetts Institute of Technology (MIT).

At the cutting edge of the technology are new designs and materials for flexible photonic sensors, which can be bent, folded, rolled, twisted and stretched to conform to human skin without compromising optical performance.

Hu, and other researchers at MIT, say such devices could be used in a range of skin-mounted, wearable health monitors, potentially revolutionising the medical device manufacturing sector. ▶

Professor Juejun Hu

## A key enabling technology

One of the key benefits of using light for healthcare is that it is non-invasive. Procedures involving photonic devices – which use systems of mirrors, lenses and LEDs to process light beams directly – do not require needles or knives or other instruments that penetrate the skin. This means less pain for patients and less complicated operations for medical practitioners.

"Instead of using a physical probe you use light to penetrate human skin and get images or chemical information about the human body," says Hu.

*"Instead of using a physical probe you use light to penetrate human skin and get images or chemical information about the human body."*

Photonic technology has been particularly central in the development of modern imaging techniques such as optical coherence tomography – a non-invasive test that uses light to capture high-resolution images of tissue. Optical coherence tomography is now used in a wide range of medical applications, including ophthalmology, dentistry, gastrointestinal endoscopy and dermatology.

"With optical coherence tomography, people use light to generate and reconstruct three-dimensional images of tissue that would be difficult to obtain using other techniques," Hu explains. "It does no damage to human tissue and has been used very widely in eye surgery as well in examining skin conditions."

The ability of light to carry information in multiple dimensions means photonics is also used for medical sensing. Different wavelengths interact with biological tissues in different ways – some are strongly scattered, others weakly scattered – providing detailed information about biological activities, such as oxygen concentration, heart rate and blood pressure.

"A simple example is oximetry," Hu says. "This is a machine that allows a doctor or nurse to read out the oxygen level in the blood. The basic idea is that you are sending different wavelengths of light to penetrate through a human finger, which is actually translucent. By looking at the absorption of light at these different wavelengths you can work out various different things."

Photons are also used to directly affect biological tissue, serving a number of therapeutic and surgical purposes. Light-based therapy is used to treat a range of dermatological conditions; laser procedures are used to correct near and far-sightedness in vision; in oncology, photonics immunotherapy has been used to treat cancer.

The photonics field is making such strong progress that, last year, it was named as one of six key enabling technologies by the European Commission's Horizon 2020 – a research and innovation programme designed to help the EU become a front runner in "market-creating innovation". The programme's proposed budget allocation between 2021 and 2027 is a mouth-watering €100 billion.

"Medical photonics research and innovation is leading towards the development of easy-to-use, low-cost screening methods that can be carried out at a general doctors premises, or even at home," said a European Commission Horizon 2020 press release. "These photonic point-of-care technologies can provide a risk assessment of age and lifestyle-related diseases within a few minutes."

**$56 billion**

Projected value of the photonics industry in 2020.

**German Federal Ministry of Education and Research**

Unsurprisingly, photonics has been identified as one of the fastest-growing areas within healthcare.

The global market is projected to increase from approximately $32 billion in 2011 to $56 billion in 2020 according to recent market research published jointly by the German Federal Ministry of Education and Research, the Mechanical Engineering Industry Association, the German Electrical and Electronic Manufacturers' Association and the German High Tech Industry Association.

"Photonic devices are penetrating into many different fields and biomedical applications," says Hu.

## Photonics flexing its muscles

While many photonic devices have already been clinically validated and are widely used in the medical sector, there is still a great deal of work to be done according to Hu. The researcher, who is a principal investigator at the Photonic Materials Group, is particularly interested in developing integrated photonic structures that are smaller and more practical than traditional devices.

"Current optical coherence tomography instruments are pretty big, bulky machines and can really only be used in a dedicated laboratory or a doctors clinic," he says. "We are looking into essentially trying to miniaturise this and make it more accessible. This is the emerging area within photonics."

Hu's group is also focused on making new materials for integrated photonics that are flexible and can be mechanically deformed. Photonic devices that could stretch and bend like human skin could be used in a range of medical applications, such as skin-mounted monitoring devices to detect heart rate, blood oxygen levels and blood pressure.

"We anticipate that the identification of new application fields, where mechanical flexibility either constitutes the key feature enabling the target applications or contributes to significantly improved device performance, will certainly accelerate penetration of the technology into diverse market sectors in the future," Hu's team said in a recent paper titled 'Flexible integrated photonics: where materials, mechanics and optics meet'.

Flexible devices of this kind are not a novel idea. The concept of flexible electronics dates back to the 1960s and is now a $5.13 billion global industry. Lighter and more durable than what came before, flexible electronic devices have seen widespread adoption in the consumer electronics and healthcare market, where they are used in lab-on-chip devices, X-ray detectors and health monitors.

But bringing this technology to the biomedical field has proved challenging. This is because the vast majority of integrated photonic devices are fabricated on rigid substrates, such as semiconductors or glass, which are deemed inappropriate for soft, curvilinear human bodies.

"If you look at how people conventionally make these miniaturised, integrated photonic devices, it is on some kind of rigid substrate," says Hu. "But if you look at biological tissues in human beings, we are made of this soft, squishy stuff. That means there is a very large elastic mismatch with traditional photonic devices."

The obvious candidates to overcome this elastic mismatch are organic polymers, from which most flexible photonic devices have traditionally been fabricated. But while these polymers have inherent mechanical flexibility, they also present their own problem: a low refractive index and poor ability to confine light beams.

"Most of the polymers have more or less the same refractive index," Hu explains. "This could be problematic because for a lot of cases you want to be able to manipulate the light probe with freedom. Polymers do not allow you to do that."

Hu and other researchers have therefore been searching for a method to make photonic devices that can do two things simultaneously – bend, twist, stretch and seamlessly integrate with biological tissues such as human skin while also maintaining strong optical performance.

**€100 billion**

Proposed budget allocation, between 2021–27, of the European Commission's Horizon 2020.

**European Commission**

*"If you look at how people conventionally make these miniaturised, integrated photonic devices, it is on some kind of rigid substrate. But if you look at biological tissues in human beings, we are made of this soft, squishy stuff. That means there is a very large elastic mismatch with traditional photonic devices."*

"My group has been working on that for the past six to seven years, and we have developed a whole array of different components along the line," Hu says. "Components must exhibit good mechanical ruggedness and flexibility that does not compromise the optical properties."

## A hybrid platform

Searching for a material that does this, Hu's group has turned to an unusual source – a specialised kind of glass called chalcogenide. Though regarded as a fragile substrate, the glass material is widely used in the microelectronics industry and possess a high refractive index with strong optical confinement.

"The glass materials' success in the microelectronics industry, coupled with their superior optical performance, point to chalcogenide glass micro-photonics as the natural next step of

technology evolution," Hu's research group said in the paper 'Chalcogenide glass micro-photonics: stepping into the spotlight'.

To overcome the inherently brittle nature of glass, Hu's team has formed the stiff material into a spring-like coil. The process has been compared with steel, which can be made to stretch and bend when formed into a spring.

"The architecture of this glass coil allows it to stretch and bend freely while maintaining its desirable optical properties," said MIT in a press release. "Tests have shown that such spring-like configurations, made directly on a polymer substrate, can undergo thousands of stretching cycles with no detectable degradation in their optical performance."

With this breakthrough, Hu believes his team now has a device that offers versatile light manipulation and transmission, and excellent mechanical flexibility. "I think what is new about our research here is that we developed this kind of hybrid platform that leverages most polymers and this inorganic material to take the best from both worlds," he says.

While this breakthrough is significant, Hu believes there is still a great deal of work to be done. So far his team has demonstrated a device that allows them to transmit light and exhibit desirable mechanical properties, "but it doesn't really carry any specific function per se", he says.

"That is something we are working towards," he adds. "We are trying to integrate this component, specifically either for biomedical applications or for high-speed data communication."

It is estimated the technology could be commercially applied within the next two to three years. While Hu may spend most of his time in laboratories and at his desk, drafting academic papers, he says this is his real ambition. "My dream is to see some of the things I develop at MIT have an impact in the real world and benefit the society as a whole," Hu said in an interview with MIT's news service. "That's why I am interested in entrepreneurship, to push them to application."

# The leading trade show for lasers and photonics

The international trade fair for photonics components, systems and applications, **LASER World of PHOTONICS** offers a complete market overview – from optoelectronics to lasers in production and imaging – bringing together key players from the fields of analytics, diagnostics and biotechnological research, as well as celebrating new talent.

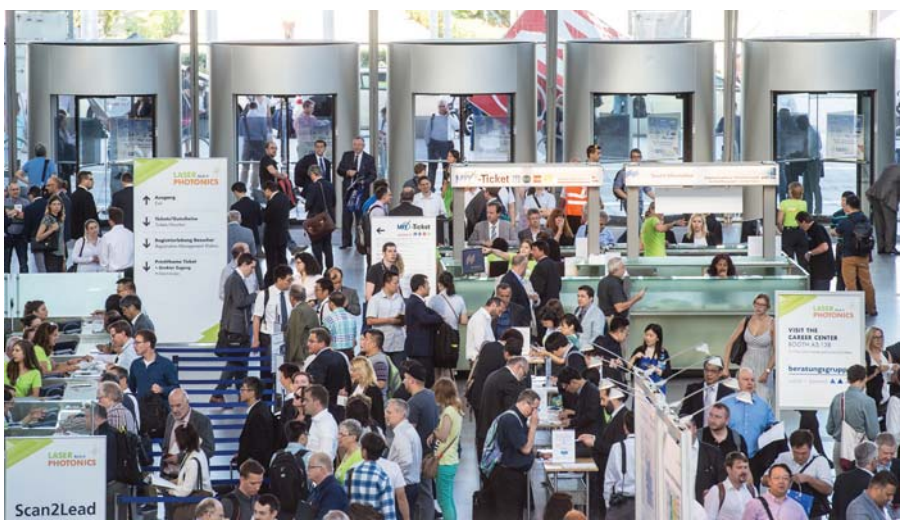
More than 1,300 exhibitors from around 45 countries will present their innovations at LASER World of PHOTONICS on 24–27 June 2019 at the fairgrounds in Munich. Also awaiting visitors in parallel is a trend-setting conference boasting seven individual conferences and more than 5,000 experts from around the world. In a nutshell, Munich is awaiting an event of superlatives that will provide deep insights into the future of photonics.

The trade show offers a complete market overview – from optoelectronics to lasers in production and imaging. One of the topics will also be biophotonics and how it is enabling ever more accurate medical diagnoses. LASER World of PHOTONICS 2019 brings together key players from the fields of analytics, diagnostics and bio-technological research. Many of the exhibitors are developing optical systems and components, but not for one application area alone; they may also be active in the aerospace industry, or at the cutting edge of progress in the semiconductor and electronics field, or contributing to quality assurance in the food industry with new imaging techniques.

## Prizes for viable solutions

Two awards at once are being handed out at this year's LASER World of PHOTONICS; the Innovation Award, being conferred for the first time, honours the best product premieres by exhibitors, while the Start-Up Award, being presented for the third time, is directed at young entrepreneurs offering innovative solutions. The awards are worth €5,000.

"The Start-Up Award contestants are living proof just how many innovative ideas are being generated by photonics," says Katja Stolle, the trade fair's exhibition director. "Which is why it isn't just the established Start-Up Award being conferred at LASER World of PHOTONICS 2019 but the Innovation Award as well. This enables us to give innovation an even bigger platform."




LASER World of PHOTONICS 2019 brings together key players from multiple industry fields and offers a complete market overview – from optoelectronics to lasers in production and imaging.

## A platform for young talent

Growth dynamics is a reason why photonics provides a very good environment for founders. The market has more than doubled in ten years. The Start-Up Area at LASER World of PHOTONICS offers young talents a platform in the middle of the trade show. Additionally, the Makeathon again provides young engineers and students with a platform for demonstrating their expertise in the photonics arena.

## World of Photonics Congress with well-known speakers

This time, Europe's leading congress comprises seven conferences – the newcomer is the OSA conference 'Imaging and Applied Optics'. In addition, the 'European Conference on Lasers and Electro-Optics and the European Quantum Electronics Conference' (CLEO/Europe – EQEC) will again be shining the spotlight on basic research in the laser technology and quantum optics fields.

Professor Anton Zeilinger will also address quantum technologies in a keynote speech, offering insights into the work of his group at the Vienna Institute for Quantum Optics and Quantum Information. The opening keynote speech for the congress on the first day of the trade show will be by Prof Karsten Danzmann, director of the Institute for Gravitational Physics at the University of Hanover and director of the Albert Einstein Institute.

Anyone wanting to gain a clearer idea of the future in photonics should schedule a visit to the trade fair in Munich on 24–27 June 2019. ●

**For further information**

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# Possible polariser application requirements

German polariser specialist **CODIXX** knows the most common requirements for choosing the right polariser for your application.

As discussed in the previous volume of *Medical Device Developments*, polarisation is a singular property of light that can significantly improve medical applications, but only if the right polariser is selected. Different polariser types are available with vastly different specifications. To find the right one, the requirements of the application should be defined and matched with the polariser.

There are several important application characteristics:

- **Wavelength range:** which wavelength range is used to be the light source or monitored effect? Applications can use the whole spectrum or just a smaller range; for example, UV, visible or IR. Most polarisers are optimised for a smaller wavelength range, so the wavelength range plus-minus a few nanometres should be known.
- **Transmission:** this describes the ability of the polariser to let light pass through as a percentage. An ideal polariser would transmit 100% of the light parallel to the polarisation axis and 50% of unpolarised light. As there are no ideal polarisers, usually between 40% and 98% of optimally polarised light is transmitted.
- **Extinction ratio or contrast:** the ratio between p-wave and s-wave. The purer the transmitted light, the higher the value, which ranges between 100:1 for low-budget sheet polarisers and $10^6$:1 for high-quality birefringent polarisers, or even $10^7$:1 for dichroic glass polarisers.

*"The requirements of the application should be defined and matched with the polariser."*

A high contrast is not essential to remove glare, but analysing contents or concentrations of a pharmaceutical substance requires a very high contrast.

## Secondary specifications

On top of these three main specifications, secondary ones need to be considered:

- **Wavefront distortion:** describes the wavefront distortion caused by passing through a transmitting component. It might cause focus shifts and spot size increases, thus causing a blurred image.
- **Laser damage threshold (LDT):** another key factor to consider when dealing with a laser light source. The LDT per square centimetre can range 1W to 500kW depending on the polariser.
- **Acceptance angle:** should be chosen adequately if uncollimated light is evident on the polariser. It usually ranges from ±2° to ±25°.
- **Size:** due to the manufacturing process, some polarisers are limited in size and are not available in larger sizes. The most common sizes are up to around 40–50mm.
- **Thickness:** some polarisers are thicker than others due to the optical path length required for the polarisation. The thickness, and therefore the required space within the application, varies between 0.2mm and 35mm.
- **Durability:** possible environmental influences like temperature, chemical or radiation exposure should be considered as well to avoid damage or destruction of the polariser.
- **Handling:** some polarisers require special handling to protect the polarisation properties during installation or regular usage.
- **Cost:** last but not least, the cost needs to be considered as polarisers can range from the price of a cup of coffee to that of a small car. In general, the lower or fewer the requirements, the lower the price. Should one of the more expensive polarisers be required, the cost can be reduced by choosing a smaller size.

These are the most common factors, which should be known in order to enable you to find the most suitable polariser for any application. Now you need to know what every polariser type can, or cannot, provide, which will be discussed in the next issue of *Medical Device Developments*, 2019 Vol. 2. ●

Finding the right polariser can be tricky, but CODIXX's expertise can help.

**For further information**

www.codixx.de

# Produce customised medical devices

3D printing solutions from **TRUMPF**, including the TruPrint 1000 3D printer, produce intricate, made-to-measure implants with excellent material properties that save medical device companies time and money.

Additive manufacturing is ideal for producing medical devices. When designing an implant, a CAD engineer will first create a computer model based on patient data and then set the 3D printer to work. What's more, products made using this technology have excellent material properties – for example, polymer devices that are robust but elastic and shock-absorbent, or implants with a porous structure that fuse well with healthy tissue but remain stable and durable. Additive manufacturing is also suitable for producing custom-fit implants on a cost-effective basis. A further benefit is that, unlike conventional machining methods, 3D printing does not produce any waste in the form of shavings or swarf. And in the manufacture of medical implants, where the material of choice is generally an expensive titanium alloy, this means genuine savings.

Furthermore, there are none of the retooling costs of conventional methods.

Conmet, a market leader in craniomaxillofacial surgery and implantology, first looked at additive manufacturing 10 years ago. At the time, however, the technology was still insufficiently mature for such applications. In 2017, the company decided to approach TRUMPF to find out how far the technology had evolved. "TRUMPF is the only supplier on the market for 3D printing that develops its own lasers and all the optical components," explains Andreas Margolf, project manager for additive manufacturing at TRUMPF. "We also have a wealth of experience in the areas of machine tools and services. That means we're able to assist Conmet with any aspect of the process."

The first task was to determine the right machine for Conmet, along with the relevant process parameters. It was soon clear that the ideal set-up was TRUMPF's own TruPrint 1000 3D printer with the laser focused to a diameter of 30µm. Equipped with a 200W fibre laser developed by TRUMPF, the machine has no problems working with the titanium alloys generally used to produce implants. TRUMPF also proved its expertise to fine tune the focal diameter at which the laser beam hits the powder bed. "Our tests showed that reducing the focal diameter to 30µm improves the surface smoothness of the implants by around 20%," Margolf explains. This makes the process slower and slightly more expensive but reduces the cost of post-processing the surface."

Conmet uses TRUMPF's TruPrint 1000 3D printer to produce customised craniomaxillofacial implants.

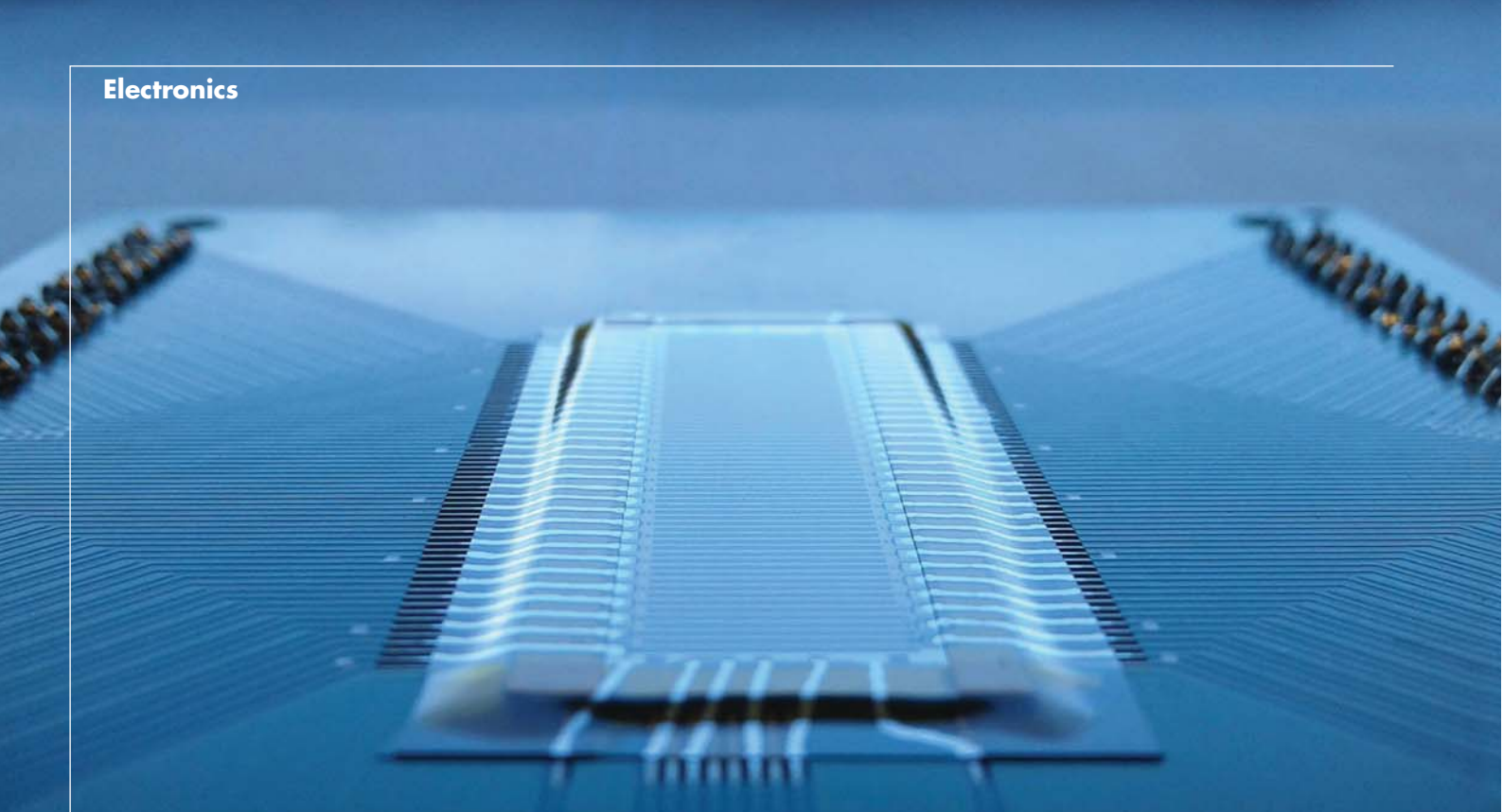
## 40% saved in production costs

Conmet has been operating with the TruPrint 1000 at its Moscow production facilities since the beginning of 2018. The company uses the new machine to produce dental components and craniomaxillofacial implants for, among others, cancer patients. Hospitals provide Conmet with CT data of patients; engineers at Conmet then design the implant, in consultation with the surgeon; and the machine prints it out. "We currently produce 60 implants a month with the TruPrint 1000, and we're planning to increase our output by 10%," says Nadeschda Morozova, project manager at Conmet. The implants not only have an especially high quality level overall – they are also substantially cheaper.

"Compared with conventional machining methods, such as turning and milling, the new process saves us 40% in production costs," Morozova reports. In the near future, Conmet intends to start producing custom-fit spinal fixation devices using 3D printing. The company also has plans to manufacture mass-produced prosthetics with the TruPrint 1000. For this, Conmet will be investing in new machinery and has once again opted for TRUMPF technology. As Morozova explains, the new machine will be a TruPrint 3000, with a larger construction chamber.

**For further information**

www.trumpf.com



# Smash the ultrasound barrier

Scientists at the University of British Columbia, Canada, have developed a portable ultrasound device that can connect to a smartphone and costs only $100. The new transducer can be used to look at any part of the body, producing instant and clear images. Research lead **Carlos Gerardo** talks to David Callaghan about the potential for this new device, which includes patients wearing it for monitoring purposes.

The future of ultrasound devices could be bright with the development by scientists in Canada of a portable scanner that embraces radical new technology and can be powered by a smartphone. Using different materials to the traditional ultrasound machines, researchers at the University of British Columbia (UBC) have produced a scanning device the size of a plaster that costs just $100.

The new device has the potential to be woven into clothes or wrapped around the body to monitor changes in performance of a person's internal organs. There are also plans for a patch-type scanner, or even tiny versions of the device being used to look inside arteries and veins.

University engineers have replaced piezoelectric crystals, commonly found in ultrasound scanners, with minute drums made from a polymer resin, which can produce clearer images with more detail. Each drum, which is the diameter of a human hair – 100µm, or 1/10th of a millimetre – vibrates according to the level of high-frequency sound waves received by the device. The resin, which is cheap and quick to produce, is made from polymer capacitive micro-machined ultrasound transducers, or polyCMUTs.

In the scanners currently used around the world the piezoelectric crystals act as a transducer by changing shape under an electrical current, and emitting sound waves that can then pass into the body. Once the waves hit an obstacle they bounce back and the crystals convert them into electric currents, which are then processed into a sonogram image. The issues with this ultrasound technology are that it is expensive to produce, has limited bandwidth and the images are not always as clear as they could be.

CMUT technology is not new, but, despite its high efficiency rating, it was restricted in the way it could be used in ultrasound due to the material used to make the drums. Rigid silicone materials have been adapted, which are costly to produce, are sometimes subject to acoustic crosstalk, and there has been a limit to how deep into tissue these scanners can penetrate.

With the new polymer drum technology, the manufacturing process is much cheaper than with silicone, meaning that CMUTs become a much more attractive option to use in ultrasound scanners. The polymer is also strong but sensitive, the impedance factor is lessened and the voltage required to make it work is low, at just 10V.

An electrode is held within a membrane made of a light-activated resin and sacrificial layer, as opposed to the silicone used in previous versions of CMUTs. An optically transparent shell will be an advantage during manufacturing, as it will allow a visual inspection of devices after fabrication. This contrasts with piezoelectric technology, where defects are detected after you create all the electrical connections.

## Inside out

"This new fabrication process has the potential to increase the use of CMUTs in the ultrasound market, including the market for wearable transducers," says Carlos Gerardo, one of the co-authors of the project at UBC.

Earlier development of polyCMUTs was hampered by the need for high voltages, in the hundreds, to make ultrasound work. This has been overcome by embedding the electrode in the membrane of the device instead of on top, and thereby reducing the power required. The frequencies achieved are comparable to the CMUTs made of silicone nitride or polysilicon.

A basic microfabrication facility operating at relatively low temperatures of less than 150°C can be used to produce the polyCMUTs, which helps to make the process even more attractive to potential manufacturers.

Possible improvements to the techniques used to produce polyCMUTs could include water-bonding technology with the SU-8 polymer, or roll-to-roll methods, where the cavities and membranes are bonded together in a vacuum environment.

"This could decrease production times and costs even further, with the possibility of fabricating ultra-low-cost ultrasound transducers," Gerardo explains.

The product still needs to be developed further. "The implementation is not immediate – we need to do a lot of experiments, and in the US and Canada there are many regulations to be met," says Gerardo. "We have produced a high-performance plastic transducer that can replace the existing technology. It is simpler to fabricate, and the manufacturing costs are much lower."

The question now is what happens next, and how can this product be further developed?

"We have ambitions for an ultrasound 'patch' that can be placed under the skin to monitor the heart for a few days or weeks. An ultrasound 'probe' could be attached to the body and used to send information remotely," Gerardo says.

The new device is not limited in its use to a particular part of the body, and can be used in exactly the same way as existing ultrasound scanners, including for cardiovascular examinations and obstetrics, for example.

**Left: Portable scanner for ultrasound devices, developed by researchers at the University of British Columbia, Canada.**

**$7.3 billion**

Current global value of the ultrasound market.

**GBI Research**

*"We have ambitions for an ultrasound 'patch' that can be placed under the skin to monitor the heart for a few days or weeks. An ultrasound 'probe' could be attached to the body and used to send information remotely."*

## Good news moves fast

News of the device has spread fast, prompting interest and contact from around the world, including the UK, Germany, Australia, the US and Canada. The UBC research team has already held meetings with biomedical manufacturers, who are interested in producing the new device commercially.

Enquiries have also come from other industries, such as gaming and virtual-reality companies, which wanted to know how this development could be used in their fields.

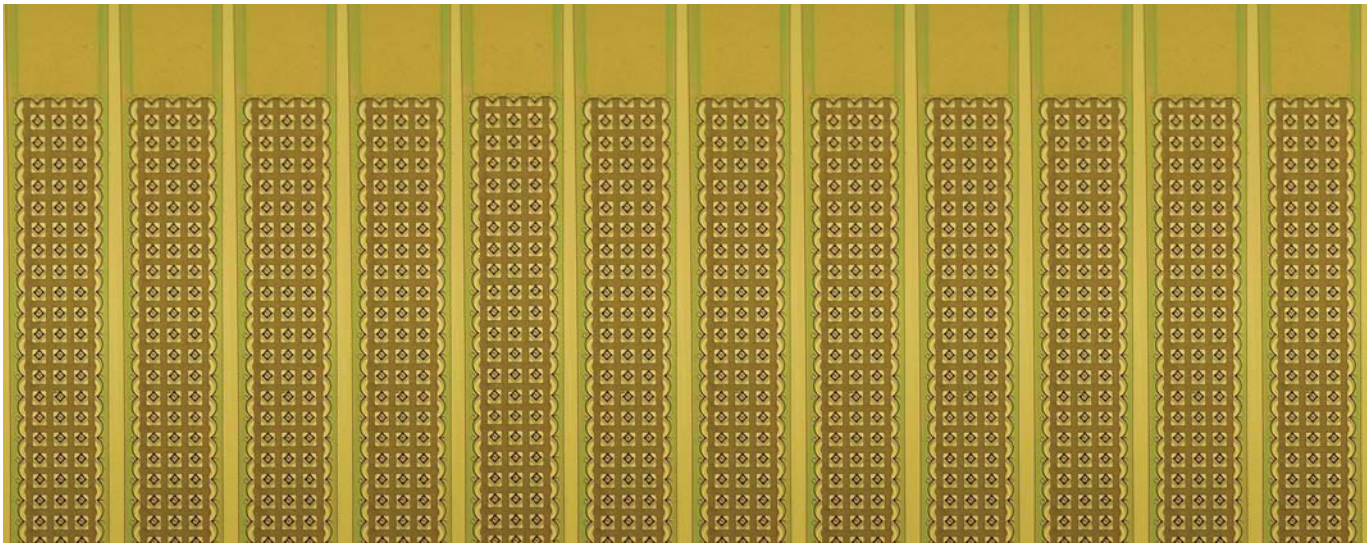
"We have been overwhelmed," Gerardo says. "It is all positive and exciting though, and we have been discussing which way to proceed from here."

There are a few questions for the researchers to consider, such as how much time they spend on other uses for the technology, while accepting the medical purposes are their main area of concentration. They also have to balance the commercial and legal aspects of developing a new technology with the need for further academic research.

"We have the potential to save lives, but at the same time we have to pass the regulations," Gerardo says.

The team will probably look at non-medical uses in areas covered with less regulation, which makes it easier, and at the same time not compromise on their efforts to keep working on the ultrasound scanning device.

There are dangers in this approach, Gerardo admits. "If we try to be too broad we won't be able to go very far, so we have keep it narrow to some extent." ▶



Enlarged microscopic image of CMUT cells.

"We are creating prototypes and seeing which ones to go with," he says. The team are going to create a small start-up company in the next few months, with a view to a partnership with a commercial manufacturer and possibly a contract.

Next year, if all goes well, the research team hope to see the polyCMUT ultrasound device on the market and available to buy. The establishment of a patent, to ensure the technology developed by the UBC team is properly protected from being copied, is a priority.

By dealing with all aspects of the development of a new product it will eventually lead to a better device, Gerardo says. "We need to invest this time, as it means we will better design things in the lab.

"We can tell people how it is done, and with the research community we have to do this. A basic lab can replicate the results – you don't need expensive equipment. But the key parameters and the tiny details we keep to ourselves for commercial purposes," he says. It is also important on the flip side to ensure they don't infringe on someone else's design.

For example, there is a US company called Butterfly Network, which has developed a handheld ultrasound scanner that can produce images of the whole body. Conditions such as liver disease or heart disease can be diagnosed relatively easily. It costs $2,000 to purchase with a user licence fee on top.

This device doesn't use the traditional piezocrystal technology, replacing it with a single silicone chip. It is battery-powered, and can be used with a smartphone. "They have an amazing product", Gerardo says. "Their technology uses something completely different to existing machines in hospitals and is similar to ours."

## On the phone

Compatibility with smartphones is one aspect Gerardo sees as really important in any new ultrasound device. In fact, a portable transducer ultrasound device attached to a smartphone is a vision the team has for their product.

"We have a dream, but we have to take it step by step," Gerardo says. "Our dream is something portable that uses batteries and is affordable. A patch would require a low voltage – we need to produce several prototypes."

Certainly the cost of the device will be crucial if it is to be used in developing countries, where money is scarce but the need is great. If the cost can be brought down below $100 then it may become a possibility for those countries. The ultrasound market was forecast to grow from a global figure of $4.6 billion in 2012 to $7.3 billion this year, according to figures from GBI Research, meaning there is enormous potential for these products.

The UBC team's polyCMUT device could be a breakthrough development that transforms the ultrasound market and its use of technology.

If the product costs less than $100 yet produces better images than existing scanners, there will surely be many takers from all over the world. Ultrasound could become available in parts of the world where it is currently only dreamt about. With the current price tag of between $10,000 for portable scanners and $250,000 for top of the range scanners, it's not difficult to see why the cost is currently prohibitive to some communities.

Existing scanners using piezoelectric crystals could be phased out, with all the implications a much cheaper alternative would have for the big-name manufacturers. Wearable ultrasound devices stand to become the go-to products for health professionals, and the ease-of-use and portability certainly make UBS's product a strong contender. As the device can be used with a smartphone, then the sky may well be the limit in terms of its potential uses, and the possibilities for future ideas are endless. ●

**$100**

Proposed cost of UBC's new scanner. In contrast, current portable scanners cost a minimum of $10,000.

UBC

**100µm**

Diameter of the drums, made from a polymer resin, inside UBC's ultrasound scanner – the same as a strand of hair.

UBC

# Fujitsu IoT Solutions

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Modules
Positioning Engine
De-centralized Mesh

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www.fujitsu.com/IoT

# Decrease work pressure, improve patient well-being and gain insight

**Fujitsu**'s IoT connectivity solutions are powerful tools for hospitals when it comes to improving efficiency and keeping track of supplies.

Hospitals deal with a large number of patients on a daily basis, which involves the movement of an even greater amount of supplies and equipment. Today's healthcare facilities are under serious pressure to have equipment available at the right time and location. Combining nursery tasks with tracing hospital equipment is an inefficient use of resources when alternatives are available.

Fujitsu Components has developed an IoT solution to cover hospital asset management; the solution can also monitor environmental conditions, such as room temperature, acceleration and humidity.

Fujitsu has developed a solution that can trace any hospital asset equipped with Fujitsu tags.

### Hospital asset management

Fujitsu has developed a solution that can trace any hospital asset equipped with Fujitsu tags. It is based upon mesh networking, which allows communication between all assets. This way, anchor nodes build a network that allows the asset tags to communicate data to the gateway. By using the mesh network, an unlimited amount of assets can be added or removed without the need for network maintenance; the assets tags simply reroute the data.

The solution offers operators a live view of where assets are located and how many are available – even maintenance information can be added. In real life, this enables the maintenance department, nurses and any member of staff to locate assets such as hospital beds, and monitor their occupation and maintenance. But the solution is not limited to just hospital beds; all types of hospital equipment can have Fujitsu tags, from various medical devices and wheelchairs, to life-saving equipment like a defibrillator. Plus the possibilities are not restricted to only tracking assets; the solution can also be applied to avoid picking errors in hospital warehousing or in patient medication distribution.

### Monitoring environmental conditions

In hospitals, monitoring environmental data can be of great importance for the patient and for a medical device's life cycle. Fujitsu Sensor Beacons can be used to monitor various environmental values, like temperature, humidity or acceleration, providing a wealth of information that can contribute to patient well-being and provide insight on variables that can influence device maintenance and stock control of medical devices.

### Patient experience and traffic flow monitoring

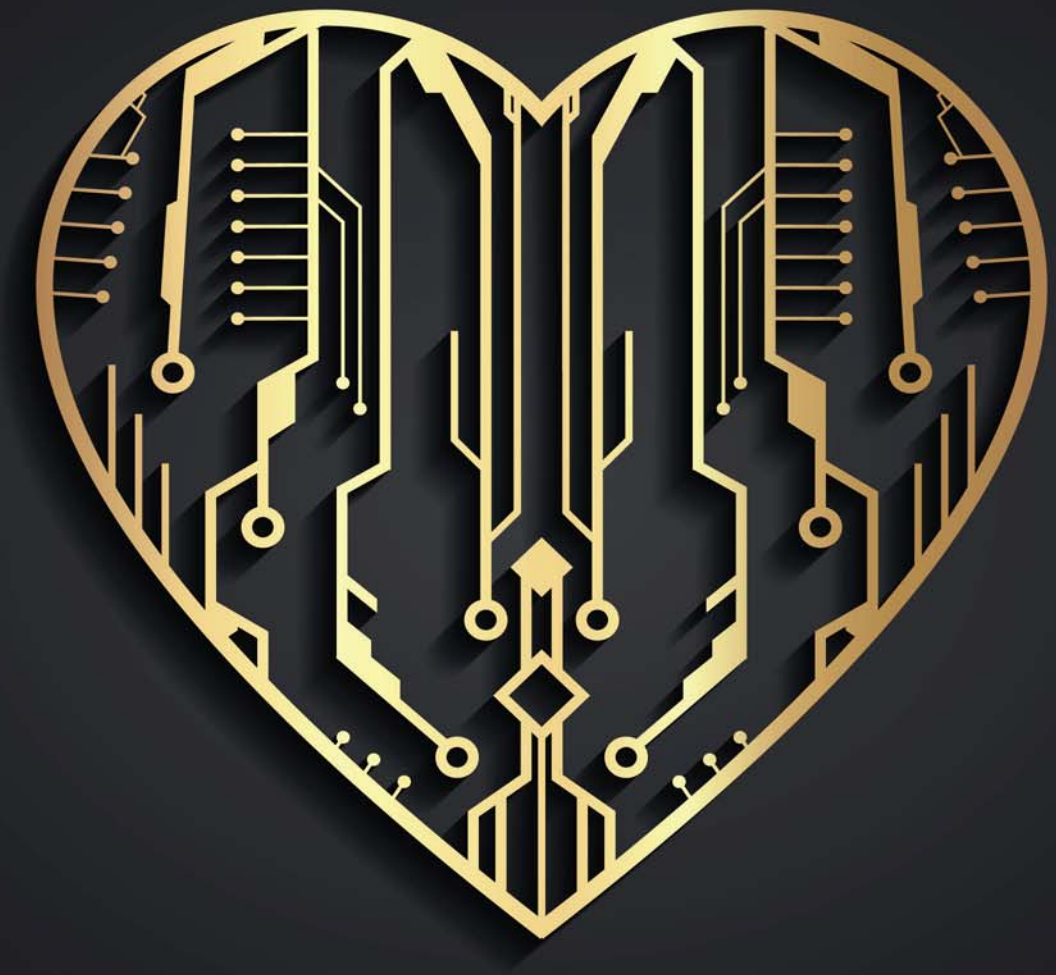
Whether used to monitor visitor experience or patient-traffic flow, indoor navigation provides multiple advantages. App-based indoor navigation can offer the visitor tailored information about appointments, waiting times and routes, therefore contributing towards a positive hospital experience. Indoor navigation also allows insight into visitor and patient traffic and enables detailed profiling of visitor behaviour.

Fujitsu Smart Beacon is a Bluetooth smart transmitter that broadcasts specific data in the form of a unique identification number, information on transmission power or a URL. The unique identification number enables smart devices – such as a phone or tablet – to recognise the beacon and relate it to a specific app. The number also identifies the group or groups to which that specific beacon belongs. Information about the transmission power can be used for navigation and localisation purposes. Combining information provided on transmission power and information retrieved from the unique identification number enables precise navigation and localisation – right down to specific rooms and areas. Indoor navigation requires a predictable transmitting characteristic, and the Fujitsu beacons are able to do this consistently. Beacons are also able to broadcast a URL that will be displayed on smart devices and can be activated by the user. This provides web-based interaction with the user that can then involve any type of information.

The Fujitsu IoT Connectivity Solutions offer great advantages for nursing and maintenance staff, as well for management. The solution provides insight on usage, efficiency and maintenance, which offers great potential for process optimisation. ●

**For further information**

www.fujitsu.com/iot



# The heart of the problem

The vast majority of semiconductors in medical devices are made from silicon, which, though the cheapest material available, is not the most efficient. Now, a team of engineers at the Massachusetts Institute of Technology (MIT) has developed a new way to fabricate ultra-thin semiconducting films made from a host of exotic materials. Michael Shaw talks to **Jeehwan Kim**, the university's class of 1947 career development assistant professor in the departments of mechanical engineering and materials science and engineering, about the potential applications of this research.

The baby was delivered stillborn and Mark C Lidwill was running out of ideas. Artificial respiration and injections of adrenalin had failed; now, the only option left open to the doctor and his assistant was a highly experimental technique of cardiac therapy. Together they plunged a needle straight into the baby's chest and into the ventricle of his tiny heart. The spindle was connected to a generator, which – Lidwill hoped – would deliver the 16V necessary to restart the patient's pacemaker.

Remarkably, the procedure worked. "The heart responded to each impulse," Lidwell wrote in an article describing the procedure. "At the end of 10

minutes the current was stopped and it was found the heart would beat of its own accord." The child would eventually leave the Royal Prince Alfred Hospital, in Sydney, Australia, fully recovered, and living proof of the first successful artificial pacemaker.

Lidwell's actions in 1928 were groundbreaking but quickly forgotten. The contraption he'd jerry-rigged with his assistant was incredibly complicated to operate, and any patient who needed to have the electrical impulses in their pacemaker regulated instead of jump-started would be tied to it, needle and cable, for life. What was needed was a wearable device, or better yet an implanted artificial pacemaker that could regulate the patient's heartbeat autonomously. It would not be until the 1950s, with the advent of the silicon transistor, to make this a reality.

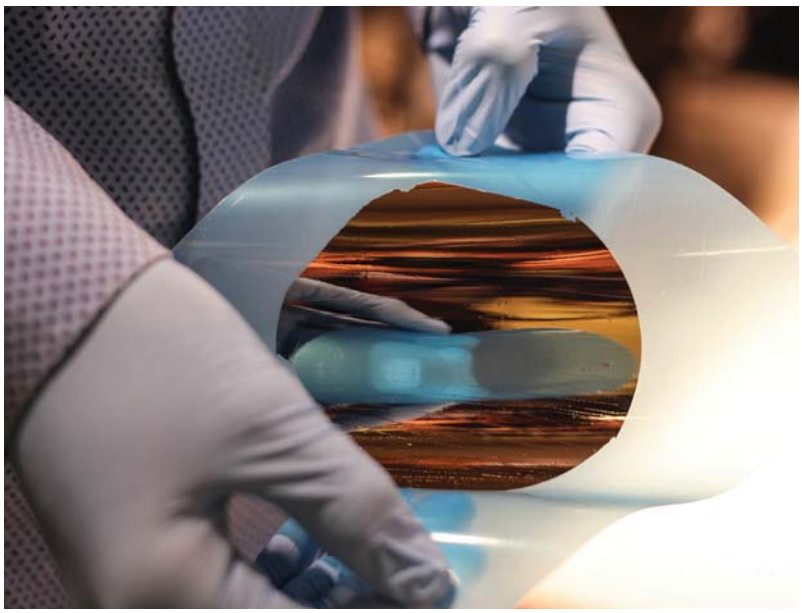
And yet, even as this development led to a succession of medical devices with ever-greater capabilities, another wall has inevitably been hit. In a medical market that yearns for more flexible electronics, affordable manufacturing methods that produce the thin semiconducting films necessary for such devices remain elusive. The electronics industry's continued marriage of convenience with silicon – which, as the seventh-most abundant element on the planet, remains the cheapest semiconductor out there – is also a sad indictment of the sector's lack of progress in fulfilling its true potential.

Why? The mobility of electrons in silicon is simply not as good as that encountered in other compounds, like gallium arsenide or gallium nitride. In fact, 'not as good' is a radical understatement; the way electrons zoom through gallium arsenide makes their passage through silicon look like a leisurely stroll, and it's the reason why the compound can be found in almost every mobile phone, the better for it to parse the radio waves beamed down to it via satellite into interpretable speech.

And yet, for all its advantages, compounds like gallium arsenide remain prohibitively expensive to manufacture compared with silicon, which comprises just over a quarter of the Earth's crust in weight. By comparison, making an 8in wafer of gallium arsenide – a compound of gallium and arsenic, this time occupying a more productive role than its traditional application as a poison – costs up to $5,000, a thousand times more than its silicon equivalent. What is needed, it seems, is a revolutionary new method of manufacturing semiconductor films, one that Professor Jeehwan Kim and his colleagues at MIT may have just discovered.

## Wafer thick

The key to the professor's new manufacturing method is, as it turns out, including another much-vaunted compound in the process – graphene. First synthesised by two scientists at the University of Manchester, UK, after they accidentally removed slices of carbon from graphite using scotch tape, the substance has since been hailed as a miracle material thanks to its own remarkable conductive potential.



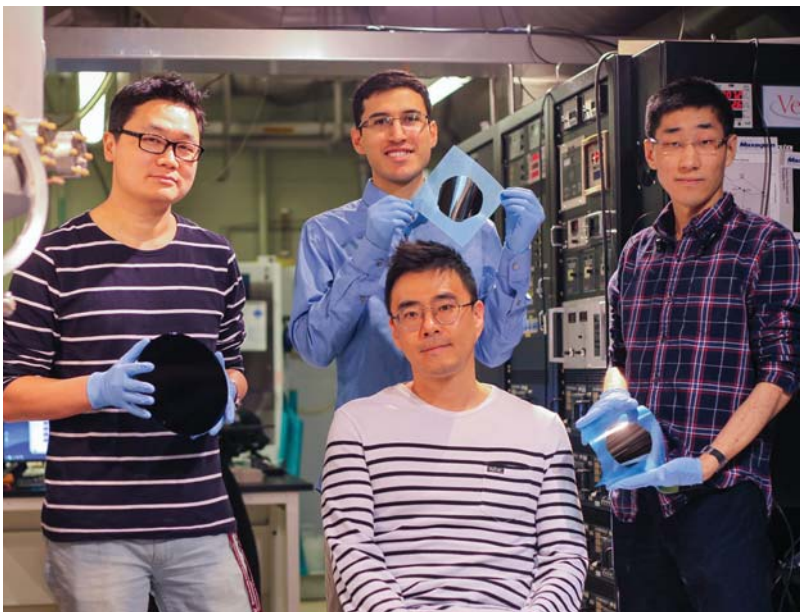
©Jose-Luis Olivares, MIT

**A layer of graphene – a substance that has been declared a miracle material due to its high conductive potential.**

Even so, graphene is also prohibitively expensive to synthesise. What Kim and his team discovered in their research, however, was that the thinness of graphene – the molecule is only one atom thick – lends itself to the wholesale fabrication of other compounds. Using a manufacturing method called 'remote epitaxy', they could produce new and exotic semiconducting films inexpensively and at scale.

*"Typically, the electrical and optical properties of single crystalline films are much better than any other electronic functional materials."*

The team began by taking a layer of graphene and placing it over an existing semiconductor compound, such as a gallium nitride wafer. Constituent atoms of this compound were then placed on top of the graphene. These particles began to form a pattern that mirrored the crystalline structure of the underlying wafer at the bottom of the structure, until an entirely new copy of the bottom section could be peeled from the top of the stack. This process, says Kim, is called remote epitaxy, and effectively allows the user to "copy and paste the crystal information of the underlying substrate", he explains. "In principle, you can do this on and on, because you go on the same material on the thin graphene and peel off… the wafer just becomes a template." ▶



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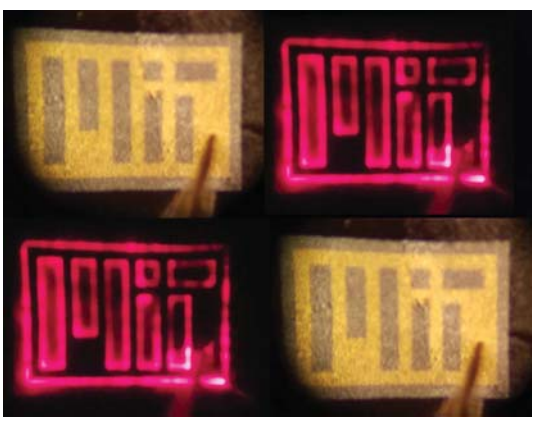
**Above: Jeehwan Kim (front centre) and his team at MIT.**

**Below: LEDs that have been grown on graphene and then peeled off.**

Kim and his team quickly discovered limits to this new manufacturing method. While they experienced success in their creation of gallium arsenide and gallium nitride films, when they decided to conduct new experiments on the same lines with germanium and silicon, they were not able to peel off any new layers of either material from the middle graphene section.

*"There's no way to put those semiconductors on the skin, because the semiconductor is rigid. By using our technology, you can make this and put it on the skin. By putting [a device in] the skin patch, you can then acquire instant information from the body through the skin pore."*

The reason why remote epitaxy failed to copy anything similar was, according to the professor, down to the ionic bonding properties of both materials. "Silicon does not have polarity," explains Kim, referring to the interactions between the atoms in the substrate and those lain on top of the graphene. The professor and his team deduced that they weren't able to copy and paste germanium and silicon because the ionic charge in the substrate and the top layer was identical, as they were from the same atomic group on the periodic table. Gallium and nitrogen, meanwhile, retain opposite charges. Not that the professor was overly concerned.



©Professor Jeehwan Kim et al

"Silicon's a chip anyway," says Kim, referring to the ubiquity of semiconductors made out of the material in multitudes of devices around the world. In the grand cost-benefit analysis, using remote epitaxy to create copied versions of an original silicon substrate might not make as much of a difference as an equivalent made out of gallium arsenide.

## Epic potentials

What difference, then, would remote epitaxy make to the field of medical devices? According to Kim, by laying each of these films produced through remote epitaxy on to one another, it could be possible to design new and more flexible types of devices.

"Typically, the electrical and optical properties of single crystalline films are much better than any other electronic functional materials," he says. The use of these films in medical device design could, Kim argues, lead to the first viable implants embeddable inside skin. After all, the largest organ in the body yields a variety of symptoms and signs to clinicians that might be more easily interpreted with such devices.

"In order to sense that kind of information from the skin pore, you need to have high-quality silicon conductors," explains Kim. "But there's no way to put those semiconductors on the skin, because the semiconductor is rigid. By using our technology, you can make this and put it on the skin. By putting [a device in] the skin patch, you can then acquire instant information from the body through the skin pore."

Kim also envisions health-monitoring devices implanted in or near major organs, the better to communicate with individual cells. He concedes, though, that this is all speculation. The full practical potential of remote epitaxy is yet to be realised.

"I think it will be five to 10 years," says Kim, on how long before medical OEMs will be able to use this new manufacturing method. Even so, the work of Kim and his team at MIT points towards new and exciting developments in the form and potential of medical devices. Just as it took the invention of the silicon chip to popularise the pacemaker and revolutionise the medical device industry, so new manufacturing methods like remote epitaxy might lead to the flexible clinical implants and wearables to transform healthcare.

# Negotiate the MDR checklist

The European Commission's new medical device regulations puts the onus on medical device manufacturers to ensure they conform to increasingly stringent regulations. **RECOM Power** knows the new legislation and advises companies on remaining compliant.

The European Commission (EC) has decided that the existing EU medical device directive (MDD) is not rigorous enough and it has been recast to the medical device regulation (MDR).

The difference between a directive and a regulation is that all member states in the EU are legally bound to abide by a regulation without any modifications (it enters law immediately), and the EC can take measures to punish countries, manufacturers, importers, distributors or even individuals if it feels that any transgressions have been made and the local authorities have not been zealous enough in ensuring compliance. The wording used in a regulation is necessarily dictatorial.

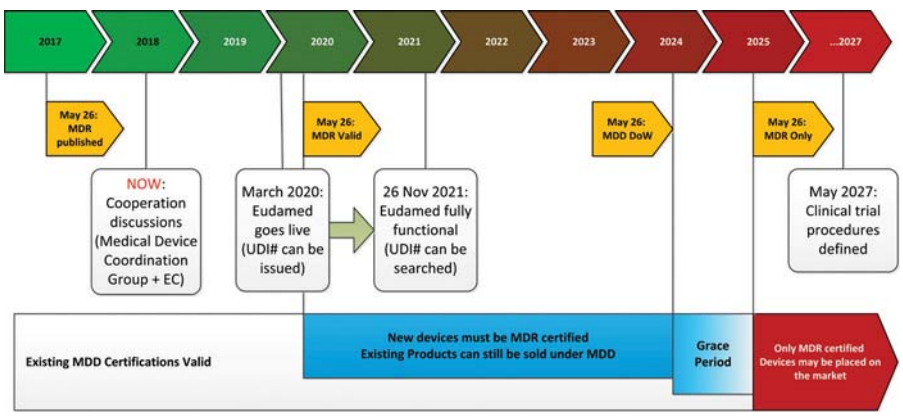
## Check it out

The following checklist from RECOM may help manufacturers wanting to stay in the medical market after 2024:

1. If you are an importer or distributor, you will have the same responsibilities and liabilities as if you were a manufacturer. Unless you have direct contact with the original manufacturer with access to the design team, supply chain management and production, you will struggle to meet the regulatory requirements for traceability and post-market surveillance.

*"The MDR will apply to all medical device manufacturers, meaning every manufacturer of a medical device or accessory will have new obligations."*

2. As a manufacturer of a component that in itself is not a medical device (for instance, a power supply), you will not be required to carry out clinical trials or apply for a unique identification code. However, you will still need to support and react to any adverse results arising from the use of the product inside the medical device over its lifetime. It is advisable to create a serial number for every product supplied, linked to full documentation (production testing results, quality control, bill of materials). A simple date code identifier will probably be insufficient.
3. If the supplied part has a potential hazard (electrical, thermal, sharp-edges or radiation), you will be required to carry out a risk assessment. This goes beyond the simple safety or EMC certifications, but will need to be an ongoing and regular re-assessment. You will need to contact each and every customer who has purchased the product on a regular basis over the lifetime of the product. It would be advisable to enter into a contractual arrangement with customers to formalise this procedure.
4. There are not enough notified bodies (NBs) accredited to meet the requirements for the MDR. It can be that a new medical product may have a delayed market entry because there is no NB available to take on the responsibility of monitoring it. Plan also for increased costs as demand outstrips supply.
5. Manufacturers will be required to have someone within the organisation responsible for regulatory compliance who possesses expert knowledge in the field of medical devices. If there is no such specialist in-house, you will need to make arrangements with an external consultant.




RECOM is ideally positioned to help device manufacturers navigate the new regulations from the EU, which are comprehensive and will have an impact on all medical device manufacturers.

The MDR will apply to all medical device manufacturers, meaning every manufacturer of a medical device or accessory will have new obligations. The MDR is perhaps unique in defining job descriptions of staff that must be employed by manufacturers if they wish to stay in the medical market and by giving the notified bodies extra duties to act as policing organisations, rather than just industry certification partners. ●

### For further information

www.recom-power.com/medical

# Next evolutionary step

Thanks to bioelectronics, devices are starting to replace drugs for a wide range of conditions. Bioelectronic medicine explores how targeted electrical signals can harness the body's natural mechanisms to diagnose and treat a range of diseases, helping the body heal itself. Emma Green speaks to **Lan Yue**, assistant professor of research at USC, about the potential of this technology for medical device manufacturers.

By definition, bioelectronics is the convergence of biology and electronics. We tend to think of it as a new term but the first reference was in 1912. According to a 2009 report by the US National Institute of Standard and Technology, this was in relation to the measurement of electrical signals generated by the body. We already have a number of applications of bioelectronics within common use, including pacemakers and medical imaging technology. Despite these developments, it was not until the mid-1990s when the term became more commonly used within the scientific literature. Today, bioelectronics is used to describe a range of applications for electronics within biology and medicine.

A number of different types of devices have been developed using bioelectronics. This includes a large variety of diagnostic, monitoring and therapeutic electronic devices, from the organ level to the cellular or subcellular level. For example, there are devices that use biosensors to detect and characterise biological materials, such as DNA, protein and cells. In addition, there are implantable devices that interface with biological systems to repair, restore or enhance physiological functions. Biolectronics also includes implantable devices, such as pacemakers, deep-brain stimulators, cochlear implants, visual implants, electrical bladder controllers, muscle implants, spinal cord and peripheral nerve stimulators.

Lan Yue, assistant professor of research ophthalmology at University of Southern California (USC) is committed to advancing bioelectronics and is currently focused on retinal applications of this technology. Despite a great deal of progress made within the field and exciting future applications, there are also a number of challenges. This is exacerbated because of the inherent convergent nature of bioelectronics. Barriers can thus arise from a lack of technological advancement, biological understanding or a combination of the two. Although there is a requirement for innovation across a number of different fields, this also allows cross-discipline collaboration among researchers and a productive platform for creative thinking.

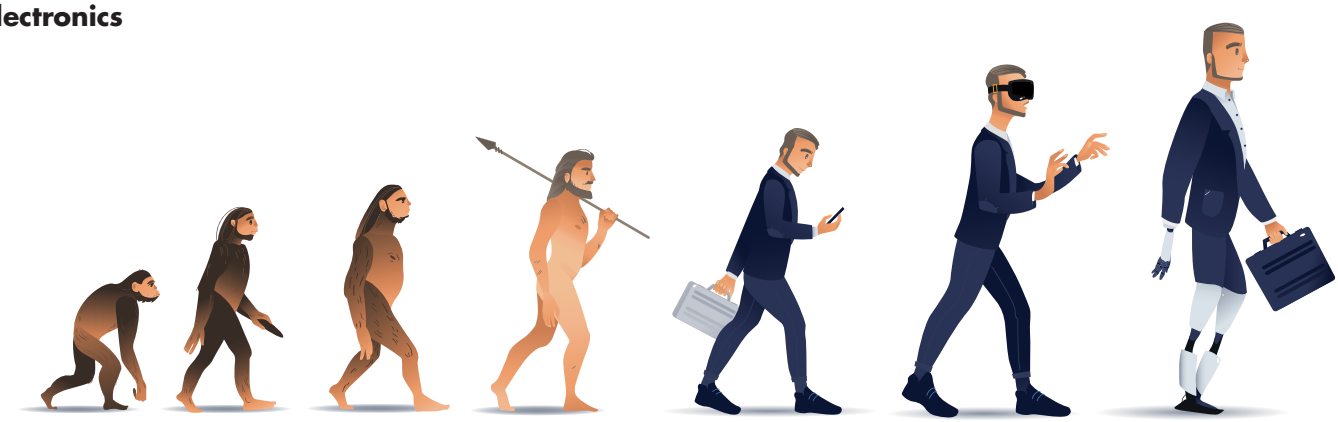
## Small problems

In terms of technological difficulties, the inherent challenge is making devices small enough to be used inside the body and producing these at a high volume. “Device miniaturisation demands advancement in microelectronics and fabrication,” explains Yue.

Fabrication methods for other fields, such as the semiconductor industry, are optimised for minimising trace widths and feature sizes. A wide variety of materials have been incorporated into the fabrication processes to improve performance while reducing costs. However, in biology and medicine, methods for building microdevices are not well established.

Reliability is a particular area of concern. The majority of micro-fabricated bioelectronic devices are either fabricated by small custom suppliers or are manufactured within academic facilities. While semiconductor technologies can be used to fabricate small features, they are not yet able to fabricate complex bioelectronics. However, with the rapid development of these technologies, it is likely only a matter of time before this is possible.

Another technological challenge is ensuring that a device is sustainable within the body. “Proper encapsulation is essential to the longevity of a device in the physiological environment,” explains Yue. ▶



There are a number of strategies to improve biocompatibility. These include employing biocompatible materials, limiting implant rejection and minimising heat generation, which all help to achieve a healthy tissue-electronic interface. Optimising the battery lifetime, functional capacity and heat management of devices is also imperative in order to obtain power efficiency and data management capabilities.

Another key challenge for bioelectronics is customisation. "A closed-loop system is desired in many cases to customise a bioelectronics device for optimised therapeutic effects," explains Yue. "This often demands advanced acquisition and interpretation of the biological signals."

Similar to other personalised treatments, as gene therapy and cell tissue engineering, bioelectronics production could be decentralised with manufacturing taking place at sites close to specialist hospitals. However, achieving personalisation while navigating the pressure to reduce cost – through the high-volume manufacture of devices and their components – is inherently difficult.

One solution is 3D-printing technologies, which offer huge potential in their ability to produce devices that meet the needs of different users in a quick and cost-effective manner. Although these technologies are still in their relative infancy; they are likely to be an increased area of focus over the next few years because of their ability to drive progress, not only in bioelectronics, but within medical devices as a whole.

There are also physiological challenges within bioelectronics. "A better understanding of the fundamental issues of the target physiological systems, particularly the processing at the bioelectronic interface and beyond, is required," says Yue. "This will enable design of

**The current status of bioelectronics in the medical device industry**

The rapid evolution within the field since the mid-1990s has been referred to as the 'bioelectronic revolution'. This is characterised by large companies, which are currently making significant investments in the area. These include the big players in the medical device space, such as Medtronic and Boston Scientific, as well as those from other scientific disciplines, such as data mining and the pharmaceutical industry. Public and private organisations, such as the National Institute of Health, the Defense Advanced Research Projects Agency and GlaxoSmithKline, are dedicating substantial resources to drive efforts within bioelectronics worldwide, with a view towards building new markets, clinical translation and adoption.

Propelled by capital injection and by the discoveries of the scientific community, a growing number of start-ups are proposing new target diseases for intervention, releasing preliminary data that can demonstrate the validity of the bioelectronic medicine approach while accepting the risks associated with early stage technology development. As a result of these efforts from the private and public sector, it is becoming easier to envision continuous improvement of these devices, leading to new models of clinical care.

Source: 'Bioelectronics: the promise of leveraging the body's circuitry to treat disease.'

the devices that better mimic the impaired functions of the target tissue while reducing biofouling."

Biofouling is a process wher a build-up of biological material accumulates on wetted surfaces. This is problematic in a number of bioelectronic devices, such as pacemakers. It affects their functionality by altering the electrical properties of the electrodes attached to the heart, making sensing and actuation difficult.

The key challenge is that bioelectronic devices must interact with living tissues that are not inherently compatible. Due to the high level of sophistication of digital electronics, the signal processing of these devices is far more advanced than the front-facing aspect of the device.

Such issues are likely to be solved by the increasing work within systems biology – the study of the interactions that occur within the body. Insights from this area will allow the development of devices that are more compatible with biological systems and tissue. In particular, there is an increasing amount of research in miniaturised and automated microfluidics and nanotechnology platforms, which is a key area of focus for Yue.

## Eye for detail

Although Yue is passionate about advancing bioelectronics more generally, her particular area of expertise is in retinal medical devices. She began her research in this area when working towards her PhD, during which time she became fascinated with bioelectronic visual prostheses, often referred to as bionic eyes. After completion of her PhD, she joined the research team of Dr Mark Humayun, a world-renowned pioneer in retinal implants. For her postdoctoral studies, she evaluated the efficacy and safety of these devices. This experience had a profound impact on her research goals and motivation. "It inspired my current work in the development of new stimulation strategies and nanoelectronic prosthesis that will, hopefully one day, restore colour vision and high visual acuity in the blind," Yue explains. ▶

Yue is currently working with blind patients who have retinal implants. She is evaluating the implant-retina interface and their visual functions with the assistance of the device. Alongside this research, Yue is developing novel stimulation strategies to enhance the visual experience of the otherwise blind patients.

The aim when creating a complex bioelectronic device, such as visual prosthesis, is to harness electrical power to produce highly specific and localised stimulation. Although an area with a lot of potential, there have also been a number of challenges that Yue has had to navigate in her work. "A lot of the difficulties that we encounter stem from insufficient understanding of signal processing of human retina to electrical stimuli," Yue explains. Further research is required to learn more about the different patterns of electrical stimulation in order to optimise the functioning of visual prosthesis.

In addition, as with all medical devices, safety is a top priority in visual prosthesis. However, this raises new challenges in the ability to improve its effectiveness. "It comes with the compromise in the fabrication capability and functional capacity of the device," says Yue.

Yue is determined to stay focused on her current area of work. "The overarching goal of my research will remain to be enhancing visual ability of prosthetic vision in the blind," Yue states. In order to achieve this, she intends to study two areas in parallel. The first of these is the development of new stimulation paradigms through continued investigation of electrical stimulation of the visual system. The second is creating and testing non-conventional bioelectronic prosthetic devices that use novel materials, such as organoelectronics and nanoelectronics.

In looking ahead in bioelectronics more generally, Yue remains optimistic, saying, "Advancement of material technology with fabrication and information technology will profoundly impact bioelectronics in the future, possibly leading to a revolutionary breakthrough."

These material developments open up the possibility to make devices that are more flexible, biocompatible, immune tolerant and with a higher energy conversion efficiency. In addition, the progress in AI and related technologies will allow the decoding of biological signals at an impressive speed and depth. Together these provide the opportunity to address difficult questions in precisely harnessing electrical power to serve for biological purposes. The devices of the future may be able to not only match the level of human functioning but also improve upon it. "It is imaginable that with the advancement in bioelectronic technology, conventional devices that aim to monitor or mimic human physiological functions may one day progress to devices that can enable enhanced performance; for example, in sensory functions and memory," says Yue. ●

# B is for bonding

PCAP touchscreens have conquered the medical industry, but it is rare to see manufacturers offering TFT displays bonded with a touchscreen unit. In Europe, only **DATA MODUL** currently offers the in-house availability of all common bonding technologies.

Thanks to developments in gloved operation or operating through liquids, as well as the optimisation of touchscreens through optical bonding, increasing numbers of PCAP touch monitors are being used at PoC and in other medical areas. However, it is rare to see manufacturers offering TFT displays bonded with a touchscreen unit. For this reason, DATA MODUL established in-house expertise in optical bonding in 2011 and has been improving it ever since.

Bonding means the connection of device components using an optical, transparent adhesive – the refractive index of which must match that of the media to be bonded. A distinction is made here between the bonding of cover glass and PCAP Touch, cover glass, and TFT. Bonding minimises distracting reflections, does not dampen the capacitive touch field, and achieves user stability against interference factors. In addition, it is not possible for dust to enter in-between the PCAP sensor and the glass. Due to the increasing demand for medical PCAP solutions with customer-specific glass surfaces, DATA MODUL is constantly expanding the range and optimising quality standards.

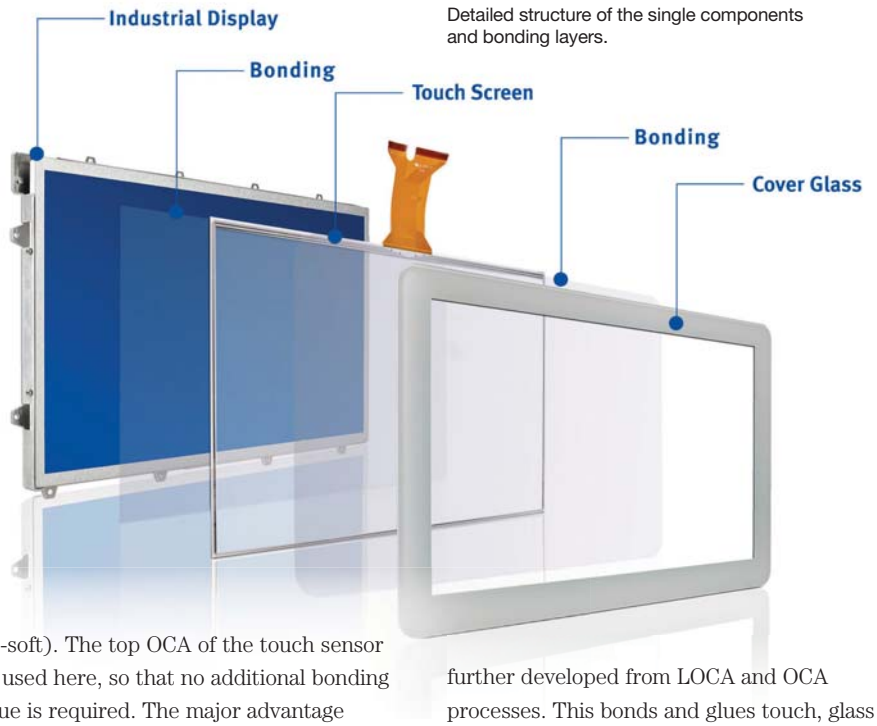
Current bonding technologies such as AirGap, LOCA, OCA, gel and the new hybrid bonding provide the best possible optimisation solutions for all display and touch variants available on the market.

### LOCA (liquid optical clear adhesive)

This liquid glue method is flexible and can be used at all display sizes. It is suited to hard-to-hard bonding and cured via UV light. The LOCA adhesive is used for bonding cover glass to glass-based touch sensors and industrial TFT displays with metal frames (bezels) to a cover glass (with or without touch).

### OCA (optical clear adhesive)

Dry bonding or OCA roll lamination applies a touch sensor film to the cover glass (hard-to-soft). The top OCA of the touch sensor is used here, so that no additional bonding glue is required. The major advantage of OCA bonding is that projects can be completed quickly and cost-effectively.




Detailed structure of the single components and bonding layers.

### AirGap bonding

This method was used for resistive touch sensors and is the forerunner of bonding technology. In contrast to LOCA, in AirGap bonding, a double-sided adhesive tape is applied around the TFT frame, which bonds the TFT and the touch or glass to one another. An air gap is maintained between the two components in the process.

### Gel pads

This method is used in processing frameless displays. Gel pads are tailored to the size of the display surface and bond the glass or touch sensors to the TFT. This would not be possible in LOCA. Diagonals from 1.3–14in and mobile applications with round memory-in-pixel displays can also be realised.

### Hybrid

DATA MODUL is one of a few companies to provide this new process, which has been further developed from LOCA and OCA processes. This bonds and glues touch, glass and display (hard-to-hard) automatically. This method is particularly suitable for high-volume projects with special requirements, like the manufacturing of medical devices.

### Gap filling

After the assembly of a PCAP touch monitor/HMI/embedded display in a housing there is always a gap between the screen and the housing frame that cannot be avoided during manufacturing. Particularly in the development of medical products, there are high hygiene requirements. One example is that gaps on devices must be avoided. Through gap filling, gaps are filled with a special glue and sealed securely. This stops impurities or liquids from entering or getting stuck in there. At DATA MODUL, a pick and place machine carries out the gap filling under cleanroom conditions. The special adhesive is suitable for temperatures from -40°C to 100°C and covers all requirements for medical devices. ●

### For further information

www.data-modul.com

# The power to succeed

In vivo networking (IVN) is a novel approach to powering – and communicating with – implanted medical devices. Jim Banks talks to assistant professor **Fadel Adib**, one of the researchers involved in an IVN project at MIT, about how the research could bring about a paradigm shift.

Major steps forward in microtechnology and new biomaterials have greatly improved the biocompatibility of devices that can be implanted in the human body, thus opening the door to a host of therapeutic uses.

Imagine devices that can monitor the condition of highly specific areas of the body, or deliver drug therapy at precisely the right time, or stimulate otherwise impenetrable areas of the brain. The opportunities are seemingly endless, but there has hitherto been one problem that has been hard to solve – power.

Devices that reside inside the body must be kept small, but they must also receive a sufficient and continuous source of power if they are to operate effectively. As these devices increasingly rely on the ability to communicate wirelessly – to deliver data about conditions within the body or to receive instructions from clinicians – the reliability of that power supply becomes even more critical. Implantable medical devices (IMDs) are becoming smaller and lighter, but the need for a battery severely limits how small they can become and, therefore, how they can be used for diagnostics or treatment.

The fact is that if a device is equipped with a battery, the power supply accounts for most of the space on the device and often means it has a limited lifespan. For instance, cardiac pacemakers rely on non-rechargeable batteries due to regulatory restrictions on the use of rechargeable batteries, which a patient might forget to charge or which, due to a technical fault, might not recharge effectively.

"One of the most important things about the new generation of implantable devices is that we want them to last a long time to enable monitoring, diagnosis and treatment," says Fadel Adib, assistant

professor in the Media Lab at the Massachusetts Institute of Technology (MIT). "We also want them to be small, so that we are not putting a large alien body into a human being. So, we need a long-term and continuous power source in a small device that can operate in different parts of the body."

## Size limitations

Fadel's group at MIT focuses on the development of new wireless systems and, recognising the application of its work in smaller implantable systems for drug delivery, long-term monitoring and deep brain simulation, he soon came up against the limitations on size created by the current crop of systems for powering these devices.

"When you are designing a tiny device that must last for a long period of time and is not anatomically specific, so that they can work anywhere in the human body, you soon come up against the question of how you power it," he remarks. "The existing literature shows a number of different approaches, all of which have their own limitations."

Researchers have tried a number of ingenious approaches to powering IMDs. One that is in the early stages of development is the biological supercapacitor under development at UCLA and the University of Connecticut. Using graphene combined with modified human proteins as an electrode, the system uses electrolytes from in-body fluids such as blood serum and urine to power the supercapacitor. In theory, the system could provide an endless supply of energy for IMDs at a size far smaller than the existing alternatives.

Body movement is another potential source of power for IMDs. Whether it is the beating of the heart, the bellows-like movement of the lungs, or the movement of the arms or legs, power is generated constantly just by the act of living, so it makes sense that some of it could be harvested to power a small device like a pacemaker or an internal sensor. Charged by internal vibrations or through wearable piezoelectric energy harvesters, there is potential for many devices to be powered indefinitely without the need to regularly replace batteries.

Adib, however, sees some limitations with many of these approaches.

"Powering a device with body movement can work well in some areas in the body but does not work so well in the brain, where there is very little movement," he remarks. "Harvesting power from movement is not, therefore, a universal solution. Generating power from chemicals within the body also only really works if the device is located in the stomach.

"We were working on both powering a device and communicating with it, so we looked at the lowest-power communication technology that is available. The most power-consuming part of communication is the amplification and transmission of the signal. That's why the battery is the largest part of a smartphone. We wanted to enable communication without the device generating its own signal, instead reflecting it from outside, because that uses the least power," he adds.

Fadel Adib

## The benefits of in vivo networking

By looking at power through the lens of communication with the device, Adib's group came up with a solution that addresses both needs in a highly innovative way. So was born in vivo networking (IVN), which can wirelessly power and communicate with tiny devices implanted deep within the human body.

Adib had been working on the possibility of wirelessly powering implantable devices with radio waves emitted by antennas outside the body, but the techniques focused on sensors and devices located in specific areas of the body. The new approach he and his team, along with Brigham and Women's Hospital (BWH), have developed does not require clinicians to know the exact location of the sensors in the body. IVN transmits power over a large area, can power multiple devices simultaneously and trigger a device to relay information back to the antennae that deliver the electrical charge.

IVN enables wireless power delivery and communication with deep-tissue medical devices thanks to an innovative beamforming algorithm that can focus its energy towards an in vivo sensor. Using a multiple-input and multiple-output (MIMO) method that multiplies the capacity of a radio link, and a multi-antenna array, the system delivers focused energy in such a way as to overcome the threshold voltage, which hinders the delivery of power, regardless of radio frequency attenuation and despite the sensor's small size. As the radio waves travel they overlap and combine, and at certain points, where the high points of the waves overlap, they can deliver enough energy to power an IMD.

"One of the biggest challenges was that wireless signals die exponentially fast in the body," Adib explains. "The signals are absorbed quickly by water, and up to 70% of the human body is water. To overcome this, we used power techniques that combine signals from multiple antennae. It is similar to the Wi-Fi infrastructure used to increase data rates."

"Using IVN, the device can either reflect or absorb the signal, which effectively creates a zero or a one, which is the basis for most electronic communication," he continues. "It powers the device and enables low-power communication with high-fidelity signals."

A beamformer serves to precode transmitted signals so that they constructively interfere at the receiver, which maximises the amount of energy received. IVN is the first system to bring the benefits of MIMO beamforming to in vivo battery-free sensors, and

eliminates the need for the transmitter to be close to or in direct contact with the body.

To absorb the energy, a battery-free sensor must convert RF signals in the environment into a DC voltage, which is achieved through an energy harvester, or rectifier. In Adib's experiments, battery-free tags fitted with rectifiers were implanted in a pig to evaluate IVN's ability to deliver power and communicate, both in subcutaneous and intragastric placements. It was capable of powering devices the size of a grain of rice located 10cm deep in tissue from a distance of 1m.

At the moment, implantable electrodes that can deliver electrical current for deep brain stimulation are normally controlled by a device similar to a pacemaker, which is implanted under the skin. With a wireless power source outside the body, this second device would no longer be required.

"We are hoping to develop end-to-end applications," says Adib. "Now, we are looking at extending the device to include a pH sensor, which could monitor reflux in the stomach. If we can measure and continuously monitor pH, we could design a device that delivers treatment by sending a command to release part of a drug when a particular threshold is reached. That kind of device, which senses the environment, could be useful for patients with Alzheimer's disease who might forget to take their medication. We have not built the device yet, but it is an example of how the technology could be used."

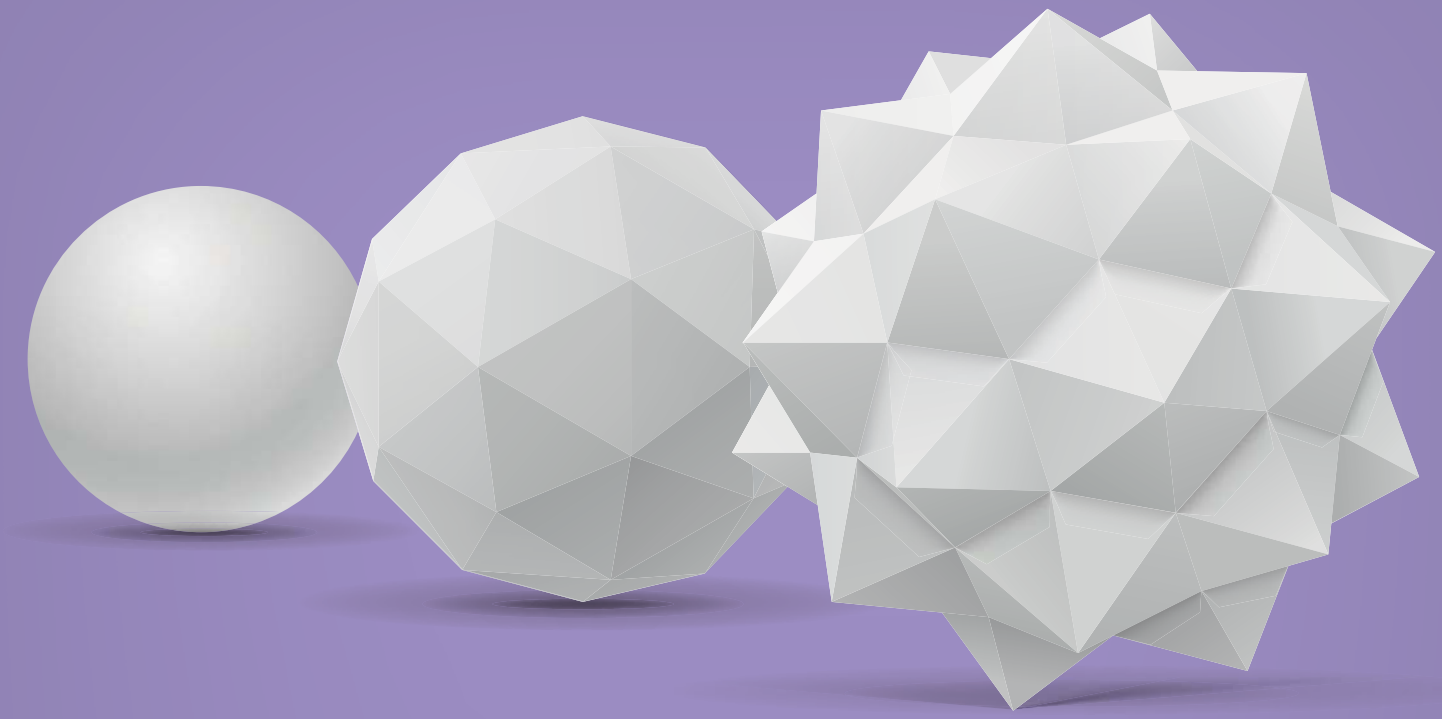
The extended charging distance that IVN offers, and that this eliminates the need to locate an IMD before charging and communication can take place, will be crucial for the development of real-world applications.

"In-body sensors have no batteries, so they must be powered before they can send a message, so we had to find a way to focus on them without knowing where in the body they are," says Adib. "Our technology allows us to focus on devices in unknown locations, although the ability to charge the device does depend on how deep it is within the body.

"The deepest, so far, is about 12cm below the skin, and we can charge that device from 1m away, so the system could be at the side of the bed. If the device is closer to the skin, it can work from up to 30m."

The paper on IVN delivered at the Association for Computing Machinery Special Interest Group on Data Communication conference, in August last year, was well received, and Adib hopes it will be the springboard for a raft of new therapeutic devices.

"The research represented the first time a miniature computer was put inside a human body," he notes. "There is a real need for these systems to have real-world applications, and it will enable a paradigm shift that will allow tiny sensors to be used in the body."



# The shape of things to come

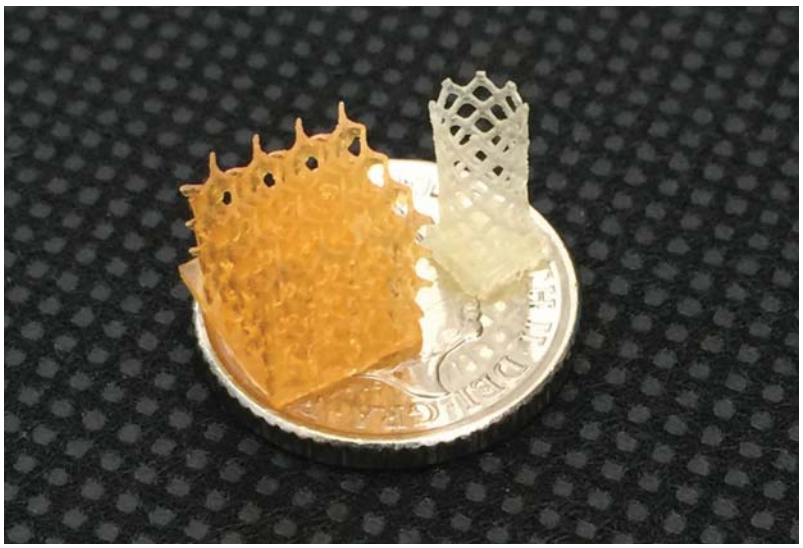
While the world continues to come to terms with the potential of 3D printing, engineers have been working on introducing a whole new dimension to additive manufacturing processes. Tim Gunn talks to **Dr Andrew Weems** of the University of Birmingham, **Professor Lorenzo Moroni** of Maastricht University, and **Dr Christophe Marquette** of Lyon's 3D Fabric of Advanced Biology laboratory about what four-dimensional printing can do to disrupt the medical device market.

People care a lot about change. It's the everything and nothing that we make and are made by. It orients our lives, our innermost thoughts and our politics. Change is struggled for, sold against, theorised, disproved, weaponised, dreamed of and feared. Now it can be printed, too.

In one sense, printing has always been an exemplary form of change. Whether it's 2D or 3D, what goes into a printer comes out different. But, as the name might suggest, four-dimensional (4D) printing adds something extra. From reclining chairs without mechanical parts to advanced implantable devices that only deform to carry out their functions when they reach the relevant area of the body, it creates objects that are able to alter themselves over time, and it allows us to bestow upon them the existential burden of becoming what they are.

Like many philosophical categories, what exactly 4D printing encompasses is up for debate. Dr Andrew Weems, an expert in shape-memory polymers at the University of Birmingham, suggests that anyone 3D printing a degradable material could argue that they were actually 4D printing, simply because degradable materials change through time. Not that he would personally make such a claim, preferring to reserve the appellation for objects that go through more controlled changes.

Weems is currently applying his expertise in advanced materials as part of a team halfway through an EU-funded project to produce a 4D stent. "We can



Simplified models of the 4D stents and porous scaffolds being tested at the University of Birmingham in their uncompressed position.

print shape-memory materials in one configuration and then deform them into some temporary shape," he explains. "Then they will return to their original shape once we apply a stimulus." Unlike traditional stents, which are compressed over a balloon catheter and mechanically opened inside blood vessels, the team's 4D stent polymers are tuned around body temperature, which means they can be printed in their open configuration and compressed for insertion before reopening in the artery.

*"A 4D-printed object is something that you 3D print and that is going to change according to a stimulus, whatever the stimulus is."*

**Dr Christophe Marquette, 3D Fabric of Advanced Biology**

## Debate over definition

Dr Christophe Marquette, director of research at the University of Lyon's 3D FAB biotechnology innovation platform, thinks a 4D object can do more than just change shape. For his team, "a 4D-printed object is something that you 3D print and that is going to change according to a stimulus, whatever the stimulus is. Specifically, what we are doing here [at 3D FAB] is printing 3D objects that incorporate biomolecules that change when they encounter other biomolecules."

The 3D FAB group's most recent paper introduces a method for 4D-printed hydrogels loaded with multiple active enzymes to reproduce biological functions in a complex shape. By co-immobilising thrombin and alkaline phosphatase in a hydrogel ink precisely engineered to release the former and retain the latter, they caused fibrin deposition, which creates a biofilm to entrap living endothelial cells, and controlled calcification of different parts of a biomimetic construct of vascularised bone. In an earlier paper, '3D–4D Printed Objects: New Bioactive Material Opportunities', the team printed a 'fanciful ball' that combined the same calcification capability with a biosensor that emitted light in the presence of glucose. There may not be a specific use for such a tool, but it does show the range of potential applications for the group's work.

"Usually [the descriptor 4D is] based on the morphology of what's printed," says Marquette. "Different parts change shape when they encounter moisture or heat. But in our case the trick is that we are printing with different compositions. If you want to have one part that emits light and another that doesn't, then you have to mix different inks with different biological components together."

This is possible because of the team's use of polyethylene glycol diacrylate (PEG-DA) hydrogel inks, which provide a moisturised environment suitable for immobilising active biomolecules, catalysts and antibodies. To quote the fanciful ball paper, it points towards a "new field of research in tissue engineering and particularly bone reconstruction, in which cells and programmed calcification might be printed together to enable the in vitro reconstruction of cellularised bone defects."

Though he wouldn't dispute the value of the research, Professor Lorenzo Moroni of Maastricht University is critical of the 'overhype philosophy' and lack of precision in the use of the term '4D', preferring to classify much of the work in the field as the 3D printing of stimuli-responsive materials. "Technically," he explains, "I think that one should only talk about 4D printing when the change happens as the 3D-printed object is being produced."

He gives the example of his work on bioprinting tissue constructs. "Calling this 4D bioprinting simply because, in time, the cells that you print in a hydrogel carrier change the composition of the matter surrounding them by digesting the hydrogel and producing their own proteins seems to me a stretch," he says. "This is bioprinting, which is 3D and where, if you make the construct well, the cells should do what they normally do – make proteins."

Then again, engineers don't work in this field for the semantics. As Marquette explains, for the 3D FAB laboratory, "the driving force was thinking, 'can we make sensing layers for in vitro diagnostics through 3D printing and not moulding or grafting?'" Then, he continues, "We wanted to see if we could get new features or new activities or new functions from a polymer with enzymes inside when this polymer has a certain shape."

This mimics sequential enzymatic reactions in the body, where macromolecular structures catalyse metabolic processes across multiple steps. The ease of 3D printing different molecule combinations in different shapes lets the 3D FAB team exercise their creativity in modelling and testing their own complex enzyme systems. Previously impossible experiments

become something like child's play. "We are printing puzzles, or Lego, and each piece is entrapping a different enzyme," says Marquette. "We can put one enzyme close to another, but not close to a third, constructing and changing the order of these pieces to see if we get any new features or new functions from the system. That's one more dimension," he laughs.

*"I think that one should only talk about 4D printing when the change happens as the 3D-printed object is being produced."*

**Professor Lorenzo Moroni, Maastricht University**

## Progress in the wider field

Weems's team isn't the only one working on 3D printing shape-memory polymers to improve the quality of stents. They might be some way from a consensus on what exactly 4D means, but researchers and engineers all over the planet believe it will prove important for patients who need implants to support arteries and airways. Under an FDA emergency use exemption, the technology has already saved the lives of infants suffering from severe tracheobronchomalacia, a condition that causes the airways to collapse. Researchers from the University of Michigan used CT scans to develop 3D-printed splints for three children, including one who couldn't have food in its stomach without having a heart attack and another whose windpipe had the floppy consistency of a "wet noodle", according to his mother.

Unlike airway stents, these resorbable polycaprolactone devices provide external support, preventing collapse or compression but allowing internal expansion, thus accommodating growth. In follow-ups over the next three years, all patients showed significant improvements in their symptoms as a result of receiving the experimental treatment. This time frame is particularly important for children with tracheobronchomalacia. Though newborns suffering from the disease have average life expectancies of days to weeks, the airways of those that make it to three usually grow strong enough to overcome the disorder. Polycaprolactone is used because it takes around three years to functionally degrade.

Similarly, Professors Yu-Gong Lee and Taeyoung Kim at the Gwangju Institute of Science and Technology, South Korea, have used shape-memory technology to model a unique bifurcated stent for use in branching blood vessels. What's more, they have a whole different vocabulary with which to explain it.

Whereas the fourth dimension is a concept most familiar to mathematicians and physicists, kirigami is origami with scissors. Practitioners precisely cut and fold a single piece of paper to create a three dimensional form. Lee and Kim's stents combine shape-memory polymers with kirigami structures to enable a bifurcated tube to pass through a tight cylindrical pathway before unfolding in response to a temperature stimulus. This particular approach needs further study before it can be trialled in a patient, but active origami has been proposed as a solution for everything from microsurgery robots to heart catheters.

## Opportunities and obstacles

Whether discussed under the rubric of space-time, origami, or stimuli-responsiveness, these devices have immense potential for decreasing the invasiveness of medical procedures and treatments. Children who once relied on paralytics to stay alive have been freed to inhabit their own bodies without fear of sudden suffocation, and it didn't require clinicians relearning how to use and apply external airway splints.

"It's very compatible with what's being done currently," explains Weems of his 4D stent. "And the other really positive aspect of these materials is that they take on the geometry of the native vessel. If there was some catastrophic failure in a stent, if something had broken during processing, which does happen, it will still take on its original shape when it opens. Compared with materials that just have an elastic response it can withstand a little bit more deformation and still return to its optimal, useful configuration without failing."

That doesn't mean there aren't still issues to overcome. The prototype for Lee and Kim's bifurcated kirigami stent is too large for clinical use, for instance. Similarly, Marquette's work at the 3D FAB Lab has shown promise 'on the centimetre scale', but the intention is to make devices 100 or 1,000 times smaller. "The idea hiding behind all this," he reveals, "is to inject some 3D-printed high-resolution sensors or active components into the bloodstream." However, the team first needs to work out whether its enzymes function in the same way and provide enough of a signal when contained in 5–10µm vessels.

For Weems, the challenge is more dissemination than containment. "We can put technology in clinicians' hands, and they can say, 'Oh, that's really cool, I might be able to use it,' but they approach problems very differently to how we do. That's great – they're doing a very different job; but it's ultimately about convincing them that what we have is worthwhile."

At Birmingham, Weems is part of what he calls a 'translational' team that brings together chemists and clinicians working in very specific areas. It's taught him that, "any medical device manufacturer that's going for a novel approach needs to find clinicians who are just as eager to try new therapies for their patients and find new ways to involve new techniques." We can print change, and maybe even hype, but understanding is harder to come by. ●

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# Take the tube to the next level

**New England Tubing Technologies**' eTubing technology is designed to meet the demands of medical device OEMs by combining conductors with electrical requirements into the walls of tubing to increase design functionally, and reduce device footprint and assembly time.

The tubing market is certainly growing, with continued development being undertaken to improve all types of medical procedures – from neurology, to cardiovascular, to medical robotics. Advances in technology and science are opening doors to new procedures that were not possible in the past and also highlighting improvements that can be made on existing procedures.

Minimally invasive surgery has become the preferred choice for scores of surgical procedures. It is used in bariatric (gastric bypass) surgery, hernia repair, urological treatments, colon resection, gallbladder and tumour removal, and is favoured as the preferred treatment for many gynaecological, pulmonary and cardiac conditions. Many of these surgeries can be done with incisions of no more than a few millimetres.

Minimally invasive surgery reduces blood loss, shortens recovery time and reduces in-patient time at the hospital. It also reduces the risk of infection, and gives the patient less scarring and pain, which, in turn, reduces the need for pain and antibiotic medications.

OEMs are looking for more performance out of their tubing. They are pushing performance targets on new devices as well as next-gen redesigns. Smaller tubing and thinner walls are being pushed to make procedures less and less invasive. When possible, customers are looking for more performance out of their tubing, whether it is physical characteristics, materials or maybe even including an electrical element within the tubing.

Every form of minimally invasive surgery uses some kind of tubing that is inserted into the patient's body. Tubing can deliver stents, as in balloon angioplasty; they may provide a camera, illumination and tools to manipulate the patient's internal anatomy, as in an ablation or resection; the very design of tubing is what makes minimally invasive surgery possible.

## Less is more

OEMs are always pushing the envelope when it comes to designs and requirements. New England Tubing Technologies are tasked with meeting these requirements or providing alternatives. Recently, the biggest challenge is getting less to do more. Everyone is looking for smaller tubes with thinner walls with the same or more functionality. A good example is the company's eTubing line. It is integrating the knowledge and capabilities of its parent company, New England Wire Technologies and New England Tubing, to combine conductors with electrical requirements into the walls of tubing. This increases functionally of the design, reduces device footprint and can also reduce assembly time.

New England Tubing Technologies can customise a tube with added elements, such as ultra-miniature coaxial cables, high-frequency cables, thermocouples and high-strength/high-flex alloys to provide more functionality in the same tubular cross-section – critical for today's minimally invasive surgeries. The eTubing designs can add analogue and digital transmission of electrical signals for sensor capabilities, powering devices and temperature/oxygen monitoring features by incorporating these customised wires or cables within the wall of the tube itself. Typical elements for eTubing include:

- power supply
- measuring/monitoring capabilities
- signal carrying capabilities
- strength members
- one or more lumen.

The benefits are more functionality in the same cross-section and a return signal wire, among others.

Etubing can be used for a wide range of applications, including handheld electrosurgical devices, cauterisation, ultrasonic devices, monitoring devices, borescopes/endoscopes, power supply and cooling combinations. ●

The eTubing designs can combine conductors with electrical requirements into the walls of the tubing.

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# Sweat the small stuff

An interdisciplinary team of scientists at the University of Massachusetts Amherst has produced a new class of sustainable electronic materials, which may lead to a greener future in biomedical and environmental sensing. **Alexander Smith**, a biomedical engineering PhD student and the founder of the start-up e-Biologics, speaks to Abi Millar about the value of these materials for medical devices.

In 1987, the microbiologist Derek Lovley made a surprising discovery. While digging through the mud of the Potomac River in Washington DC, he encountered a strain of bacteria with properties that had never been seen before.

The bacteria, which he christened *Geobacter metallireducens*, were able to survive without oxygen or sunlight thanks to their unusual dietary habits. They 'eat' and 'breathe' metals such as iron, feeding on waste compounds and passing their energy onto metal oxides outside the cell.

It didn't take Lovley long to realise the implications: since these bacteria 'eat' organic compounds, they could potentially be used to clean toxic waste. By the early 2000s, Lovley had found 70 types of *Geobacter*, which were variously used to decontaminate an oil spill and a uranium mine.

The possibilities, however, didn't end there. When a *Geobacter* bacterium 'breathes', it excretes electrons, passing them down tiny wires that protrude from its surface. These wires – dubbed 'microbial protein nanowires' – make the bacteria a natural electricity source.

"The bacteria produce these protein nanowires as part of their metabolism and also to communicate with their neighbours," explains Alexander Smith, a biomedical engineering PhD student at the University of Massachusetts (UMass) Amherst, who works with Lovley. "Because of that, these microbial filaments are electrically conductive, and that's a pretty interesting property – they're basically like a biologically made electronic material. You can fit thousands of these protein nanowires in the width of one human hair."

Over the decades since *Geobacter* were discovered, research in the field has advanced rapidly. Most recently, Lovley's team has found a way to combine the protein nanowires with a non-conductive polymer, producing a flexible electronic composite material. The material in question, which can function even under harsh conditions, is suitable for manufacturing sensors and electronic devices.

Once limited to small quantities of protein nanowires (those that were produced naturally), the researchers are now working on scaling up production, generating the nanowires in commercially useful quantities.

"We can genetically modify the bacteria to produce even more of these protein nanowires in abundance. We're then able to purify the protein nanowires and discard the rest of the cell, so that we can use the nanowires to make materials," explains Smith.

They have made the jump from microbiology to engineering, from mud to material science. This could open the door to all kinds of commercial applications.

"In the past, Derek's research has been about characterising these microbes and studying their properties," says Smith. "He was also involved in projects where they were using the microbes for different applications such as bioremediation and fuel cells. But it wasn't until recently that we discovered how these protein filaments could be purified from the bacteria and used as a material. All of a sudden we have the opportunity to produce a biologically made material that can be used to make devices for different applications."

## Green electricity

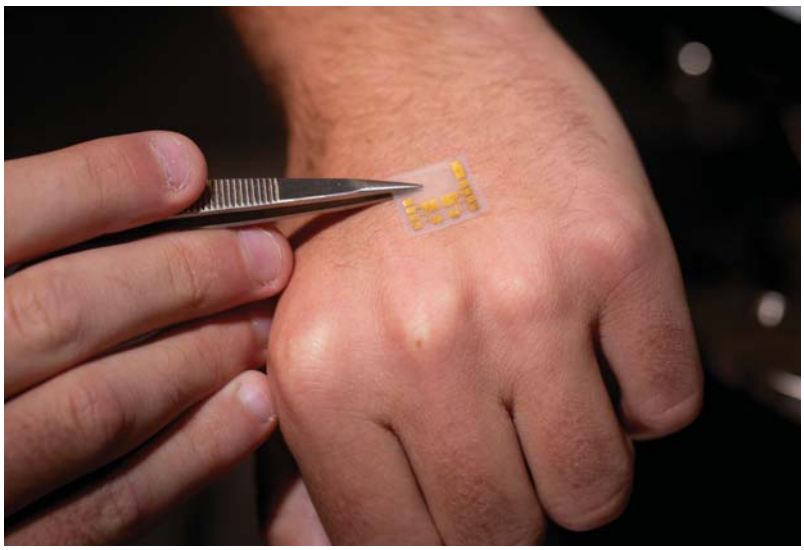
The advantages are obvious. Not only are these protein nanowires electrically conductive and super-sensitive – easily rivalling human-made materials such as carbon nanotubes or silicon nanowires – but they're highly sustainable to produce.

In fact, protein nanowires could spell the beginning of a truly green field of electronics, free from the toxic components that make electronic waste such a concern. While today's electronic devices are predominantly considered disposable, they are non-biodegradable and difficult to recycle. With the dawn of electronic biologics, this could be about to change.

"The process to make carbon nanotubes and other traditional materials is pretty nasty, requiring toxic chemicals and reactions," says Smith. "By contrast, these protein nanowires are produced by the *Geobacter* naturally – all we have to do is feed the bacteria with renewable feedstocks. So we have this sustainable and inexpensive way to produce the protein nanowires even at scale, eliminating a lot of the toxic chemical production that's used with current technology."

Another benefit of the nanowires is their versatility. Through tweaking the *Geobacter*, it is possible to produce different types of nanowires suitable for different forms of biomedical and environmental sensing.

"Since it's a biologically made protein, we can genetically modify different strains of protein nanowires so they are sensitive to very specific analytes," says Smith. "One of the biggest challenges in sensors nowadays is making them really selective, so that's a challenge we can conquer with our protein nanowires, by functionalising them with highly selective molecules."



**e-Biologics is developing a skin sensor patch, which can be used to detect the early signs of diabetic ketoacidosis.**

Solving this challenge has been Smith's key focus during his PhD career. An enterprising and commercially minded young researcher, he had read about Lovley's work in the field, and quickly caught wind of the possibilities.

"I was on a mission to look for technologies at the UMass Amherst campus that could be viable products," he says. "I came across Dr Lovley's patent for biological microbial protein nanowires, and as I was reading about them I decided I needed to talk to this man more. So I sent him an email out of the blue, and he agreed to meet with me the next day. As he was telling me about them I just became more and more fascinated and saw the potential. I said, wow, we need to commercialise these, they're so cool. Derek said that one of the big challenges, though, is finding the right application and the right businessperson to translate the research. So I rounded up some business mentors and we formed a team."

*"The process to make carbon nanotubes and other traditional materials is pretty nasty, requiring toxic chemicals and reactions. By contrast, these protein nanowires are produced by the Geobacter naturally – all we have to do is feed the bacteria with renewable feedstocks."*

The result was e-Biologics, a start-up dedicated to commercialising the protein nanowires. Five months after Smith's meeting with Lovley, his fledgling company won first prize in the UMass Amherst 2018 Innovation Challenge, going home with $30,000 in funding.

That summer, he participated in the Berthiaume Centre Summer Accelerator, which provided further funding and gave him a crash course in launching ventures. The company is

Alexander Smith

now moving towards making device prototypes and applying for patents.

"My PhD research is focused on developing the technology for the protein nanowire devices, and then my activities with the start-up company will be taking the technology that I'm developing and putting it to use for practical applications," explains Smith.

To begin with, the e-Biologics team is focusing on a single biomedical application, which Smith describes as the original vision for their minimum viable product – something that will pave the way for more complex biomedical sensors. It is a skin sensor patch, worn like an Elastoplast, which can be used to detect the early signs of diabetic ketoacidosis

Protein nanowires can be stabilised in water, which makes them ideal for detecting metabolites in sweat. They are particularly good at gauging acidity, with their conductivity changing in response to changes in pH.

"With the help of my business mentors, I came up with the concept of a wearable device that would analyse your sweat continuously and non-invasively to measure biomarkers that can indicate the early onset of diseases," says Smith. "Sure enough, there's a condition called diabetic ketoacidosis, which particularly affects people with type 1 diabetes and is indicated by changes in pH."

The device will be linked to a smartphone app that alerts the wearer to the possible onset of ketoacidosis. It will be marketed to high-risk patients with type 1 diabetes, and could ultimately prevent many hospital bills and trips to the emergency room.

*"With the help of my business mentors, I came up with the concept of a wearable device that would analyse your sweat continuously and non-invasively to measure biomarkers that can indicate the early onset of diseases."*

This, however, is only the beginning. As Smith explains, the protein nanowires constitute a kind of platform technology that could be used for all kinds of purposes in the future.

"While these protein nanowires are responsive to pH initially, we can genetically tune them so they can respond to other analytes as well," he says. "The vision is that we could measure many analytes simultaneously in a very small space."

They would look not just at sweat, but also at other biological fluids such as urine, saliva and breath. This could provide an assessment of many diseases, such as Parkinson's disease, Alzheimer's disease and cancers.

"Because the sensor is so small and biocompatible, our vision is that it could be placed pretty much anywhere in or on the body with a very small footprint, and would be able to measure many analytes simultaneously, providing a comprehensives assessment of a patient's health," says Smith. "Not just diseases, but applications like nutrition and fitness tracking as well. Providing personalised monitoring of a person's health in real time is very exciting."

## Industrial use

Since the nanowires can also be used as gas sensors, there are potential industrial uses in the works too. In these cases, the sensor would be integrated into something like a microchip, which could be used for gas sensing within chemical processing. This in itself could have implications for human health.

"During production of industrial materials such as fertiliser, if toxic gases are produced and people inhale them that can make them sick," says Smith. "So we can make sensors that detect the presence of dangerous gases to prevent health problems from occurring."

While e-Biologics is still in its early stages, the future certainly looks promising. The next step, says Smith, will be to rent a space in the University Of Massachusetts Institute for Applied Life Sciences, where the company will set up shop and continue to produce the technology. He is also looking to apply for further sources of funding, such as non-dilutive government grants.

Over the next few years, the team hopes to move on to testing their sensing devices with animals and eventually humans. Eventually, they want to move beyond their prototypes into a whole host of applications.

For Smith, putting these protein nanowires to good use is "a goal not just for the start-up but also for my life". And for his mentor, Lovley, who has spent over three decades focusing on the *Geobacter* bacteria, the latest developments are no less exciting.

"Derek has studied these protein nanowires for their interesting microbiological properties, but he's thrilled to see them used in an actual application that is clinically relevant and can help people," says Smith. "He loves the interdisciplinary nature of the project, combining microbiologists with engineers and businesspeople – it's this whole new start-up environment that has been super productive for research and for translating the research. At one point he told me, 'I never imagined that these applications could arise when I was studying *Geobacter* rolling around in the mud.' And now it's got the potential to save people's lives."

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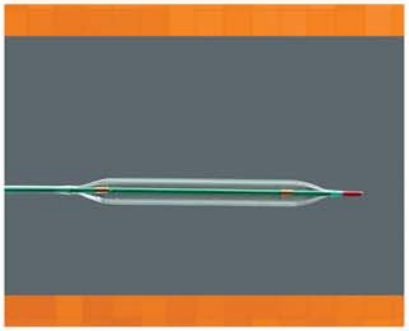

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# The right design choices have lasting implications

As an authorised distribution partner for TE Connectivity medical tubing, ODU medical connectors, and AlphaWire medical wire and cable, **Lapp Tannehill** partners with medical device and equipment development and manufacturing companies to help them make the right design decisions.

In today's medical market, front-end decisions that designers make can have a lasting impact on manufacturability, patient and practitioner satisfaction, and time to market.

Lapp Tannehill works alongside a range of manufacturing companies developing many different devices.

## Designing for manufacturability of interventional devices

Selecting the right process aids while designing for manufacturability (DFM) of interventional devices such as stents can have a significant impact on manufacturing time and costs. Use of traditional FEP medical tubing process aids may cause difficulties and inefficiencies that are easily avoided with strategic design and concurrent engineering. The use of flexible polyolefin-based solutions, such as TE Connectivity's MT-LWA medical tubing, can realise processing efficiencies with an easy-to-peel (without the use of blades), no-need-to-skive design, or eliminating adhesives and mastics in joining operations.

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## The right medical electrical connectors for signal and power transmission

Choosing the right medical connector for patient monitoring and diagnostic equipment often requires easy, ergonomic electrical connections over many mating cycles. Additionally, requirements for a 'break-away' function for emergency release can also be essential in critical situations.

Medical connectors such as the ODU MEDI-SNAP Break-Away connector provide effortless, ergonomic connection, while also featuring 'snap locks' that can unmate the connector with one pull of a specified force on the cable. An over-moulded plastic, plug-and-play design shortens development time, and reduces cost and weight.

## Fit-for-purpose wire and cable

As medical equipment technology becomes ever more capable, intelligent and complex, the need for space-saving solutions to wire routing and harnessing challenges becomes more pronounced. The AlphaWire ECOGEN and MicroCoax series of medical-equipment-focused wire and cable are ready to meet the miniaturisation, space-efficiency and weight-savings demands of the industry, while providing the requisite signal integrity and physical robustness that has always been essential.

AlphaWire EcoCable and EcoFlex control cables in flexible and shielded/unshielded configurations are up to 47% smaller and 65% lighter than traditional PVC jacketed cable, while EcoWire hook-up wire provides similar benefits for internal wiring of equipment.

The AlphaWire Micro Coax series of coaxial cables are available down to a smaller 50 AWG size with outstanding dielectric properties for the low capacitance and consistent impedance required for coaxial applications, such as medical probes, endoscopy, oximetry systems and more.

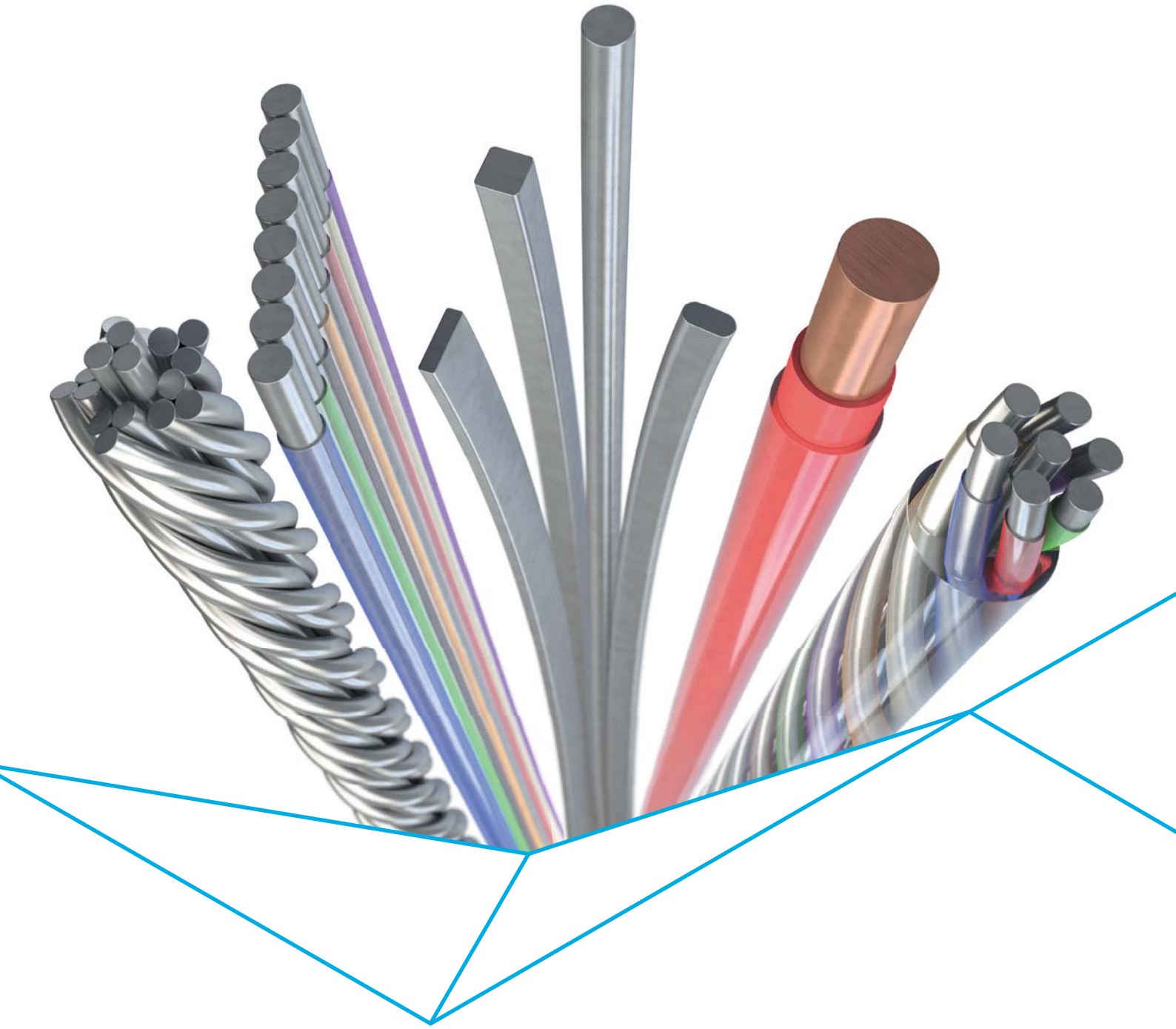
## Finding the right partnerships

Successful medical device and equipment design goes beyond achieving design targets and selecting the right componentry. The right partnerships can go a long way in ensuring that a successful design translates into equal success for patients, practitioners, regulatory processes, organisational goals and business financial goals.

Lapp Tannehill has been partnering with medical device and equipment development and manufacturing companies for several decades. As an authorised distribution partner for TE Connectivity medical tubing, ODU medical connectors and AlphaWire medical wire and cable, it are able to assist in early stage design selection, while also ensuring an optimised manufacturing and supply chain. ●

**For further information**

www.lapptannehill.com/medical



# DESIGNING MEDICAL DEVICES? LET US INSPIRE YOU!

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# Medical devices – it all comes down to the wire

Ultra-fine medical wire is an essential component in many medical devices. Gary Davies, production unit manager at **Sandvik**, talks about the company's collaborative approach to designing EXERA wire, and how this leads to highly specialised products that increase the efficiency of automation processes.

It's no secret that medical devices are developing at a rapid rate. Increasingly, smaller, more intricate solutions are required to reduce the invasive nature of surgical and diagnostic procedures, minimising patient trauma and limiting recovery time. As well as demanding high-quality products, developers are frequently looking for unique materials to solve design-related problems. As demand grows, manufacturers are partnering with specialists to help automate their methods of production.

Sandvik, a manufacturer of ultra-fine precision medical wire, is satiating this demand, working with manufacturers to develop high-tech medical devices.

According to Gary Davies, production unit manager at Sandvik, the high quality of EXERA wire, which is made with diamond dies by experienced craftspeople, is the result of a rigorous development process. "We follow strict internal qualification and validation guidelines in order to fine-tune processes to meet our customers' high-precision requirements," he says.

EXERA wire can be used in cochlear implants, in lead wires; vascular therapy, in guide wires and pacing leads; for monitoring thermal and glucose levels; and for neurostimulation.

## Unique designs

Fulfilling these demands often involves altering certain products to unique design preferences. "One thing we do, aside from the manufacturing, is tweaking certain products to suit the needs of our clients – whether we are coiling the wire, stranding it, cutting it to a particular length or stripping the ends. It's about making things easier for developers," Davies says.

Partnership with medical device manufacturers has led to the development of ultra-flexible leads capable of stimulating multiple nerves with the same transmitter, as well as composite wire configurations that combine steerable strength members with highly conductive signal-transmission materials. EXERA wire is available in a wide range of surface treatments. Single-wire configurations can be electroplated with custom thicknesses of gold or nickel and layered in polymer, PTFE and multilayer coatings. Customised multi-filar arrangements and cabled wire are also available.

*"One thing we do, aside from the manufacturing, is tweaking certain products to suit the needs of our clients – whether we are coiling the wire, stranding it, cutting it to a particular length or stripping the ends. It's about making things easier for developers."*

Sandvik's wide variety of alloys, forms, thicknesses, arrangements and coatings provides developers with a range of options. The configuration and materials used in EXERA wire allows device manufacturers to automate production methods more efficiently.

"Many of our customers are embracing automation. So they're looking for solutions that can add value to their products. We work with companies to solve those design-related problems, whether that involves using a specific type of material, not only on the alloy side, but also the coating side," explains Davies.

A creative and collaborative approach is the key to achieving these efficient, polished products.

"We're not afraid to try new alloys or new coatings to meet the requirements that developers have, whether that involves doing some preliminary lab-scale melting of alloys or trying out different coatings. It's always rewarding going down the development path with our customers," Davies says.

In its quest to help medical device manufacturers refine and develop new processes and products, Sandvik is at the cutting edge of health technology. It is also a company willing to help developers of all shapes and sizes.

"We're willing to work with anyone," says Davies. "Not just large corporations, but smaller innovators, to support them and help make their new idea a reality."

For Davies, it is motivating to know that such devices are improving people's lives in subtle and drastic ways.

"We've had end users come into the factory and shared their story about a certain implant that has made their life easier, and it really hits home. It's great to know that you're helping people," he says. ●

**For further information**

https://exera.sandvik


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# Catheter safety and performance with tie layer

Headquartered in Orangeburg, South Carolina, US, **Zeus** is the leading extruder of performance polymers, serving multiple industries with a long-standing and reputable presence in the medical sector.

As engineers and medical professionals continue probing for improved products to boost patient care, they face the daunting challenge of getting new concepts to manufacturing reality. Often, the ideas are there to tackle a specific problem or issue but not the manufacturing know-how.

For Zeus, meeting such challenges is its strength. One of the company's guiding principles is to innovate and lead with new products and designs to address application needs just like these.

## Performance catheter components

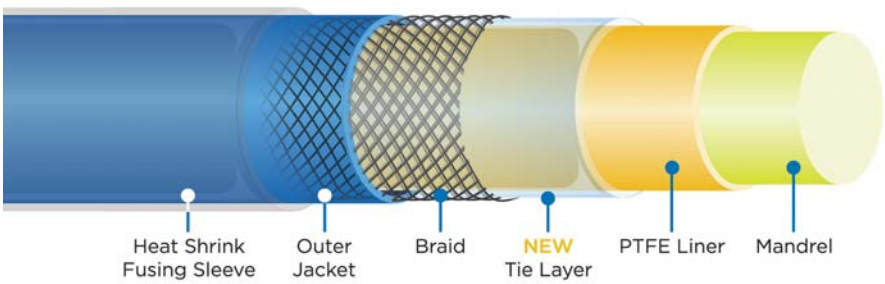
A core element of Zeus performance extrusions for the medical industry is its components for catheter construction. FluoroPEELZ peelable fusing sleeve vastly improved the removal process after the reflow step of catheter construction. LCP monofilament is an MRI-compatible non-metal braiding material and Zeus's polytetrafluoroethylene (PTFE) base liners are the thinnest available for use as a free extrusion.

Now, adding to these is Zeus's new tie layer – a thin polymeric coating applied to the etched OD of the PTFE liner designed to reduce delamination and improve mechanical attributes of the finished catheter shaft.

## Catheter tie layer – continuing innovation

This new tie layer represents a significant step forward for catheter construction. The tie layer is applied as a coating to an etched PTFE extruded liner – a process unique to Zeus. Applied in this way, the tie layer promotes more uniform adhesion of the reflowed jacket to the etched PTFE liner.

Secondarily, the tie layer will typically be of a similar or same material as the jacket, creating a like-for-like bond during jacket reflow. With the tie layer bonded to the liner during the coating process, the summary effect of the tie layer is to increase the liner-to-jacket bond strength. Preliminary testing has shown that the tie layer increases liner-to-jacket bond strength up to two-and-a-half times compared with catheters made without it. Depending on the material and durometer chosen, the tie layer has been shown to improve catheter performance, deliverability and increased column strength.




The increased layer bond strength of catheters made with the tie layer helps to address the serious safety concern that come with delamination.

The tie layer's most important advantage is safety. The increased layer bond strength of catheters made with the tie layer addresses the serious safety concern of delamination – the separation of layers within the catheter. Aside from delamination defects discovered during final inspection – the most costly yield loss and a major contributor to raising production costs – it carries high liability of delamination problems occurring in a clinical environment. There, delamination failures have direct repercussions for patient safety. The increased bond strength from the tie layer also supports a more mechanically consistent device with more reliable performance characteristics.

These attributes lead to more efficient catheterisation procedures and lower risk to patients.

## Tie layer – versatility and safety

The tie layer is versatile and suitable for a variety of applications, and can be produced in a variety of durometers. While currently offered in a variety of materials, including Pebax, nylons and polyurethanes, Zeus will also continue to make tie layers available in other materials.

In keeping with its history of leading the way, Zeus has identified a tie layer to be an ideal solution for those catheter manufacturers wanting to secure a PTFE liner to the ID of a metallic tube, such as a laser-cut hypotube. This versatility afforded by the tie layer allows device designers and makers to precisely tailor the performance of their device to deliver life-saving therapies in some of the most tortuous vasculature.

With industry buzz words like 'continuous improvement', Zeus catheter componentry is advancing this industry. And, as exemplified by the tie layer, any improvement to manufacture, design or device implementation will undoubtedly result in improved patient safety. ●

*Pebax is a registered trademark of Arkema France.*

**For further information**

www.zeusinc.com

# Glass healing

Bouncing, bending and bonding to bone, glass is looking more and more like a miracle material. The liquid-like solid is showing its worth in everything from healing wounds to replacing intervertebral discs. Tim Gunn talks to **Professor Julian Jones** of Imperial College London and **Professor Aldo Boccaccini** from the University of Erlangen-Nuremberg about the properties of bioactive glass that make it so valuable for medical devices.

"Hamburger. Hot dog. Ice cream," whispered Professor Gerry Merwin, the very hungry ENT surgeon who had just implanted the world's first Bioglass device into another human being.

"Hamburger! Hot dog! Ice cream!" repeated his joyous patient. She could hear again. The glass prosthesis in her middle ear was conducting sound waves, just as the tiny bones she had lost to infection once did. She would not be deaf to her second child's first cries, nor the voice confirming her order at the drive-through. What would you do as the local anaesthetic wore off in a Florida hospital in 1984, your hearing restored by the unprecedented ministrations of a lunch-deprived man, but cry hamburger, hot dog and ice cream?

It was with that calorific mantra that a human-made material, Bioglass 45S5, first began to bond with living tissues inside a human body. On the surface of the device, a rapid series of chemical reactions were forming hydroxyl carbonated apatite (HCA), which, due to its similarity to bone mineral – hydroxyapatite (HA) – is able to interact and integrate with living tissue. The cells in the stapes and ear drum were using it as the basis for the new bioactive bonds that would hold the prosthesis in

place as securely as bone itself. Unlike the bioinert alternatives, this implant would neither slip nor be pushed out of place, thus protecting the young mother's ears from further damage.

It had been 15 years since materials scientist and children's author Professor Larry Hench discovered Bioglass, but even after he watched over the success of its first in-human trials, he could hardly claim that he fully understood its potential. In fact, over the next few years, Hench and his research team began to realise that, more than simply bonding to living tissue, the material was capable of regenerating it. This too was attributed to the formation of HCA on the surface of implants in the body, although that didn't explain why synthetic HA was comparatively ineffective. Whereas HA supported new bone growth at the bone-implant interface, 45S5 also did so within the implant itself.

## Second life

It was not until the early 2000s that Hench and his new research partner, pathologist and tissue engineer Professor Dame Julia Polak, developed a clearer idea of what was going on. The most pronounced healing effects of bioactive glass are caused by the release of ionic dissolution products as the material reacts with the body. In particular, as 45S5 glass degrades it releases sodium ions, calcium ions and soluble silica, a process that stimulates osteoprogenitor cells and facilitates the production of new bone. This realisation marked the beginning of what Professor Aldo Boccaccini calls the "second life" of bioactive glass. "The gene expression of bone cells was being activated by the ions released from the glass," he explains. "They were moulding the formation of new bone tissue by acting directly on the cells."

Shortly after, Boccaccini's own team demonstrated that ions released from bioactive glass devices could also promote angiogenesis in soft tissue. As was clarified later, calcium ions assist in the migration and proliferation of epidermal cells and accelerate blood-clotting, while silicon ions advance neovascularisation and stimulate the formation of collagen. For Boccaccini and others, it was becoming clear that, "If we control particular aspects of the chemical composition and the kinetics of releasing ions, these glasses can communicate with different cells and provide different biological responses."

Indeed, bioactive glasses are now found in toothpastes and cosmetics, as well as orthopaedic particulates and wound-healing systems. Until recently, however, such materials had not overcome their primary limitation. Bioactive glass is still glass, and glass is far too brittle for many functions required by the human body.

## Injury luck

"That was an accident," laughs Professor Julian Jones, in an offhand reference to the time he made a glass that could heal itself. The team Jones leads at Imperial College London was trying to engineer a bioactive material capable of taking cyclic loads. He was messing about with one of their latest 3D-printed test cylinders. Unlike melt-derived glasses, it had been formed through the sol-gel method, a chemical process whereby solid ceramics and metals are grown from small molecules, and printed before they have fully solidified. "I was squeezing it going, 'It's almost there, I think that's almost what we're looking for,'" Jones recalls. "It was just a bit stiff, and by squeezing it I cracked it across the diameter."

As far as Jones was concerned, that crack showed why 'almost there' wasn't good enough. Insufficiently intrigued by the fact that the chunk had not just exploded, he put it down and turned to his fellow researchers to discuss how to improve on the design. The sol-gel method made it possible for the team to mix biodegradable polymers into bioactive glass on the molecular level by growing them together through a series of chemical reactions. Unlike a composite, the resulting hybrid would act as one material. The team just had to get the mixture right and their bioactive glass would be able to take the cyclic loads the human body exerts on its constituent parts. After 20 minutes of brainstorming, Jones picked up his stress-tested glass again. "I checked all the others to make sure I hadn't mistaken the one I put down, but I hadn't. The crack was gone."

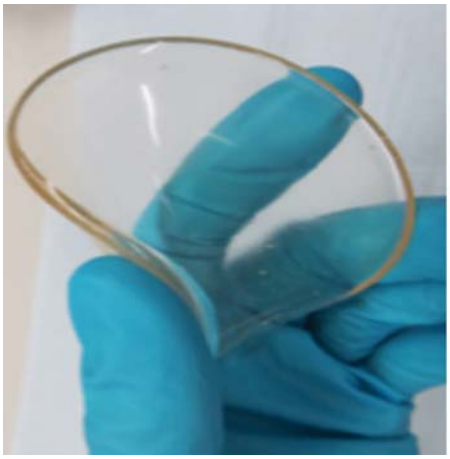
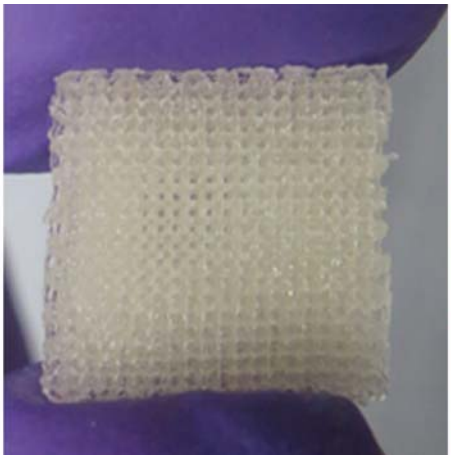
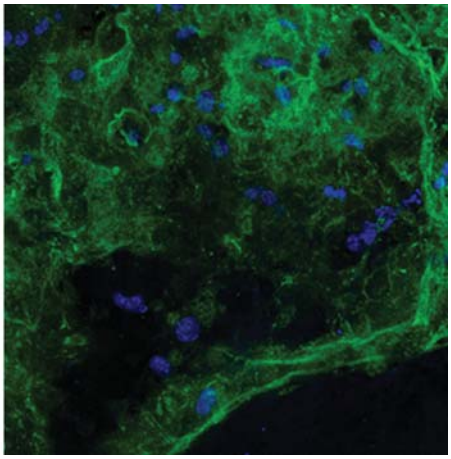
**15**

The gap, in years, between the discovery of Bioglass and its first in-human trials.

*"What people want and really need is regeneration of cartilage lost due to arthritis. If we can develop better ways of detecting the onset of arthritis, then these sorts of technologies may translate to that once we've proved them in sports."*

**Professor Julian Jones**

The accident of creating a self-healing implant material was one of a few strokes of luck in the story of bioactive glass. Incredibly, Hench chose the optimal chemical composition for his Bioglass on the first try. Jones and his team's attempts to develop the best possible bioactive bone implants also resulted in a glass hybrid that could bounce and bend – a perfect fit for repairing cartilage, which is even more difficult than regrowing bone. At present, sports injuries like a torn meniscus can take months to heal. Regenerating the cartilage

**Bouncy bioglass is flexible (left) and can be 3D printed into scaffolds (centre). When the scaffolds have a certain pore size they stimulate cartilage cells to produce a high-quality articular cartilage matrix (right) unlike any other existing device.**

requires surgeons to dig into the surrounding bone to release stem cells, but these can only produce a dense and fibrous form of scar-like tissue, which lacks elasticity and quickly wears out. By contrast, when Jones's bouncy scaffolds are printed in the correct channel size, they can enhance and guide stem cells to produce the particular architecture of joint cartilage, which grows through microscopic holes in the glass as it biodegrades.

"If you're repairing bone, you need big channels that bone and blood vessels can grow into," explains Jones. "For cartilage you don't need any of that; what you want are channels small enough for individual cartilage cells to communicate with each other."

Furthermore, the material's ability to bond with tissue and take cyclic loads means that patients could return to pre-injury activity levels within a few days of receiving the implant. That would be a boon for sportspeople in the short and long term, minimising recovery time while ensuring that the damaged tissue regenerates to meet the demands of continued stress and activity.

Sports injuries are a relatively limited application, but non-biodegradable variants of the 'bouncy' bioactive glass scaffolds could also be used to replace intervertebral discs. "Obviously," admits Jones, "what people want and really need is regeneration of cartilage lost due to arthritis. If we can develop better ways of detecting the onset of arthritis, then these sorts of technologies may translate to that once we've proved them in sports."

## Never can say goodbye

Jones and Boccaccini began their work on bioactive glasses with Hench in the late 1990s and early 2000s. "He used to say, 'Oh, I will retire in three or four years, so you can take over some of my research,'" recalls the more Argentinian of the pair. "But 10 years later, he was still there." Today, only Jones remains at Imperial, but both material scientists have defined and been defined by the second lives of bioactive glass.

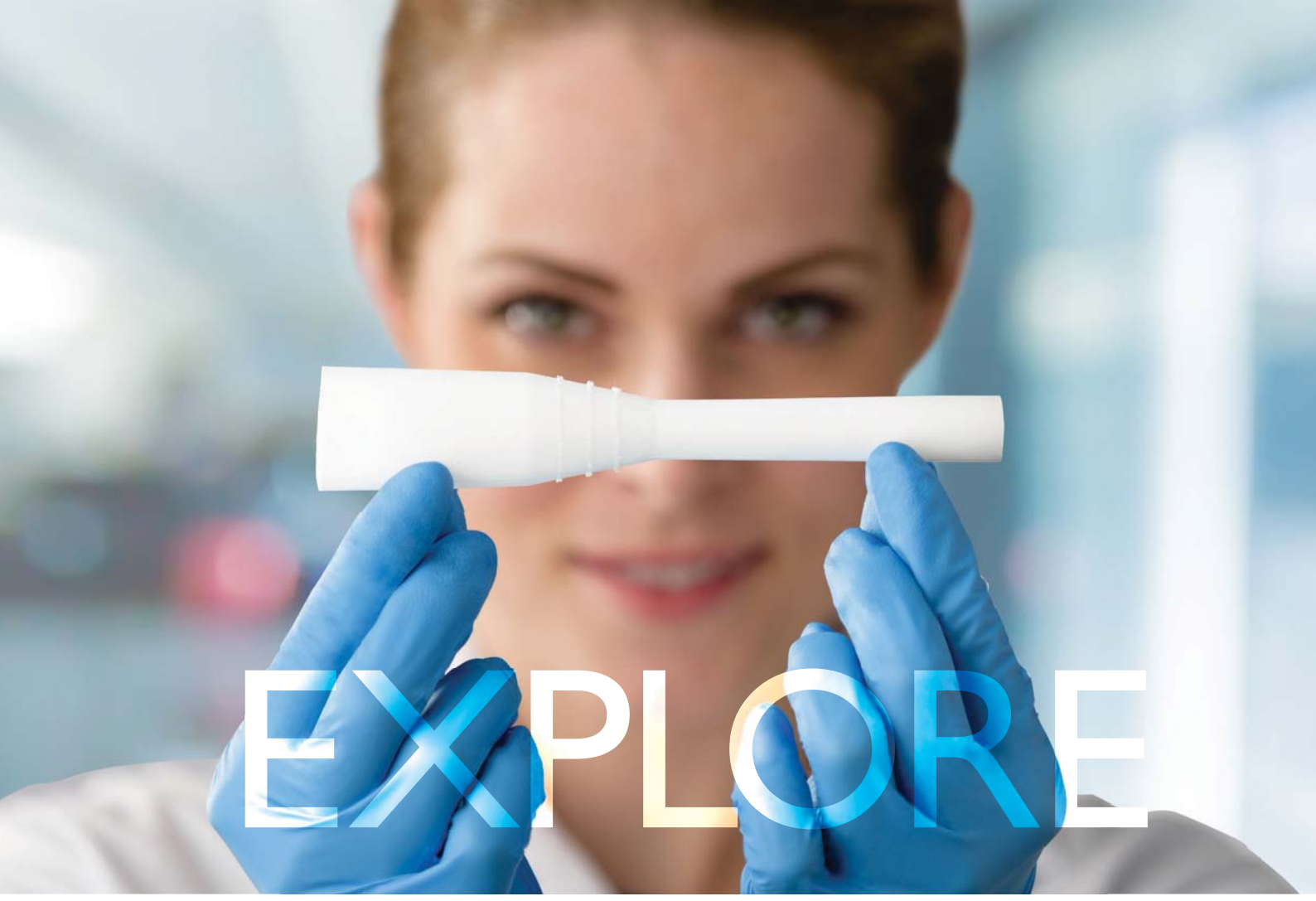
As Boccaccini explains, the discovery of the effect of bioactive glass ion products on vascularisation made the material applicable across the whole human body. Cartilage is a notable exception, which is why it is so difficult to regenerate, but most of the body is vascularised. "The blood is everywhere, so you are not necessarily bound to use glass simply for bone repair," he says.

To take one example, nickel and cobalt ions can be added to bioactive glasses to mimic hypoxia and aid wound healing. "In simple terms, when the glass starts dissolving, those ions will absorb oxygen from the area of the wound," explains Boccaccini. "Low oxygen content triggers a number of mechanisms, recruiting endothelial cells to build blood vessels and attract oxygen via the bloodstream." Equally, bioactive glasses could be used for drug delivery devices that synergistically release therapeutic dissolution products alongside their drug payloads; or as a coating for wound dressings and other implants, where they can release antibacterial ions as required.

In fact, Jones believes ETS Healthcare's Mirragen bioactive glass wound dressings have the potential to take the chronic wound care industry by storm. "There isn't a good way to regenerate diabetic ulcers at the moment," he says, "and bioactive glass could be the next big thing." The product can heal wounds up to 40% faster than its direct competitors.

Boccaccini is similarly excited by Mirragen, but urges caution. "All these things are coming, but more research has to be done," he stresses. "There is still a gap in the data on the long-term effects of the release of ions and the degradation effects of bioactive glasses in realistic in vivo models. It's the obvious thing to do, but it's very expensive."

As Hench once wrote, "Being a pioneer and ahead of one's time is, on the whole, not desirable." Still, since his death at 77 in 2015, Jones, Boccaccini and others have been happy to take on that mantle. However long the next stage of development takes, it is quite a legacy.




# Device Design Possibilities with Biomedical Textiles

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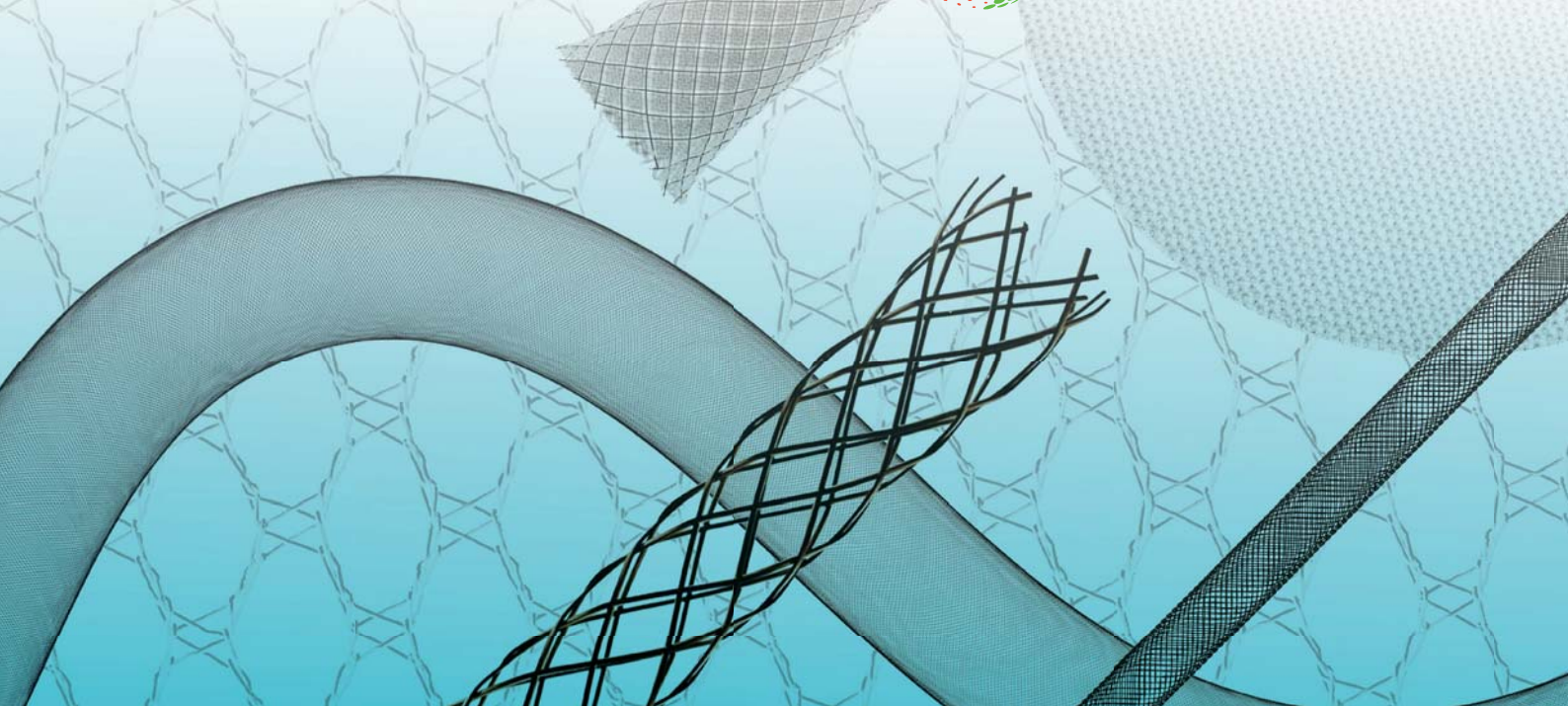


# Patented textile-forming technologies

**Secant Group** combines textile engineering expertise with speciality manufacturing technology to create high-performance biomedical structures to facilitate repair and recovery of the body.

Secant Group offers several market-leading capabilities, such as its patented Drop End technology. Tubular woven implants are manufactured with this technology, which drops warp ends circumferentially within the tapered region to maintain a consistent density around the entire construct.

In other technologies, the ends are dropped next to each other, rather than circumferentially, leading to regions with different porosity. The Secant method is superior for maintaining specific characteristics, such as porosity and flexibility along the length of the textile structure. Tubular woven fabrics may be used during surgery to repair or replace various damaged or diseased lumens within the human body; for example, in vascular surgery, in which a woven tubular prosthesis is used to repair a blood vessel.

Secant Group can use patented manufacturing capabilities to customise implantable devices.

*"Another patent granted to the Secant Group is for its supported lattice for cell cultivation technology. It saw a need to create a lattice for cultivating living cells to form living tissue, so surgical implants could act as grafts to heal damaged tissue and correct disorders."*

Another notable patent granted to the Secant Group is for its supported lattice for cell cultivation technology. Secant saw a need to create a lattice for cultivating living cells to form living tissue, so surgical implants could act as grafts to heal damaged tissue and correct various disorders. One example for this application is a tubular support lattice for a coronary bypass graft.

This tubular support substrate is comprised of resilient filamentary members interlaced together to form a coarse mesh and another plurality of flexible filamentary members braided together to form a fine mesh. The coarse and fine mesh filaments are then braided together with the resilient filamentary members to form the construct. The finer mesh built with flexible fibres creates small interstices that provide a bed adapted for growing living cells in a two-dimensional array across the cell cultivation lattice.

This creates a substantial continuous surface of living tissue that forms a tube usable as a graft for a coronary bypass operation.

## Woven tubular grafts

Woven tubular grafts with regions of varying flexibility is another Secant Group patent. Woven grafts have numerous advantages, such as impermeability, low porosity and small bulk, which are important characteristics for several medical procedures, such as repairing a vascular aneurysm. However, a disadvantage with woven textiles is their lack of flexibility due to the warp and weft yarns interlacing at 90° angles, causing them to lock in place.

By tuning the flexibility within certain regions of a woven graft using elastic materials and tensioning techniques, Secant can provide areas with more radial expansion and others with less radial expansion. By weaving in radial flexibility, the graft can radially expand to match the diameter and shape of the artery. In regions where a set diameter is desired, and no radial expansion is wanted, Secant can apply greater tension on the weft, which inhibits the yarn from expanding any further. For example, the region adjacent to an aneurysm needs to maintain a set diameter so that the hydraulic pressure of the blood as it is pumped through the artery can relieve pressure on the aneurysm. The same techniques can be used when making straight or bifurcated tubular grafts.

Visit the Secant Group website via the address below to learn how it can use patented manufacturing capabilities to customise your next implantable device.

**For further information**

www.secant.com

# Make it stick

When choosing a motor, the need to balance multiple factors such as service life, cost, speed and temperature conditions, as well as the huge range of potential applications of the technology, can be a challenge. Emma Green speaks with **Thomas Mayer** from Sonceboz and **Carl Bugeja**, an embedded-software developer, about how to effectively navigate decisions about motors and the magnets that allow them to run.

At the heart of many pioneering medical devices are new designs of electric motor and motion-control systems. In pushing forward their design parameters, technology companies are continually seeking higher efficiency, more speed, and increased power from smaller, more robust and quieter equipment. It is therefore up to the designer and manufacturer to ensure that motors can meet these needs, regardless of the particular application and setting.

Central to motor technology, past and present, are magnets. The initial discovery of magnetism began with lodestones, which are very weak, naturally occurring magnets. Next came electromagnets, which are made of iron laminations with copper wire coils around them. Later, alnico and ferrite, also known as ceramic magnets, were incorporated. Since magnets were expensive and not particularly strong, motor designers tried to use iron to contain, direct and focus the magnetic flux within the motor.

Magnetic iron is relatively cheap as a bulk material. However, the machines needed to punch, stack, glue and grind these metal components are expensive. With the advent of more powerful magnets, it is now possible to make motors that don't incorporate iron into the switched magnetic circuit. A large diameter motor has more volume available for magnets and coils, which allows the designer to choose between

maximising torque or efficiency by reducing power density. This action allows the temperature to be more easily controlled, which is critical for a number of medical devices.

For Carl Bugeja, an embedded-software developer, the attraction of working with motors is the ability to use them for robotics. Although his work has not yet been applied in medical devices, it has huge potential for the industry.

After graduating from an electronics engineering degree from the University of Malta, he immediately began working on a drone start-up, co-founded with a fellow classmate, but soon ran into a challenge.

"We were trying to design a tennis-ball-size coaxial drone, but after some time we had to end the project because of funding issues," he recalls.

Despite this unfortunate outcome, Bugeja was not put off by the experience and instead was keen to build upon it going forward.

"I learned a lot, especially from going through the design process of trying to miniaturise every piece of electronics that goes into tiny drones," he says.

## Fit for purpose

Companies are also pushing boundaries in the motor technology space. One such organisation is Sonceboz (SBZ), which has a strong track-record in developing innovative electric motors and mechatronic drive solutions. For Thomas Mayer, sales and application manager in the MedTech department at SBZ – and a former Boston Scientific employee – getting to the heart of the issue is key when developing a motor.

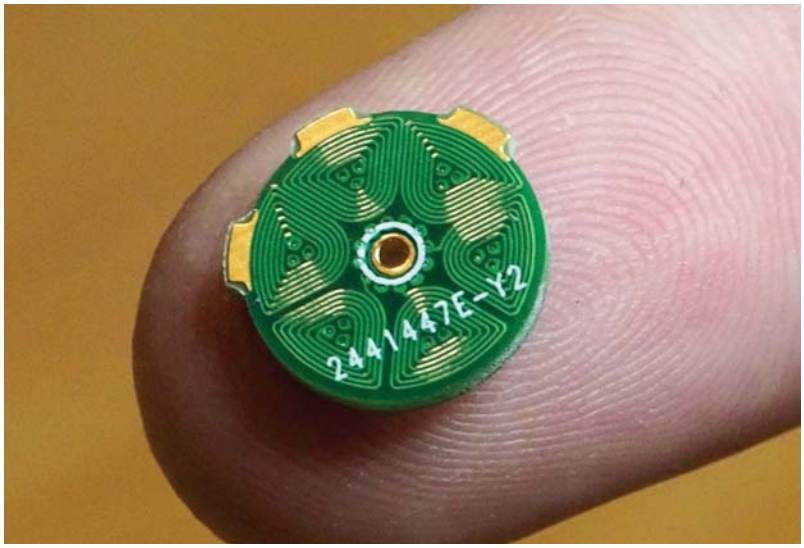
"When we are in a discussion with a particular customer, we ask what problem they have, where they want to use it and what is ruling out the selection of a standard motor," he explains. "We focus on solving complex problems that you can't fix with something off the shelf."

Although some of the important factors, such as efficiency, speed and power, remain consistent when working to optimise motor technology, there is certainly not a one-size fits all when it comes to using them for medical devices. The solution implemented could vary immensely depending on the application.

"A motor that is used in a ventilator for respiratory care is a different story than the kind of device you use in dialysis or a lung machine," acknowledges Mayer.

The MedTech department in SBZ caters to a wide range of medical device applications so Mayer is used to juggling shifting priorities depending on the context.

"In laboratory analysis equipment, you want to have precision, but also compactness and reproducibility so that you always get the same result with each motor," he explains. "In haemodialysis, the most important thing is to have a low-noise motor, and because you have it close to the patient, you want to keep the heat emission as low as possible and you also need the ability to control the revolutions of the motor."




**Bugeja has recently developed a PCB motor with an axial flux motor that uses PCB traces for electromagnetic coils.**

Unlike SBZ and most other medical device manufacturers, efficiency and power are not the primary goals of Bugeja's work.

"What I'm mostly interested in is designing motors that are cheap and easy to manufacture, which are still good enough to power tiny lightweight robots," he says.

*"Most healthcare systems and economies on a global scale are facing a challenge when it comes to cost-efficiency and those two factors combined lead to an increase in home-based care."*

## Printed circuit board traces

One of Bugeja's recent developments is a printed circuit board (PCB) motor with an axial flux motor that uses PCB traces for electromagnetic coils. Unlike conventional electric motors, which have copper wire windings, Bugeja's designs put those windings on the PCB itself as traces. This allows for inexpensive integration of low-torque electric motors into a device without having to add an electric motor to the bill of materials.

Oftentimes, motors used in medical devices were not originally intended for this application. However, developments in the technology tend to offer benefits to a number of sectors, including med-tech. This cross-pollination serves as a key driver of progress within and between industries. Bugeja's PCB motor, while not being developed specifically for medical devices, holds great promise in this area.

"This motor can be a simple solution for anything that requires low torque and high speed," Bugeja explains. ▶

### Carl Bugeja's axial flux motor

Bugeja developed an axial flux motor that uses printed circuit board (PCB) traces for electromagnetic coils, an idea he came up with while trying to design a new quadcopter. From his previous experience in designing drones, he knew that the size of the motors would define how small the robot could be. Bugeja tried to minimise this by integrating the motor's stator on the same PCB as the drone.

Although he was confident about using this approach on a large scale, he initially struggled with trying to miniaturise it to the same size as other micro brushless motors. However, he soon found a solution, by defining a maximum 16mm diameter limit and trying to fit as many windings as possible.

Despite the success of Bugeja's original motor design, he recently tried to make the PCB motor smaller still by adding two extra layers, which enabled him to reduce the number of turns per layer and get it to 11mm. The total height of the motor is 3.6mm and its weight is just 0.5g. Currently, Bugeja is doing further testing on his PCB motor and designing more porotypes in order to further improve the torque.

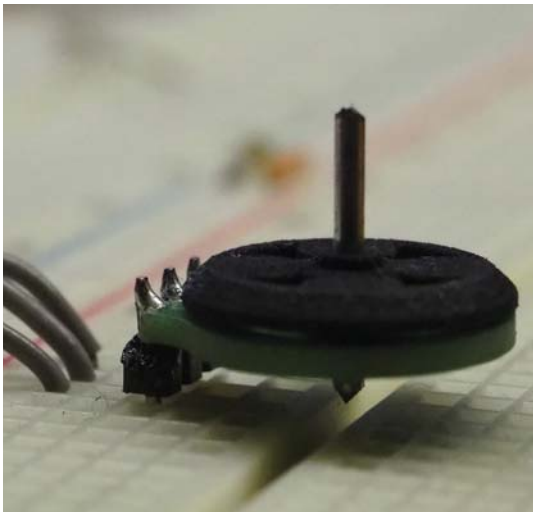
Similarly, SBZ is currently focused on modifying existing motors that have been used for an alternate purpose. "Right now we are working on adapting automotive technology to be able to use in a wearable tracker device," Mayer explains.

Although this technology is a highly promising area of development, the work at SBZ has not been without its difficulties.

"We had to modify the overall geometry somewhat and then also find ways of controlling the motor to squeeze out as much torque and power, while maintaining a high level of efficiency," Mayer says.

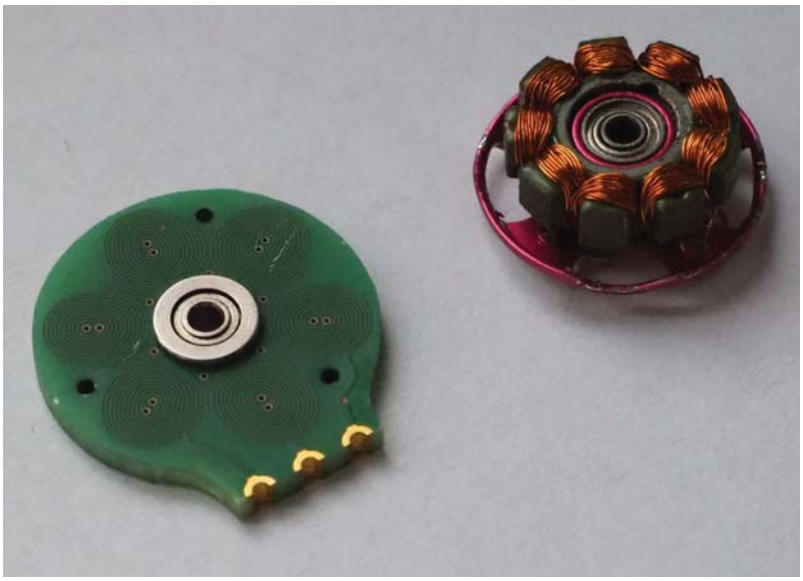
## The rise of home-based care

Another facilitator of innovation is the rise in patient-centric models of care, which has implications for a number of fields, including the pharmaceutical medical device industries. This approach aims to achieve a more precise picture of the disease by considering the specific circumstances of the patient. This information can then be used to design and administer an individualised treatment option that will produce better patient outcomes.



**Above: Bugeja's PCB motor in action.**

**Below: Unlike conventional electric motors, which have copper wire windings, Bugeja's designs put those windings on the PCB itself as traces.**



While the effect of this movement on medical devices may not be immediately obvious, it also entails a transformation of patient care from being based in hospitals and outpatient clinics to taking place within the home. In light of an ageing population, and the associated increase in chronic conditions, the application of the patient-centric approach is becoming more important than ever.

Mayer is acutely aware of the need to cater motors for devices that can be used outside of traditional care settings.

"Most healthcare systems and economies on a global scale are facing a challenge when it comes to cost-efficiency and those two factors combined lead to an increase in home-based care," Mayer explains. "Putting more responsibility into the patient's hand, taking medication in their home environment, is an area where we believe we can add value."

Constantly improving motor technology is a key part of achieving sustained success both inside and outside the med-tech industry. The inherent challenge in the refinement process is what keeps Bugeja engaged and excited. Clearly a creative thinker, he is currently exploring other ideas based on his PCB technology.

"I recently tried to put the same electromagnetic PCB coils on flexible PCBs," he explains. "I am now trying to integrate flexible PCB electromagnets into lightweight robots, to act as their legs and even fish fins."

For SBZ, staying in its lane and maximising efforts within that space are key strategies to ensure longevity in the field. Although excited about the technology, Mayer is keen to emphasise that motors are only one aspect of the work at SBZ.

"We are not trying to compete with other motor manufacturers," he says. "Our goal is to find a challenging application where we can add value by combining our motor technology with electronics and also gearboxes. I think that is an important part of our business success." ●

# Old spark, new ideas

Although the use of plasma treatments for medical device coatings has been around for some time, in recent years it is enjoying something of a renaissance. Andrew Tunnicliffe talks with **Professor Denis Dowling** about its potential and its limitations.

From the often magnificent lightning displays in the sky or the aurora borealis, to its use in car headlights and the televisions we watch, plasma is everywhere. Said to be the fourth state of matter – the first three being solids, liquids and gasses – it is an excited gas produced by adding energy to it, causing electrons to leave the atom. While natural plasma has been in existence for as long as time itself, it wasn't until the 1920s that American physicist Irving Langmuir first recorded and then researched its properties. He coined the name plasma to describe the ionised gas as it reminded him of a blood plasma. Since then it has been used for myriad applications, not least in industry.

For several years now the medical device sector has been increasingly turning to plasma to coat its products. In 2016, industry experts spoke of the growing use of plasma-enhanced chemical vapour deposition (PECVD) as a means of depositing coatings to protect products against corrosion and wear.

Today, plasma has become commonplace during the manufacturing of medical devices.

"Almost every medical device company looking at polymer processing will have a use for plasma," explains Professor Denis Dowling, director of the I-Form Advanced Manufacturing Research Centre at University College Dublin.

Plasma can be used to prepare surfaces prior to printing, for adhesive bonding, as well as for depositing metals and functional coatings – all of which have uses in applications ranging from the fabrication of medical device sensors, to enhancing cell attachment to metallic implants.

"There is a diverse range of either surface activation treatments, etching treatments, or functional coating treatments where the technology is applied," Dowling adds.

Although medical devices aren't the only products to require coatings – others include semiconductors, engine parts, and packaging, to name but a few – the challenge they pose is unique because of the nature of their use for clinical application. The ultimate aim is to increase hardness, gripping surface and resistance to wear; but with a coating that is biocompatible.

## Plasma spray coatings

In recent years medical device original equipment manufacturers (OEMs) have turned their attention to hydroxyapatite coatings deposited by plasma-spraying, particularly in the field of orthopaedic implants. This coating is vital as it has the same composition as bone; this means the metal implant knits with the bone, otherwise there is potential for loosening of the device. For plasma spray coatings to perform at their optimum, the surface and its preparation is essential, as Dowling explains.

"It comes down to the surface – tailoring the surface for what you want to achieve," he says. "For example, you can use plasma to put down a layer of diamond a few microns thick. However, if that layer goes on to a surface that is not particularly hard, effectively you won't get the form of layer that is a harder resistance because the structure underneath doesn't support it. It is like an egg; it has a hard shell, but it is soft underneath. So it provides some protection but it won't take any impact."

Therefore, Dowling says that when it comes to selecting the coating it is essential to understand how the material will perform and how the device is ultimately going to be used.

"You are tailoring the type of energy that you put in to the material properties, mechanical properties, thermo properties, of what you are applying it to and what you want to do," he explains.

Going back to his example of diamond, he says, the plasma used to deposit it could be a microwave discharge operating at 900°C. However, if you are using a polymer or a low melting-point metal such as aluminium, it will melt and decompose before you can apply the coating. For these substrates, you would have to select a different wear-resistant coating such as metal nitrides, which could be deposited at much lower temperatures.

"You select the deposition conditions that are appropriate for the substrate you are working with," Dowling says. "If you are dealing with polymers, generally you don't go over 50°C or 80°C to avoid any damage to the substrate, whereas if you select ceramics you can go to much higher temperatures."

This is why he uses the term 'surface engineering' a lot, but rightly so. Clearly the success of any coating is hugely dependant on understanding its compatibility with the material being used, and the ultimate application of the device.

## An unbreakable bond

One of the areas plasma coating has really changed is bonding, says Dowling. On his visits to device manufacturers' plants in Ireland, he has seen a shift towards the use of atmospheric plasmas for bonding.

"10 years ago there were very few, but now you see them routinely," he says. "Before, they [manufacturers] would have stopped the production line and put the devices into a chamber where they were bonded. Now plasma is in the process, making it continuous and meaning you can avoid that. Increasingly, as newer devices come through, the use of these plasma processes are built in, making it is so much quicker."

As Dowling eludes to, traditionally plasmas for use in manufacturing were applied using a vacuum process. The component was placed into a chamber, the pressure of the chamber was then reduced and gas was introduced to treat the surface by forming a discharge. Once complete, the chamber was repressurised. Today, for some plasma treatments there are atmospheric pressure alternatives thanks to technological developments in recent years.

Not only is this more cost effective, there are benefits for the environment, and health and safety.

"Polymers can be activated by dipping them into a solvent," says Dowling. "If you took a polymer and dipped it in an alcohol you have the effect of activating the surface and, as a result, you enhance its wettability. However, you then have the problem of these organic solvents evaporating off, with health and safety issues there, whereas plasmas are much cleaner and generally very well contained.

"They are also very fast; the process can range from seconds to minutes. So they are environmentally a lot cleaner and much more controllable than conventional chemical processing."

For medical devices, bonding is critically important. Therefore, plasmas are routinely used in order to enhance the surface of a medical device prior to the bonding of two polymers. Dowling and his colleagues are currently carrying out some significant research in this field.

"In our own research we have shown that a type of coating known as plasma polymerised can be used to deposit nanometre-thick layers that exhibit superhydrophobic properties, with a water contact angle >150°C," he explains. "One application of these non-wetting surfaces, for example, is to protect the electronics of mobile phones when they fall into water. ▶

**10%**

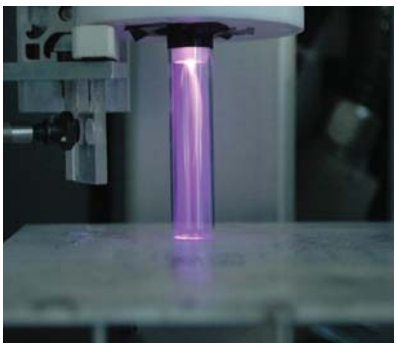
The amount in which fabricate polymer materials are thinner with the application of plasma technology.

**University College Dublin**

**2,000°C**

The temperature at which it is possible to deposit from ceramic materials.

**University College Dublin**



**Left: Plasma technology being used to properly prepare a surface for a biomedical application.**

**Right: kINPen by NeoPlas uses cold atmospheric plasma to treat wounds and skin ageing.**

"Another application of plasmas is to produce surfaces that wet very easily; the term is 'activated'. We are using this approach to activate polymer particles."

These particles were subsequently used in either injection moulding or 3D printing.

In the case of the injection moulding, the polymer particles were passed directly into the moulding equipment, while for 3D printing the particles were melted and extruded into a filament, which was then used for printing. Dowling says the parts produced exhibited an approximately 10% enhancement in mechanical performance.

This is associated with the cleaning of the particles with the removal of weakly bound water and organic molecules. Their removal increased the bonding between the particles, therefore enhancing the mechanical strength of the fabricated polymer part.

"We started out with a barrel plasma source that could treat approximately 1g of polymer particles," says Dowling. "The capacity of the source was initially increased to 20g at laboratory scale and then to 500g for pilot scale treatment."

One application of the developed technology is to fabricate polymer medical devices that are at least 10% thinner but exhibit the same mechanical strength.

"A high level of technical know-how is required when using plasmas for advanced coating and etching applications in sectors such as medical devices and in semiconductor processing," says Dowling. "Manmade plasmas are usually in the form of discharges formed between two electrodes."

That discharge is formed, under low pressure or the opposite, via myriad different systems of varying design, shape and size, but fundamentally they all are used for the same purpose; either for removing material, to etch, or for deposition. For coating, says Dowling, typically a line of sight method has been the one of choice.

"In other words, it is anything that the source can see, that the electrode can see, that gets coated," he says.

## Discharges: benefits and complexity

However, although in principle it seems simple, it isn't.

"There are a range of different types of discharges," says Dowling. "You engineer the type of discharge according to what type of material you want to deposit. For example, because of the energy contained in a thermo discharge, they are best suited to things that require a lot of energy to break bonds.

"If you're thinking of a ceramic material, such as hydroxyapatite, you have to go up to about 2,000°C in order to be able to deposit from that. If you are talking about putting down a polymer layer, there is a technique known as plasma polymerisation, where you take a monomer of the polymer and spray it into the discharge, where it gets crosslinked to form the polymer layer. That is done under much lower energy conditions. So much like surface engineering, you tailor the type of discharge according to what you want to apply."

Although atmospheric plasma has gained traction in recent years, it isn't suitable for everything, particularly for the deposition of metal coatings.

"With coating, it comes down to the process and what is required," Dowling explains. "Is it metal, a polymer layer, a low-friction coating and so on? So, for those applications involving metal coatings, you do have to stop and take them [devices] out; it wouldn't be something you could put in line because it's simply not technically feasible."

However, when atmospheric plasma can be used, the cost benefits and more positive impact it has on the environment are a real bonus.

Although plasmas can be applied simply for applications such as polymer activation, once you move away from those simple applications and start putting down functional layers, the skill set increases considerably. The level of time and expertise required to carry out those processes would be substantial.

"At a basic level, plasmas can be used routinely as a low-tech solution," says Dowling. "But once you are trying to achieve superior coating performance or etching, the degree of complexity of the process, and the cost associated with those processes, go up considerably. It then becomes a cost-benefit consideration. There will be a point where it may or may not be worth it in terms of the value added of the component."

It may have some limitations but the use of plasma for medical device coating has been around for a while and is here to stay – and it may very well evolve still further.

"There is much wider adoption of plasma than previously, with a range of newer coatings that are being deposited," Dowling concludes. "Almost all surfaces can be coated. However, the choice of coating should be appropriate."

That is the conundrum for device manufacturers, one they seem to be getting to grips with. ●

# Coat with confidence

**Formacoat** has cultivated an enviable reputation as one of the world's pre-eminent providers of coating services for clinical instruments. *Medical Device Developments* talks to Mark Gross and Jesse Manley, the company's CEO, and research and development engineer, respectively, about how they are reacting to new developments in the coating market.

Formacoat is moving, says its founder and chief executive Mark Gross.

In need of new warehouse space, the company's headquarters will up sticks from its current base in Savage, Minnesota, US, to the town of Chaska, some 12 miles down the freeway.

"For some, it's a longer drive," Gross cheerfully points out. "For me, it is only a mile and a half."

New travel arrangements for certain employees aside, the move is just another sign of Formacoat's burgeoning reputation in the coating sphere. Incorporated in 2002, the contract manufacturer for medical device coating services has proven expertise in pairing the right hydrophilic or hydrophobic coating with some of the most intricate and advanced clinical instruments. Its success in this area has been demonstrated by its expanding customer base and rising staff numbers.

"We have reached a point where the space we are in no longer works for us," Gross explains. "So, we are building a new facility that will increase our square footage fourfold."

This will provide room enough for new ultrasonic spraying tools and equipment for precision coating applications.

Some expansion space and funds will support Formacoat's pursuit to help medical OEMs navigate the US Food & Drug Administration's position on particulate generation in certain coatings.

"It has pushed coating manufacturers to develop new formulas and strengthen their products so that they are better at producing lower levels of particulates," explains Gross.

Formacoat anticipates being at the forefront of delivering coating options and services to customers that live up to these new standards.

"Part of our response to particulate generation is that we are going to begin doing in-house particulate testing earlier in the development process," says Jesse Manley, a research and development engineer at the company. "We are going to do dynamic testing that integrates not only liquid particle counting, but does so with the standard lubricity-durability pinch testing that we do to qualify all coatings, for all customers."

### The right coating for the job

Because Formacoat does not manufacture or sell coatings – instead sourcing coatings from corporate and academic partners – the company has a vast array of options open to it in order to find the most appropriate coating for any device.

"What I learned early on in the business is that not all coatings are equal," says Gross.

*"By offering different coatings from different vendors, if one doesn't work, we can switch to another very easily."*

"By offering different coatings from different vendors, if one doesn't work, we can switch to another very easily."

This versatility also allows Formacoat to break away from traditional thinking surrounding how certain coatings fit with certain applications.

For example, Gross and his colleagues are currently working with coating vendors to develop soft-touch coatings that, the CEO says, "feel like peach skin".

Formacoat has also joined with another coating vendor to offer a chemical grafting coating for catheters.

"It does require heat, but the coating is formed in liquid and is a very good coating for doing IDs of products," explains Gross. "We are currently performing cutting-edge research and development towards commercialisation with this coating."

In the past year, Formacoat has also developed new methods for encapsulation with polymers of substrate materials and has made inroads into creating new heatable coatings with partner vendors.

Looking ahead, Gross and Manley anticipate greater interest among customers in coatings that do more than passively provide lubricity to individual medical devices. A great example of this would be Formacoat's use of a hydrophobic, 'matrix-entrained liquid' coating, which possesses a high degree of repellence against materials that might lie against it inside the body.

"It has valuable applications for antimicrobial activity, but without there being any drugs involved," explains Gross. "Bacteria simply can't adhere to its surface. That means it is great for dosing and stripping applications, where you're trying to remove products or contaminants from a surface during a medical procedure."

That coating is still in its nascent commercialisation stage, but Formacoat has plenty of other projects to keep it busy as its staff wait to make their move into the new facility.

"We have got coatings that are heatable and surface-blocking coatings that prevent proteins from bonding to device exteriors," Gross says, confidently. "Our world of coating applications is pretty much exploding." ●

**For further information**

www.formacoat.com

# Proven Solutions from a Trusted Partner

For over 45 years, Argon Medical has been a global leader in the manufacturing and distribution of interventional radiology, cardiology, vascular surgery and spine access devices and accessories. With manufacturing facilities in Wheeling, IL, Athens, TX and Rochester, NY, our highly skilled employees are committed to providing off-the-shelf or contract manufacturing solutions to fit your needs. We operate major facilities in a controlled manufacturing environment and offer a wide range of specialty devices, components and services that can be configured to your requirements. We are a vertically-integrated GMP medical device manufacturer and take great pride in maintaining an effective quality system, regulatory expertise and ISO 13485:2016 certification.

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- CNC Swiss machining
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- Coating

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# A point well made

**Argon Medical OEM** is recognised as a leading manufacturer and supplier of high-quality needle point geometries for bone, biopsy and vascular access – with a solution to suit the needs of all customers.

Trusted, high-quality needles are required for interventional procedures such as kyphoplasty, vertebroplasty, bone access and bone marrow biopsy, as well as orthopaedic and spine surgeries. Although the need for such bone needles is common, finding a specialised needle that specifically matches your requirements can be a challenge because the procedural outcome, ease of use, and patient and clinician comfort is greatly impacted by the needle's point geometry, cannula design and handle ergonomics.

Grinding the needle point geometry is a critical process in manufacturing a perfect needle. This is especially evident in bone access and bone marrow harvest needles where the point geometry directly affects insertion force and patient comfort, and can impact the overall success of the procedure.

From custom point geometries to specific cannula designs, Argon Medical OEM offers CNC Swiss Machining, and a variety of metal processes, such as swaging, bending, flaring, electrochemical 'burr-free' cutting and chemical etching.

Another important feature of a bone needle is the ergonomic handle design. Handle designs have improved greatly over the years to improve needle control and clinician comfort.

Additionally, adding custom features to the handle design, such as a pad-printed logo or a specific handle colour, can enhance marketing efforts and increase brand awareness.

As a leading provider of bone access needles, Argon Medical OEM offers a comprehensive range of ergonomically designed handles in a variety of shapes and colours.

As a leading provider of bone access needles, Argon Medical OEM offers a wide variety of ergonomically designed handles in many shapes and colours.

*"Grinding the needle point geometry is a critical process in manufacturing a perfect bone needle."*

Argon Medical OEM provides a wide variety of point geometries, including: the double-diamond point designed to easily penetrate hard bone; an industry-leading 'match-ground' tip where the needle and stylet are uniquely matched one-to-one during grinding, for a perfect needle point; and electrochemical grinding and notching for custom features specific to customer needs.

### Cannula and ergonomic handle design

Cannula design is also an important feature for bone needles. Some design options to consider are shaping the tubing or wire to strengthen the hub bond, modifying the funnel entry for accepting a device into the tubing inner diameter, designing the cannula to capture and retain outstanding-quality bone marrow specimens, or adding centimetre depth markings.

### Off-the-shelf and packaging options

Some projects prioritise speed and time-to-market, when there simply isn't enough time or budget to source a customised bone needle. For such situations, there are off-the-shelf options that are ideal. Argon Medical OEM has a vast portfolio of ready-to-order needles specifically designed for bone access, bone biopsy and cement delivery, with leading edge design features built in for optimal ease-of-use and patient outcomes.

Argon Medical OEM provides a wide variety of point geometries to cater to customer needs.

Packaging is another important consideration for your bone needle project. Packaging options range from bulk non-sterile to custom single-pack sterile.

Although sourcing your needle bulk non-sterile might seem to be the easiest and least-expensive solution, partnering with a supplier in order to provide a sterile, private-label-finished device can help reduce overall lead time and total cost of ownership.

Argon Medical OEM offers a wide variety of both custom and standard packaging options, including form-fill-seal, vacuum forming blister trays, peel pouching, and private label and custom packaging.

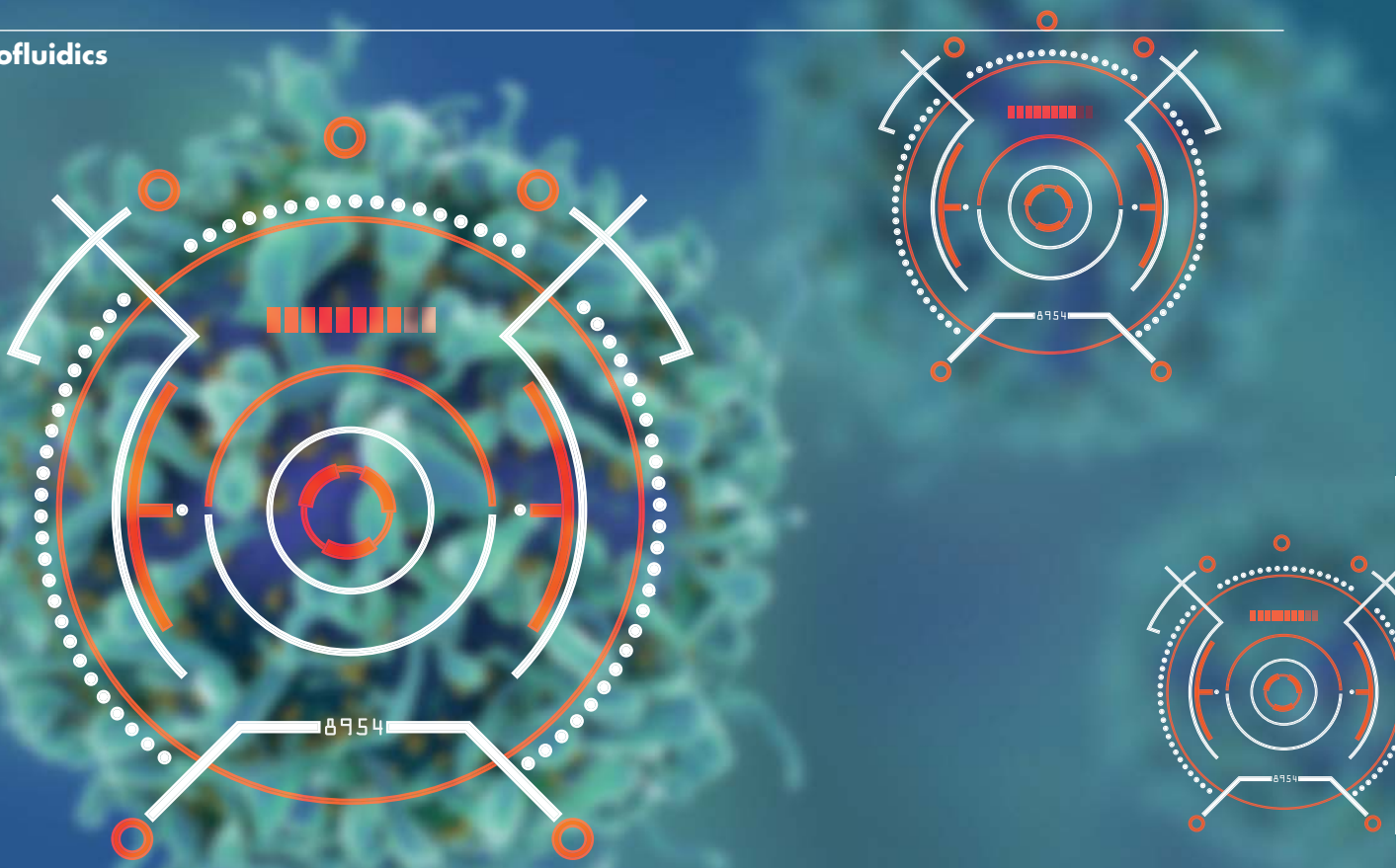
### Quality as standard

Argon Medical OEM is a proven quality supplier of needles for bone, biopsy and vascular access, and a respected leader in medical device manufacturing, with custom and standard product offerings for components, accessories and private-label-finished devices.

Argon's experts are available for the company's clients to contact and discuss their projects. ●

### For further information

www.argonmedicaloem.com



# Cancer detector

Cancer DNA changes in response to its environment, favouring alterations that help it survive long term. These include large and small changes, and the latter can be almost invisible. **Chrissy O'Keefe** and a team at Johns Hopkins University have created a digital microfluidics platform to help detect these changes. She talks to Kerry Taylor-Smith about how this technology could revolutionise cancer detection.

Identifying scientific markers of cancer is key to early disease detection and treatment planning – often possible long before a diagnosis has been made or symptoms develop. It can also help doctors to track disease progression and guide treatment in established cases.

However, searching healthy cells for small changes to DNA in cancer cells is akin to searching for needles in haystacks. That's because while some changes are significant – and relatively easy to detect – others are so small they evade analysis. And it's these changes that can give cancer DNA an edge and affect patient outcomes – early detection can boost survival rates by as much as 90% in some cancers. In what could signal a major breakthrough for oncology research, a team from the Department of Biomedical Engineering at Johns Hopkins University has developed an innovative device to help make identifying these small changes easier and more efficient.

HYPER-Melt – or high-density profiling and enumeration by melt – is a digital, microfluidics-based platform that allows researchers to manipulate and analyse minute volumes of fluid. By separating blood samples into smaller and smaller chunks, the device makes them easier to individualise and analyse. This makes it easier to identify disease-carrying DNA and to separate it from healthy DNA.

HYPER-Melt is the brainchild of Chrissy O'Keefe, a PhD student who has been under the mentorship of Professor Jeff Wang, a microfluidics expert in the university's Department of Mechanical Engineering and at the Institute for NanoBioTechnology (INBT), and senior INBT research scientist Tom Pisanic.

O'Keefe and her team have published their work on HYPER-Met in a *Science Advances* paper entitled 'Facile profiling of molecular heterogeneity by microfluidic digital melt'. The research is the culmination of more than five years' work in the field.

O'Keefe says the device, which is based on hardware and software components, evolved from an interest in studying the heterogeneity of a sample on a molecule-by-molecule level.

"Cancer, along with many other diseases, is highly adaptable and contains many heterogeneous cell types," she says. "It is constantly changing and evolving to ensure it can survive and thrive in its environment – in the body. We wanted to develop a technology that could detect and quantify this variability so we could better understand tumour evolution. We wanted to look at this at its earliest stages, as well as at later stages where the cancer adapts and avoids treatment or causes a relapse. In particular, we were interested in studying cases where molecules may be very rare – such as cell-free DNA from a blood sample."

## Collecting signatures

HYPER-Melt works by investigating small sequence variations of tens to thousands of single molecules of DNA. It digitises molecules into 4,096nL chambers and uses a thermal-optical platform to simultaneously amplify and obtain the high-resolution melt signatures of each chamber.

In practice, the workflow is similar to a standard bench top PCR experiment. The user prepares their mastermix and target on the bench top, and loads the mixture into a syringe. When the syringe punctures the seal of the chip, the mixture enters the device by vacuum-assisted loading, and a partitioning fluid is pressurised through the channels to digitise each chamber. This process is fast and efficient, taking no longer than five minutes.

The final step involves the device being placed on the flatbed heater to undergo digital PCR and high-resolution melt (dPCR-HRM) using the same time frame as a microtiter plate experiment.

O'Keefe says there are a number of reasons why the technology could revolutionise cancer detection. "HYPER-Melt allows highly parallelised molecular profiling of rare molecules," she says. "The platform uses a simple, all-in-one workflow and demonstrates highly sensitive detection that is roughly two to three orders of magnitude higher than current techniques.

"For example, digital analysis in a microtiter-plate system is limited to tens of molecules, which limits the amount of information that can be collected. Microfluidic manipulation, on the other hand, enables the acquisition of more information per sample from thousands of individual molecules in parallel, while minimising reagent usage. In addition, the ability to assess various sequence changes of a given locus provides more in-depth information than current PCR-based gold standards."

She says HYPER-Melt could be used to study the genetic and epigenetic make-up of a population and pave the way for an increased understanding of disease development and progression.

This new microfluidics digital platfrom can aid those searching for subtle DNA changes in cancer cells.

"HYPER-Melt is readily extendible to applications like precision medicine. The ability to profile disease populations within a patient can help identify genetic or epigenetic therapeutic targets, as well as small clonal populations that may be resistant, which could help in developing and adjusting treatment regimens."

The device is best suited to samples with rare and heterogeneous molecules. Liquid biopsies, which contain trace amounts of cell-free DNA in the plasma, could be a key focus of HYPER-Melt-based research.

"Many diseases, such as cancer, are highly variable so that they can adapt and grow in their environment," says O'Keefe. "HYPER-Melt can be used to assess this variability throughout the development of disease by simply taking a routine blood sample."

In particular, it could benefit doctors working to detect cancers that ordinarily require invasive procedures like biopsies, endoscopies and colonoscopies to secure accurate diagnoses.

She said the device could also be used to monitor cancer evolution in response to therapy. "The ability to detect small, rare sequence changes could give an early indication of evolving therapeutic resistance."

## The impact of high-resolution melt technology

Similar current devices are based on digital PCR platforms, with the most popular version being droplet digital PCR (ddPCR), which can isolate and detect single molecules. It's a sensitive technique that can find rare biomarkers; however, it is limited to a few known or targeted sequences.

HYPER-Melt, on the other hand, offers greater insights through its ability to assess unknown sequences, and identify a spectrum of modifications using high-resolution melt.

"Typically, digital PCR produces a binary yes/no result for each chamber. However, high-resolution melt

Chrissy O'Keefe

allows us to acquire additional sequence information about each amplicon," says O'Keefe. "High-resolution melt measures sequence variations by using an intercalating dye to detect changes in fluorescence during a thermal ramp. For example, in this study we looked at methylation changes – an epigenetic modification that affects gene expression. High-resolution melt allows us to assess the whole range of potential methylation changes, even those relating to unknown targets. One of the largest technical challenges in developing this platform was detecting real-time variations in fluorescence from thousands of nanolitre-volumes in parallel. Once acquired, though, we can obtain the sample's entire sequence profile."

Hyper-MELT could offer clinicians significant cost and time savings compared with other current technologies, such as sequencing, says O'Keefe.

"Sequencing, which is commonly used for genetic profiling, can provide exact sequence information," says O'Keefe. "However, it is an expensive technology and it also takes a long time to achieve the requisite sensitivity (<0.1%) for challenging samples with rare molecules, so it is not particularly suited to clinical use.

"By comparison, HYPER-Melt can achieve much higher sensitivity – 0.00005% – with much lower cost; in fact, for roughly the same cost as a microtiter plate. In addition, it has a simple, rapid workflow with few hands-on steps, and provides an easy-to-interpret result, making it an efficient and relatively simple means for molecular profiling."

*"Cancer is constantly changing and evolving to ensure it can survive and thrive in its environment – in the body. We wanted to develop a technology that could detect and quantify this variability so we could better understand tumour evolution."*

O'Keefe said HYPER-Melt was aimed at achieving the outcomes of digital PCR and sequencing, and then building on these outcomes in terms of developing better sensitivity, efficiency and reliability.

O'Keefe says the pace of development in microfluidics is presenting exciting opportunities for the scientific community. The improved performance and reliability of commercial microfluidic technologies, such as ddPCR, have sparked a boom in research.

"One simple advantage of digital techniques like microfluidics is absolute quantification," she says. "Researchers can simply count positive chambers to exactly quantify their sample without using standards, and this enables more accurate measurements for applications such as copy number variation.

"Another powerful advantage is the ability to detect extremely rare molecules. As a result, we are seeing more and more digital microfluidics being used in cancer studies to detect single nucleotide polymorphisms and rare mutations, especially in liquid biopsies."

## Bringing the device to market

Each of the prototype devices consists of a single polydimethylsiloxane (PDMS) pattern layer sandwiched between glass, and is made using an ultra-thin soft lithography technique. PDMS has several advantages, such as ease of fabrication, biocompatibility and optical properties, says O'Keefe.

"In addition, the gas permeability of PDMS allows rapid, vacuum-assisted loading. Glass, which can be easily bonded to PDMS, serves to provide a flat, rigid surface for heating while maintaining optical transparency."

Having a beta-ready version of HYPER-Melt available within three years is a key target.

"There are still many improvements that we need to make before a packageable version of HYPER-Melt is ready for market," O'Keefe concedes. "One major milestone would be to establish sufficient sensitivity and specificity of the platform in a clinical setting. If the platform demonstrates sufficient performance, then we can start to tackle scalable manufacturing methods and high-throughput assessment of samples.

"Currently, one of the device's biggest drawbacks is the relatively low throughput of the system. HYPER-Melt can analyse roughly five samples at a time, which limits its use in large studies that require the assessment of hundreds to thousands of samples. We're therefore looking to improve the throughput for larger-scale studies by focusing on developing a more advanced thermal-optical platform."

O'Keefe and her team are working with partners at Johns Hopkins University and other medical institutions to advance and refine the HYPER-Melt technology and usability to prepare it for market.

The team hopes to evolve the technology so it can be used as a diagnostic tool to detect tumour-derived DNA in liquid biopsies. "We believe that the high sensitivity of this platform, coupled with the multidimensional data set, can improve early detection of some types of cancer, especially those without reliable screening techniques," she says.

Follow-up studies are focused in particular on lung cancer and ovarian cancer. Using lung cancer as an example, O'Keefe says the technique could be used following a CT scan to provide secondary, non-evasive analysis, potentially replacing the need to run a biopsy. In the case of ovarian cancer, which does not currently have a reliable diagnostic technique that can be used prior to symptom evolution, there is real potential to develop new biomarkers that could pave the way for early detection, diagnosis and treatment.

# Liquid flow

A number of disposable sensors are now available to monitor fluid control in medical devices, and these tend to be low-cost because there are no electronics located in the sensor. IVAM CEO **Dr Thomas R Dietrich** talks to Kerry Taylor-Smith about the potential of these sensors for mobile and point-of-care diagnostics.

During medical treatments, the outcome of therapy and the overall well-being of a patient so often depends on the reliable and continuous administration of drugs or intravenous fluids at low or ultra-low flow rates. However, such procedures and therapies are faced with the same challenges – precisely measuring and regulating lowest flow rates of medicines and/or fluids down to the microlitre per hour.

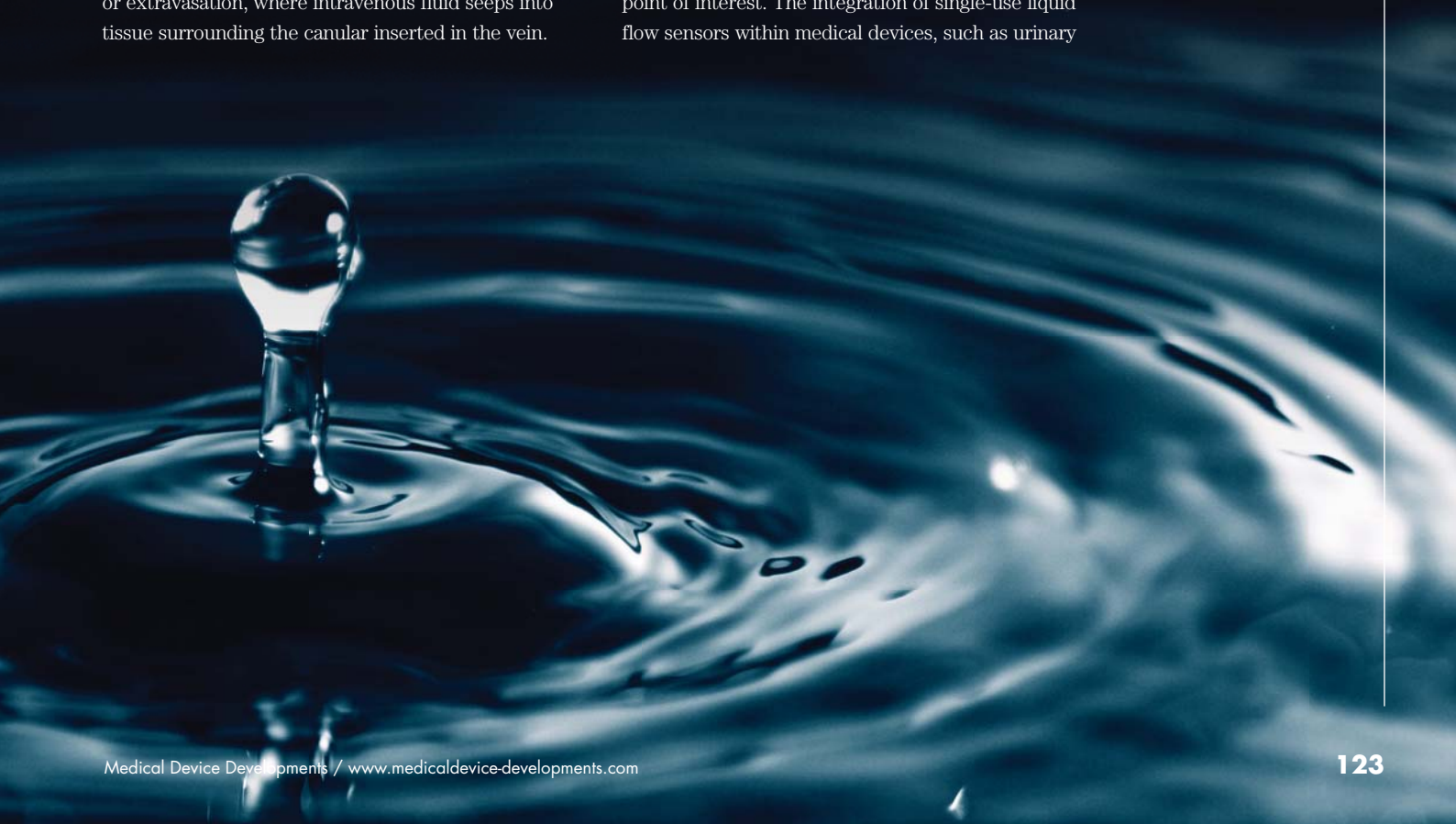
Smart infusion pumps provide well-controlled drug delivery over an extended period of time, but are unfortunately susceptible to failure. The technology lacks the ability to directly measure the flow rate of the drug inside tubing, leading to undetected failures or oversensitive pumps giving false alarms.

Typical failures include occlusion (a blockage or closing of the blood vessel or a hollow organ); air in the line; free flow; cross flow, where multiple infusions are taking place at the same time; and infiltration or extravasation, where intravenous fluid seeps into tissue surrounding the canular inserted in the vein.

## Smart chips

Disposable liquid flow sensors containing smart chips could be a game-changer in the biomedical field, from controlling the flow of valuable ingredients in bioreactors to monitoring infusion therapies at low and ultra-low flow rates in a clinical environment. They have been designed for single-use, high-volume biomedical applications such as drug delivery systems, and their in-built failure detection features can help counteract failures such as cross flow and extravasation.

Smart chips within the sensor can combine microelectro mechanical systems (MEMS) and CMOS (complementary metal-oxide-semiconductor, a class of integrated circuits) on a single silicon wafer, and have the potential to improve diagnostics and automation. This unique technology is safe and reliable, not to mention highly precise, and is capable of detecting the smallest change in liquid flow rate in real time at the point of interest. The integration of single-use liquid flow sensors within medical devices, such as urinary



catheters or infusion sets, is simple: the sensor chip is completely isolated, encased in a plastic housing – meaning it cannot come into contact with bodily fluids or medications – that can be secured in the fluidic line using standard Luer lock fittings. The sensor is also low-cost – it has been stripped back to a bare minimum without sacrificing mechanical, electrical and fluidic connections, making it ideal for disposal after use.

The straight, open-flow channel has no moving parts (meaning nothing to break or fail), which provides excellent reliability, and its small size results in efficient and highly repeatable measurements in real time, offering unprecedented reliability and safety. It can, for example, spot occlusion in a matter of seconds by noticing a decrease in flow rate even at ultra-low flow ranges. Medical-grade wetted materials also offer excellent chemical resistance and outstanding biocompatibility as well as sterilised operation.

"A disposable liquid flow sensor provides liquid flow measurement capability from inside medical tubing, such as an infusion set or a catheter," explains Dr Thomas R Dietrich, CEO of IVAM, an international microtechnology business network and technology marketing expert based in Dortmund, Germany. "Because of its low cost, it is suitable for disposable applications."

*Treatments will become more effective as they become easier to monitor and control. Patients' safety is improved by the automatic detection of failure modes like clogging, free flow, air bubbles, or leaks in the tubing connection.*

Drug delivery from an infusion set, an infusion pump or other medical devices can be measured precisely and in real time. "Inside a disposable liquid flow sensor, a microchip measures the flow inside a fluidic channel," says Dietrich. "Flow rates, typically in the range of zero to several 100ml per hour are measured with a typical accuracy of 5% of the measured value. Inert medical-grade wetted materials are used to ensure sterile operation with no contamination of the fluid."

The sensors' measurement method is based on a micro-thermal principle; an incredibly tiny heating element on the chip releases an insignificantly small amount of heat into a bypassing liquid to obtain a thermal flow measurement. The shape of its heat cloud is monitored by two temperature sensors positioned symmetrically up and downstream of the heat source, which detect minute temperature differences with incredible sensitivity: these fluctuations are directly related to the flow rate inside the fluidic channel. Using this principle, liquid flow sensors can continuously and reliably measure low flow rates typical of medical applications.

## Intelligent, compact and cost-effective

Single-use liquid flow sensors have the potential to revolutionise drug delivery. They are considered more effective as it is easier to oversee and regulate the flow of medication or IV fluids, and their smart chips are helping to improve diagnostics and automation. The result is better patient treatments, improved safety and support for overworked hospital staff.

"Treatments will become more effective as they become easier to monitor and control," says Dietrich. "Patients' safety is improved by the automatic detection of failure modes like clogging, free flow, air bubbles, or leaks in the tubing connection." This serves to increase the accuracy of drug delivery and automatic diagnostic equipment.

Such single-use liquid flow sensors can detect a drop in a primary infusion flow due to cross-flow errors from a secondary line where multiple infusions are taking place simultaneously, and includes bubble detection to identify air inside the infusion tubing.

Furthermore, the sensors are so sensitive that they can even detect a heartbeat, a direct indication of an intact connection of the infusion cannula to the vein of the patient. The absence of a pulse could indicate an interrupted connection caused by a kinked tube, ruptured tubing or a dislodged cannula, which could lead to infiltration or extravasation (leaking of intravenous fluid into the tissue surrounding the vein). Such incidents can occur when damage is caused to the vein during catheter insertion and can cause irritation if the fluid is a non-vesicant agent, or damage to nerves, tendons and joints if the fluid is a vesicant agent such as a chemotherapy drug.

These intelligent, compact and cost-effective liquid flow sensors have the potential to change drug delivery from the ground up, offering safer, more mobile and reliable care in hospitals and peoples' homes.

"Disposable liquid flow sensors make the use of point-of-care diagnostic tools affordable for everyday use," says Dietrich. "Even patients and family members without any medical education can use automatic equipment for diagnostics and drug delivery."

The use of these devices at home is made possible as the sensors are cheap and easy to use. "This will give elderly and chronically ill people the opportunity to stay longer at home and avoid long clinical stays or movement to nursing homes," explains Dietrich.

## Multiple benefits

It is known that being mobile can reduce the length of a patient's hospital stay while simultaneously improving their quality of life. However, ambulatory infusion pumps can be problematic in terms of ensuring the required flow rate is accurate – during a typical day it can be difficult for a patient to follow the handling instructions that ensure the specified performance,

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resulting in real-life flow rates deviating drastically from the intended values.

The use of a single-use liquid flow sensor could help overcome this by allowing the continuous delivery of highly concentrated medication over several days. This could be especially useful for those receiving chemotherapy where the constant administration of chemotherapy drugs over time has a better pharmacodynamic influence on effectiveness and toxicity compared with traditional bolus injections every day. There is even the potential for these single-use liquid flow sensors to be incorporated into wearable drug delivery devices, further enhancing a patient's quality of life while they undergo treatment.

Another issue is the clogging of the restrictor of the pump – usually a thin capillary in the pressure drop element – or at the injection site. It can take hours before an occlusion is noticed by the medical team or the patient themselves, but the use of a disposable liquid flow sensor within the infusion set can spot such a failure much more quickly – even within seconds.

Such disposable liquid flow sensors can also prove useful in treating babies and young children who require much smaller doses of drugs due to their low body weight. Once integrated into an infusion set, the single-use liquid flow sensor allows for the accurate monitoring of administered flow rates – critical if excreted fluids are also being monitored – as well as overcoming other common failures related to current infusion technology quickly and reliably.

But these sensors aren't just for administering drugs and fluid to the body, they can also measure and record things coming out of it. They can also help to diagnose acute kidney injury (AKI) by automatically measuring and recording urine output, a task currently carried out manually at regular intervals by nurses. Using disposable liquid flow sensors in this manner could allow for a timelier diagnosis and potentially prevent the onset of AKI, while also eradicating human error and freeing up medical staff's time.

Integrating disposable liquid flow sensors into infusion tube sets has the potential to progress infusion therapies and allow for controlled drug delivery on a much broader scale. Measurements and vital signs could be obtained and stored automatically and electronically, eliminating human error and saving valuable time, which medical staff can dedicate to actually treating patients.

They could detect currently unnoticed failures and maybe even prevent them, increasing patient safety and well-being. Introducing such a ground-breaking technology could also present massive savings for the healthcare system, while decreasing workloads and stress for hospital staff.

# Cutting-edge porous solutions

Jack Chan, global marketing director for medical segment at **Porex** (Filtration Group), explains how the company's sintered POREX Virtek PTFE solutions are designed to address today's diverse medical device challenges.

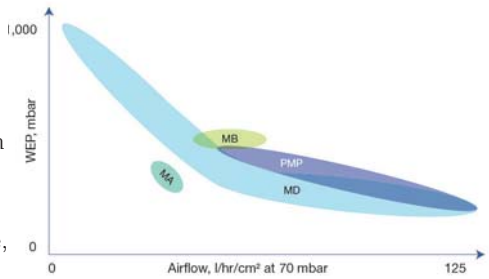
Whether used to treat illnesses, injuries or anywhere in-between, medical devices are essential tools that help to improve health and well-being, and save the lives of billions worldwide. As critical as it is to have access to these devices, it is also vital that they are functioning properly to safeguard both patients and medical professionals.

Recently, the EU updated its current directive for the regulation of medical devices. The EU's medical device regulation (MDR), set to come into effect in May 2020, requires medical device manufacturers to provide more in-depth clinical data to prove safety and performance claims, and more stringent equivalency standards, in order to get their products to market. Thus, it is imperative that manufacturers carefully consider the components at the core of their medical device design to ensure the safety of individuals in any healthcare environment, whether in a hospital or laboratory facility.

## Sintered PTFE: touch and versatile

Design manufacturers seeking to increase safety, functionality and reliability in current and next-generation medical devices can utilise a sintered polytetrafluoroethylene (PTFE) membrane as a component. This durable, high-performing technology, which more effectively vents, diffuses and filters air, gas and liquid, allows medical devices to perform exactly the same every time. The medical-grade PTFE hydrophobic material provides a high bacterial filtration efficiency of 99.99% or higher, superior water-entry pressure, optimal airflow and a fluid barrier.

Sintered PTFE, a membrane featuring an open-cell, omnidirectional 3D pore structure that is design-flexible, is extremely versatile. It can be tailored in thickness, porosity and pore volume to individual device needs. The unique composition, comprised of well-controlled particles, creates additional robust strength.




The medical-grade PTFE hydrophobic material provides a high bacterial filtration efficiency of 99.99% or higher, superior water-entry pressure, optimal airflow and a fluid barrier.

*"POREX Virtek sintered PTFE venting solutions are designed to address today's diverse medical device challenges."*

When a medical device is not outfitted correctly, everyday procedures can present critical risks. For example, an instance in which a defective vent causes a safety IV catheter to leak can expose healthcare professionals to blood-borne pathogens, putting them in harm's way. When properly designed with porous venting components, medical devices such as the arterial syringe, IV catheters and others can prevent an incident like this from occurring.

This, in turn, permits greater durability and reliability of the porous PTFE components, potentially extending their use and the lifespan of the medical device as a whole. The sintered PTFE material is unlike other porous PTFE membranes that product designers and manufacturers may use to vent medical device applications. Traditional porous PTFE membranes often require a supporting layer or scrim to reinforce the strength, whereas sintered PTFE is superior in manufacturing processes, due to their delicate nature. Sintered PTFE, which can retain its properties through the rigours of high-speed automation or heat, pressure or vibration welding, can be used in a wide range of applications. This material is optimal for infection control, injection therapy, and medical and pharmaceutical packaging, among other applications that promote safer medical device usage and performance.

Components, particularly those that enable venting, play a critical role in how well medical devices function and perform. POREX Virtek sintered PTFE venting solutions are designed to address today's diverse medical device challenges and replace the production and operation of faulty, unreliable devices that can harm the individuals they are meant to aid.

Learn more about the applications for POREX Virtek PTFE solutions that are creating a safer, healthier and more productive world at the Porex website.

*References available on request.*

**For further information**

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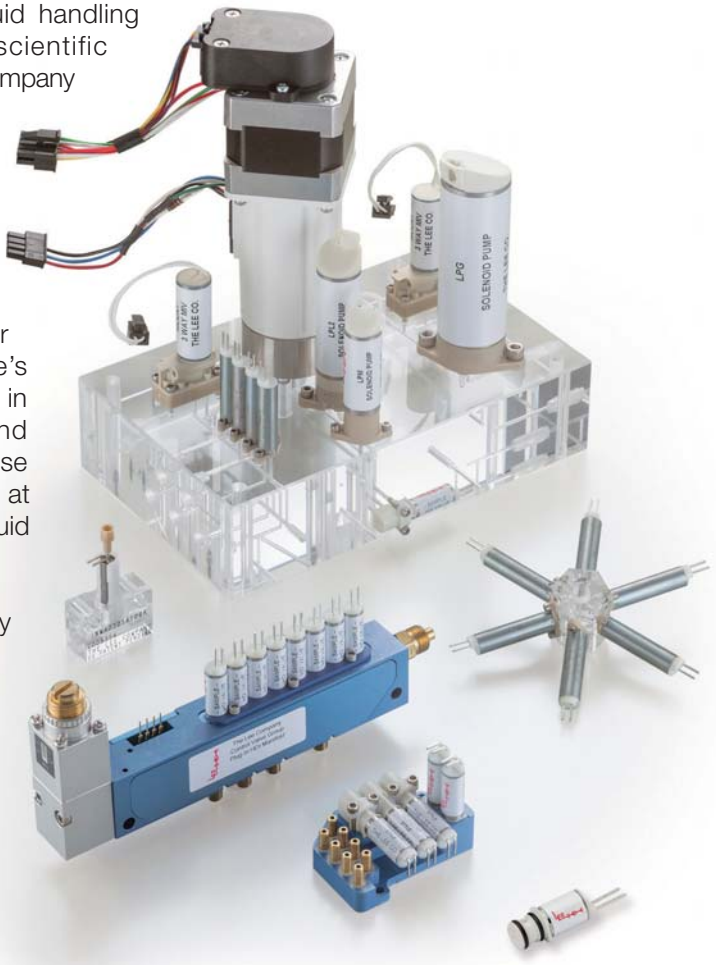

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# Many hands make light work

The global market for sustainable packaging is rapidly developing. However, medical device companies are still lagging behind their personal-care, food service and shipping counterparts. **Peylina Chu**, executive director of Healthcare Plastics Recycling Council, speaks to Emma Green about key principles to consider in bringing the medical device industry up to speed.

**Opposite page: Northshore OR bags specifying their use for recyclables or hazardous waste.**

It is estimated that one million tonnes per year of non-infectious medical plastics are available for recycling in the US, with equivalent amounts in Europe and Asia. However, notwithstanding its environmental impact, plastics have offered huge benefits to the industry. These include enhancing patient safety and making lighter packaging to save fuel and costs when transporting supplies.

Over the past few decades, there has been growing awareness of the environmental hazards related to the disposal and recycling of packaging, numerous government initiatives and increasingly stringent regulations. Despite these drivers, the complex and dynamic nature of the medical device industry makes it more difficult to implement environmentally friendly practices into the supply chain.

Peylina Chu, director of Healthcare Plastics Recycling Council (HPRC), is up for the challenge. She is passionate about identifying and addressing barriers throughout the supply chain. Together with a small, but highly active, group of members and advisory board, Chu is keen to educate relevant individuals and organisations, and promote opportunities to recycle medical plastics more widely.

Two aspects are particularly problematic within the industry. The first of these is the amount of regulation around patient safety. "They need to be able to get approval of a particular plastic device or plastic packaging to make sure that it is safe for patient use," explains Chu. "This means that any design changes need to go through that rigorous approval process, which is very expensive."

The second is what Chu calls the 'ick factor'. "After being used and disposed of, a lot of recyclers are concerned about infectious materials, perhaps a syringe, or stuff that's not the usual consumer or residential trash." Further complications arise due to he lightweight nature of the materials, which makes them expensive to transport, and the lack of recycling centres. In light of these difficulties, adopting a collaborative approach is key.

In order to ameliorate issues further down the supply chain, it is imperative to make packaging recycling friendly right from the start. "This is where we've been working with the sustainable packaging coalition to make sure that we are talking about the same issues when it comes to designing the packaging," explains Chu. "Things like not mixing materials within a single package, not having a metal screw cap on a plastic bottle and trying to minimise the paper labels that are used on plastic packaging."

Although all of these issues can be dealt with by recyclers, this is an extra step. "It costs more money, it takes more energy and it just makes that whole recycling process less profitable," says Chu. It is thus better to prevent these problems from occurring in the first place. ▶

## Get the word out

There are also efforts by the HPRC to teach hospital staff about what and how to recycle. This includes being proactive about identifying materials and treating them appropriately. "One of the best practices that we like to talk to hospitals about is removing packaging before the patient is even brought into the operating room," Chu explains. "That way, you can make sure that those plastic packaging materials are kept clean, they don't have infectious materials or blood on them, and instruments are not accidentally tossed into the bin."

At the end of the chain, the HPRC are tackling the practices of recyclers. This includes providing education and encouraging more communication. "There's a lot of this material out there and they may not have thought to talk to hospitals about recycling," Chu says.

Emphasising the value of these plastics, particularly compared with consumer materials, is central to getting this buy in from recyclers. "They have a tighter spec, and in a lot of cases the materials are sterile," Chu explains. "The material is also denser, so if it's properly sorted it can actually have a higher market value."

Although the HPRC is only concerned with recycling efforts, this is addressed from multiple angles because of the variety of companies involved. This includes suppliers, medical device manufacturers, academic healthcare facilities, healthcare systems and recyclers. "I like to say that we're an inch wide and a mile deep," Chu says. "We only focus on recycling but we look at recycling from a lot of different perspectives, and I believe that our group does some quite meaningful things for the industry."

One of the surprising aspects of the HPRC is that members are often companies who would not otherwise be working together. "Even though this group includes competitors, this is an area where they can come together and see that by collaborating they've got a better chance of being successful in the industry," explains Chu.

Central to the success of this cooperation is the enthusiasm and dedication of the individuals and companies involved. "They are individually passionate about the

environment and the planet but at the end of the day, it's got to make sense for their own business," Chu says.

The result of this collaboration has been a number of publicly available resources for individuals and organisations interested in expanding their sustainability efforts. "We have a toolkit that's free for hospitals to download, it's called HospiCycle," explains Chu. "It's for hospitals that are interested in starting up a recycling programme or improving or expanding upon an existing recycling programme."

This also includes resources to help aid the design of more sustainable design methods. "We also have guidance for manufacturers, talking about how designing for recycling is really important," says Chu. "There's things that make it easy to recycle, and things that make it more difficult to recycle."

## Across the pond

To date, the majority of the work of the HPRC has been conducted within the US. However, in recent years the coalition has begun to expand its remit to Europe. Chu is acutely aware of the large differences between countries in Europe, as well as those between Europe and the US.

Interestingly, the environment within Europe has tended to be permissive rather than restrictive in integrating recycling into working practices. "In some ways, the regulatory landscape, economy and healthcare systems actually help the recycling scenario in Europe compared with the US," Chu says. "We're finding that some of the challenges that we find within the US aren't as big of an issue, or even an issue at all, within Europe."

Technological progress within Europe has also been beneficial for the aims of the HPRC. "There are a lot more drivers and I think there's greater urgency and advancement in technology in Europe than in the US." ▶


**Above: Employees at the Casella sorting facility.**

**Page 132: Many recyclers are concerned about infectious materials, such as syringes, or other materials that are not typical consumer or residential waste.**

**Page 133: Designing packaging to make it easier to recycle is hugely important.**

Significant international events, such as the China ban on waste imports, might be expected to cause disruption to recycling efforts but have actually been a positive influence. "One of the things that I see here in the US is that now, because of the China ban, the return on investing in a recycling facility or new recycling technology in the US is becoming better," explains Chu.

This is having a much wider impact than just medical plastics. "We're now seeing investment in recycling facilities and technology within the US that will certainly benefit the medical industry if not other industries that we would never have seen without the China ban."

*"We're focusing on those unique nuances of healthcare packaging, educating recyclers and hospitals about how to generate that clean stream of materials so that it doesn't have blood and other yucky stuff on there."*

### Healthcare Plastics Recycling Council

The HPRC is a private technical coalition focused on inspiring and enabling the recycling of plastic packaging and products used in the delivery of healthcare. It adopts a unique approach through identifying barriers to recycling along the value chain. It then develops resources to remove, or at least minimise, those issues. Some of their past and current work includes:

- **Design guidance:** intended for manufacturers, this guidance provides 'dos and don'ts' to improve recyclability of healthcare plastics.
- **HospiCycle:** a free toolkit for hospitals looking to start or expand their plastics recycling programme.
- **Materials testing phase 1 and phase 2:** targeted to recyclers, HPRC is testing hard-to-recycle flexible films to assess various technical properties so that recyclers can see the value of these materials.
- **Chicago project:** a regional recycling project involving multiple hospitals and recyclers to better understand challenges and factors for success within a geographic region.

Source: HPRC

Learning from these other sectors has also been helpful as they face similar issues with plastic packaging. "One of the issues that we're working with here in the US is multilaminate packaging, which is also a challenge within food, beverage and consumer types of packaging," Chu explains. "You can now get a piece of clear-looking packaging that looks like polypropylene or high-density polyethylene but is actually sandwich materials, but you can't tell from just looking at it."

Although the HPRC has a narrow focus, Chu acknowledges that other strategies are needed to improve sustainability within the medical industry. "We are concentrating on recycling specifically but I know that all of our member companies are also focused on reducing the amount of plastics used in their packaging," says Chu. "That's something that's very important as well."

Looking to the future, it is clear that there is still a lot to be done to improve the sustainability of medical packaging. This involves action from a number of different stakeholders, including manufacturers. "They could look at improving their packaging design," says Chu. "There are still paper labels being used but there needs to be a transition to recyclable plastic labels or even printing directly on the packaging." Such developments have already begun to be implemented in the food industry and this trend is likely to continue over the next few years.

At the other end of the chain, increases in sustainability efforts will open up new avenues for financial gains. "We're focusing on those unique nuances of healthcare packaging, educating recyclers and hospitals about how to generate that clean stream of materials so that it doesn't have blood and other yucky stuff on there," Chu explains. "As recyclers better understand this, there will be a market pull for these materials – brand-owners stepping up and saying yes we want to buy recycled materials."

Although the medical industry is inherently complex, Chu remains optimistic about the sustainability of packaging. "It's a time of a lot of different moving parts right now, which I think are going to be positive for much of healthcare plastic recycling and plastic recycling in general," Chu says.

The drive for more environmentally friendly practices across industries is only going to increase in upcoming years. However, it is imperative that large-scale changes to the environment are made to be able to accommodate these strategies. "We're hoping that, with this new-found momentum and visibility, a lot of large organisations will start rethinking our recycling infrastructure, how that can be improved and the capital investments that need to be made."

# Seal the deal

**Atlas Vac Machine** is the oldest medical device tray sealer brand solely focused on cleanroom packaging applications. President John A Abraham explains how the tray sealer technology, as well as the seal tooling nests, calibration, field service and correct operation training, is the company's core expertise.

For the medical device manufacturer, packaging is one of many issues to be considered when launching a new device. However, all too often the packaging, as well as its core process elements, is afforded little attention on the project timeline. Just as any deficiency in the medical device itself can result in a recall, so can the failure of the packaging performance.

The capabilities and productivity of the latest tray sealers have been enhanced with automatic shuttles, safety-rated light curtains, servo-driven presses and, most importantly, data acquisition. This can result in better payback on the capital equipment investment – but only if the features are fully understood and utilised.

As with most validated capital equipment, a tray sealer is in operation for years, and often well over a decade or even two; therein lies a drawback.

The new Model 1830S All Electric Medical Device Tray Sealer from Atlas Vac Machine.

*"Something as simple as reviewing an IQ checklist can save a packaging engineer hours of backtracking should someone who is uninformed install the equipment incorrectly upon receipt."*

When it is time to acquire new equipment, user specifications are often based on equipment perceptions and rigid processes rooted in older technology. Understanding what is available now and how it can be applied productively may create some competitive advantages if curiosity overtakes rooted perception. Remember, the equipment designer has been listening to many 'voices of the consumer' as a guide to what features are valued in this specific market.

### Multiple benefits

Automatic shuttles provide repeatable cycle times, while reducing package component displacement and repetitive motion injury. Light curtains provide safe hands-free operation so the operator can provide additional value-added labour internal to each cycle period. Servo presses produce a different and more exact sealing pressure profile compared with pneumatic systems.

Important advances have been made in data acquisition, down to the exact details of each package that is sealed at this nexus of device, package and label before it leaves the clean room. Potentially, such data capabilities challenge the upstream and downstream systems to integrate thinking to the betterment of the enterprise.

Given that these new features may not have been available on an in-use tray sealer that has been in the facility for 10–20 years, it would be a wise (but too frequently overlooked) step to take a day to learn the details for proper set-up, use and calibration of a newly acquired tray sealer. Yes, it is all in the equipment manual (which is often shelved, skimmed and/or lost), and a hand-in-hand review through the equipment manual is essential to provide the packaging engineer with the ability to train others (maintenance, calibration, operators), as well as to find IQ data recommended by the OEM.

### The importance of OEM training

Training at the OEM factory – which is free at Atlas Vac – can offer numerous advantages. Something as simple as reviewing an IQ checklist, and the related equipment features, can save a packaging engineer hours of backtracking should someone who is uninformed install the equipment incorrectly upon receipt.

OEM factory training is essential, as well as required by ISO, for the maintenance tech supporting the equipment. Predictably, injuries can occur where an untrained technician who knows nothing about the controls and functions bypasses all the safety systems in a trial and error attempt to address some reported 'malfunction'.

We often see third-party calibration services brought in who are ISO 17025 certified, but have zero familiarisation or training (an ISO requirement) in the operation, maintenance and calibration of Atlas Vac tray sealer control systems. This has resulted in damaged components, adjustments to system components specifically designated as 'non-adjustable', undocumented software modifications, and incorrect temperature, pressure or timing performance. This results in customer packaging sealed unknowingly at inaccurate recipe values. Atlas Vac offers technical support for your designated third-party calibration service provider.

Providing production with the most advanced equipment is an investment that will payoff over the next decade (or two), but free training is priceless in more ways than one. ●

### For further information

www.atlasvac.com

# CREATE WITH **CONFIDENCE.**

## A partner you can rely on.

At Brentwood, we want you to have confidence in your product. Our design team works with you every step of the way from concept through production. We are here to ensure that you achieve a final product that not only meets your specifications but makes both your team and ours proud.

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**610.347.5109** or visit us at **www.brentwoodindustries.com/medical**

BRENTWOOD Medical

**CONFIDENCE.** Today, Tomorrow, Together.

# Design outside of the box

Innovative packaging designs from **Brentwood**, a global provider of formed plastic solutions to multiple consumer, manufacturing and environmental industries, resulted in significant time and cost savings for dental solutions manufacturer Dentsply Sirona.

Dentsply, a US-based company, and Sirona, a European-based company, formed Dentsply Sirona in 2016. Dentsply Sirona manufactures professional dental solutions that include preventative, restorative, implants, imaging services, treatment centres and software solutions. Dentsply Sirona's headquarters are in York, Pennsylvania, US, a short one-hour drive to Brentwood's Specialty Products Group located in Reading, Pennsylvania.

## The challenge

On 25 October 2017, Dentsply Sirona came to Brentwood looking for an improved packaging solution to its current off-the-shelf injection-moulded polycarbonate boxes sourced from China. These boxes held the company's restorative dental products including crowns, abutments, screws and dentures. For the new packaging designs, Dentsply Sirona wanted to focus on a premium look, easier-to-use packaging, and a solution that reduced costs. These new packages will be used for Dentsply Sirona's Atlantis product line, a fully customisable treatment box tailored to each patient's specific implant needs.

## The solution

Brentwood and Dentsply met for the first time within 12 hours of receiving the initial project specifications. Brentwood understood that Dentsply wanted a premium look that was easier to use and significantly reduced costs compared with its current packaging.

Three days after the designs were provided, a 3D-printed prototype part was sent to Dentsply Sirona's product line manager in Spain at no charge.


Dentsply Sirona wanted to make sure that the packaging design reflected the company's global brand image, so an additional aspect in the design was making the lids of all the packaging a specific blue colour.

Brentwood's engineers developed a detailed action plan and began work on the first round of designs. They produced concept drawings within 24 hours (beating other companies by several days). Brentwood's quick turnaround time was a critical factor in decision-making for Dentsply Sirona's product line manager in Spain.

Dentsply Sirona held focus groups to test the original designs and identify areas of improvement. A pivotal design change involved the condition that the abutment trays needed to be opened with one hand. Brentwood's team of designers delivered new concepts to Dentsply Sirona's product line manager within 24 hours. Three days after the designs were provided, a 3D prototype part was also sent to the product line manager at no charge.

## The result

Brentwood's team of engineers developed multiple aesthetically pleasing package designs, abutment trays that are easy to open with one hand and a solution that reduced costs for Dentsply Sirona.

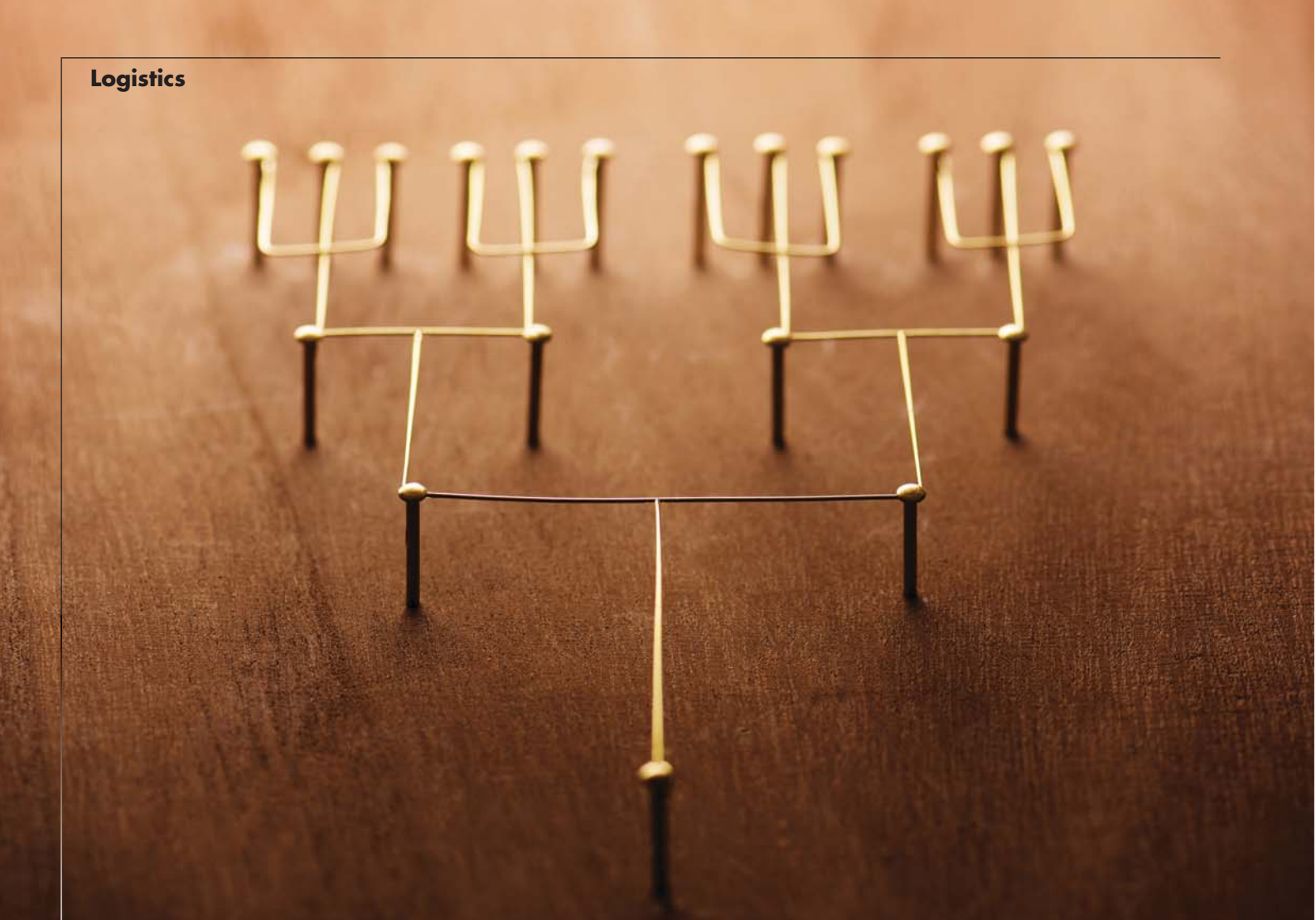
The new packaging line includes three different styles of abutment trays to hold screws and implants, and two different-sized box designs to hold guides and dentures. The abutment design is a nested, sliding tray that can be opened with a thumb, moving forward or backward. This design keeps the implants secure during transport and allows the dental care provider to access the abutments with ease.

Since these customised boxes will eventually be available worldwide, Dentsply Sirona wanted to make sure that the packaging design reflected the company's global brand image. This additional aspect in the design involved making the lids of all the packaging a specific blue colour. Brentwood's team worked with several material suppliers to formulate the perfect blue material that matched the Pantone colour of Dentsply Sirona's brand. Each tray and box packaging includes a clear bottom and Dentsply Sirona blue lid.

In summary, Brentwood's talented packaging design engineering team successfully met the unique and challenging needs of Dentsply Sirona. ●

**For further information**

www.brentwoodindustries.com



# Chains of command

Heavy regulation from design to delivery can make logistics highly challenging. Optimising the shipping process provides time and cost savings, as well as the ability to offer exceptional customer service. Kim Thomas talks to **Bruce J Stanley**, president-principal at the Stanley East Consulting Group, about key strategies designed to maximise the efficiency of logistics procedures.

An efficient, well-oiled supply chain is essential to the smooth operation of any business, whether that business is selling food, cars or clothing. However, it is particularly important in the world of medical devices, a sector that is highly regulated and where companies typically carry large amounts of inventory.

Bruce J Stanley, president-principal at the Stanley East Consulting Group, has a wealth of supply chain experience in the healthcare industry, and now advises global biotech, medical device and pharma businesses in the management of their supply chains. So what does he see as the main challenges facing medical device companies aiming to make their logistics procedures as efficient as possible?

The biggest concerns, he says, continue to be geopolitical issues, and regional regulation of medical devices and healthcare. There was an optimism in the industry a few years ago that companies "could create a product and ship it anywhere around the world like it was Amazon", but this has proved not to be the case.

More recently, Brexit has made it harder to know where to place facilities to serve EU countries. Before Brexit, "You could put a facility anywhere in that geopolitical area.

Now it is not so easy any longer. If anything, Stanley adds, "The geopolitical and regulatory issues are probably even more paramount today than they were five years ago."

This is why one of the major pieces of advice he gives clients is, "Stay close to your regulating body, whether it is in London, whether it is in Washington DC, whether it is in Singapore." It doesn't matter how innovative the client's logistic model is, he says, "The reality is you have still got to play by the local regional jurisdiction because if you don't, you won't be able to ship the product."

## Medical products are not like DVDs

When it comes to managing distribution, says Stanley, some medical device businesses imagine that it is possible to mimic the innovative distribution model of companies such as Amazon.

"They think, 'If they can do it in DVDs and books, we can certainly do that in healthcare'," say Stanley, urging caution.

"It takes a lot of courage for companies to make that leap because people don't die if they don't get their DVD on time, but people can be injured physically and die if the [medical] products aren't where they need to be when they need to be, so there is some degree of hesitancy about saying, 'Well, we will just use that model and drop it in here'."

In fact, Stanley says, the real reason for Amazon's success lies in its collection and analysis of customer data. It has, he points out, "figured out a way to translate the data into really workable operating parameters", resulting in near-seamless logistics.

Many in the medical devices industry are keeping an eye on Amazon's expansionist tendencies.

"This is what scares a lot of the people in my industry, because once Amazon figures out some of the other stuff, they are going to be a force to be reckoned with, because they do understand how to use their pristine data, turn it around, capture it, reuse it in such a way that everybody benefits," says Stanley.

It follows that the companies that have risen most successfully to the challenges of medical device distribution, he says, are those that maintain "pristine data, whether it is customer data, product data or patient data".

As companies come to realise that their data is a type of intellectual property, they become keen to protect it, and some of Stanley's work involves offering advice on the multiplicity of tools they can use to manage their data more effectively.

"They have CRM tools for pricing and contracts and sales, and distribution and so on – and at the end of the day, they are all the same," he points out. "Basically, they have all the same functionality."

The important thing is not which tools businesses use but how they make best use of the data.

So how can businesses make sure that their data is pristine? Stanley says that many companies are reluctant, for security reasons, to use third-party organisations to manage their data. Although he agrees about the importance of security, he is also a strong advocate of making use of the global standards organisation GS1, which he describes as an "industry forum that helps create the mechanisms so that organisations, companies, hospitals and governments can actually have consistent, clean data."

*"Organisations like GS1 provide the platform for companies to stay current 24 hours a day, seven days a week, every day of the week, without missing a beat."*

## Predictability leads to success

The ability to have consistent data that adheres to the same naming conventions makes a substantial difference to an organisation's ability to keep track of crucial information in supplier and customer databases. GS1's Traceability in Healthcare standard, for example, makes it possible to see the movement of medical devices right across the supply chain, tracing backward to identify the product's transfer history, and forward to see its route to the hospital or clinic.

"Take the identifier for what a customer is – you could have 10 different identifiers, or a product could have five different catalogue numbers," says Stanley. "Organisations like GS1 are trying to drive global standardisation in such a way that when you pick up a syringe in the US it has got the same classification, the same catalogue number, as in Belgium or Germany or Norway."

Keeping data up to date is a major challenge, he points out – data that is correct today could be wrong by tomorrow.

"Organisations like GS1 provide the platform for companies to stay current 24 hours a day, seven days a week, every day of the year, without missing a beat," he says. "That is what is different now from maybe 10 years ago when each entity thought they had to create their own data profile. Now they can use organisations that help them keep it consistent and current all across the board, everywhere."

The impact of having data that is both clean and up-to-the-minute is transformative when it comes to managing the supply chain.

"What we see now in healthcare is predictability models being utilised in such a way that manufacturers can start to predict with a better degree of certainty what their customers are going to need or what surgeries are being done," Stanley explains. ▶

Bruce J Stanley

They can even take into account what regulations government agencies are creating and how that affects manufacturers upstream, to the extent that now they have, "good predictability on product flow, product consumption, product usage and, for that matter, product discontinuation with some degree of certainty that they couldn't do before".

## Look beyond healthcare for data analysts

In a world where collecting and understanding data has become essential to keeping the supply chain running, the key skill set, says Stanley, is that of the data analyst.

"You just can't have anyone looking at data," he says. "Now you need analysts who can ask, 'How do we use this in such a way that actually creates optimisation up and down the network?'" Data analysts, he notes, "can pick trends, and predictability is hugely helpful".

This makes it imperative, he says, that businesses employ staff with excellent data analysis skills.

"In healthcare you see a lot of data analysts coming from banking, because people in healthcare realise that these people think differently than we do. It is one thing to have an esoteric view of, 'Well, we are in healthcare because we help patients and cure cancer', but in order to optimise the system or process you need people to think differently."

Stanley and his colleagues have done a lot of work with the banking industry, learning how its approach to data analytics could be applied to healthcare.

"They deal with billions of bits of information routinely – financial, transactional and customers and identifiers, all the kind of stuff that healthcare wrestles with," Stanley explains. "So I always encourage healthcare providers and manufacturers to look to these other industries that may not seem connected, but are really connected when it comes to the capabilities of the people that do the work."

At the same time, it is more important than ever to understand the different regulatory environments under which data is held.

"Data is protected differently from region to region around the world," Stanley points out. "Companies that are global always have to always take that into consideration."

This is another reason, he says, why he encourages global clients to have a presence in the country where they are doing business.

## Sometimes you have to make hard choices

Although Stanley sees good management of data as integral to successful supply chain management, another area that he believes is essential is stock keeping unit (SKU) rationalisation.

"You see any kind of company and they say, 'We have been making this for 50 years and everyone loves it', and the reality is that they may not love it as much as people think," he says. "Companies that tend to be state-of-the-art now are the ones that make the hard choices on SKU rationalisation. They look at their cost. They look at their sale price. They look at their market, they look at their gross profit on those products."

It is a very hard decision to make, he acknowledges, but one that is "crucial to this optimisation of supply chain, because it affects everything from the end-user patient all the way upstream to the supplier or the items that the manufacturer makes on behalf of the patient".

So, what are the big mistakes Stanley sees businesses making time and time again?

"The first one is that they are going to latch on to what they think is the new state-of-the-art technology and never really take a pause to see how that is going to affect how they work and what they do, and their market, their customers and their product line," he says. "So in many cases, the biggest mistake they do is apply new technology on old processes. And then there is just a mishmash and it never works right."

It is surprisingly common, he adds, for businesses to implement technology without understanding how it is going to help their bottom line.

"Often I have asked a lot of CEOs and company leaders, 'How do you work? How do you know what you do?' And I am shocked many times that good companies with good leaders can't really tell me how they work."

Too often, he says, companies "have never done the heavy lifting to do a self-assessment and research what they do, how they do it, and what the costs are." Once you have that knowledge, he says, "Bringing in systems is so much easier because then you go, 'Well, this one really helps us get to that level'. So that is probably the biggest mistake – that people want to rush to new technology because they think it is great."

Ultimately, he says, success is predicated on mastery of the business's core data.

"Once I know with crystal clarity what my customers are, where they are, what their needs are, where they are moving – because they could be moving to a new technology or new procedure – once I have got that in my hands, all the other things are somewhat ancillary because it will tell you where to go. It will become so obvious to someone looking at that data that the rest of it is simple."

# Considerable care from origin to destination

Transporting pharmaceutical products from origin to destination by air is an exclusive and specialist service that requires high levels of care and attention. **Turkish Cargo** flies to most countries in the world and supports a huge network, including freighter destinations.

Turkish Cargo maintains its ongoing activities in order to realise the best transportation of time and temperature-sensitive pharma and healthcare products, to make the Turkish Airlines network even more integrated via Envirotainer operation requirements by adding QEP accreditation to its most important stations.

Envirotainer's QEP accreditation is proof of the brand reliability within the temperature-controlled freight industry, and the result of hard work and dedication to the customers. Negotiations with Dokasch-TS, an active container supplier, have been concluded successfully and the operation started.

Turkish Cargo's biggest difference on cargo business is its network that enables customers to send pharmaceuticals shipments to almost 260 destinations, with new passenger routes consistently opening in Europe and Asia. In order to ensure a high level of reliability and security throughout pharmaceutical shipment, QEP accreditation provides the improvement of ramp-handling processes.

## The only way is up

Turkish Cargo has increased the number of QEP-accredited stations to 40 for handling pharmaceutical products; moreover, last in/ first out procedure, prioritised loading and unloading, a total of 90 minutes on tarmac for transit shipments, quick ramp transfer and thermal dolly are implemented to minimise the ambient exposure in the pharmaceutical-handling process.

Also, specific SLAs/SOPs are signed with esteemed global solution partners and valuable forwarding agencies for risk mitigation and lane assessment. SOPs cover handling, storage and transportation processes of pharma shipments.


Turkish Cargo operates the best equipment to ensure that pharmaceuticals maintain temperature.

*"Turkish Cargo has increased the number of QEP-accredited stations to 40 for handling pharmaceutical products."*

Turkish Cargo was awarded IATA's Pharmaceutical and Healthcare Products Transportation certificate 'Center of Excellence for Independent Validators' (CEIV) at its Istanbul Hub, in August 2016.

The company successfully maintains the recertification process that will be performed by IATA every three years. The process of CEIV Pharma-certification for new airport has already begun.

## All in regulation

The company regularly monitors sector requirements in order to transport according to Operational Quality and Pharma GDP standards, completes the deficiencies and continues to realise activities in this direction.

In this respect, the company is a member of Pharma.Aero, which aims to achieve excellence in reliable end-to-end air transportation of pharmaceutical products. CEIV Pharma certificate is accepted as the standard by the Pharma. Aero organisation.

In order to keep up with the times, some investments should be made continuously in pharma air cargo. The investments must first be made into the facilities, training, and certification required to transport pharmaceuticals safely and securely. Recent cold-chain technology developments provide ensuring temperature condition that are maintain within acceptable limits during transport.

Using the right cold chain equipment is important to reassure pharmaceutical products maintain optimum temperature. Cold chain equipment can be used especially healthcare products. In this way, Turkish Cargo builds a bigger and more special dedicated pharma facility at Istanbul Airport. ●

**For further information**

www.turkishcargo.com

# Your cargo is special

Equipped to carry all types of air cargo in full compliance with global industry standards, and with an in-depth knowledge of the healthcare and pharmaceutical industry, **AirBridgeCargo** has been providing high-quality cargo carrier services to clients around the globe since 2004.

AirBridgeCargo (ABC) is a global cargo carrier with an expanded international route network that connects customers in the largest trans-regional markets of Asia, Europe and North America, and covers more than 30 major cargo gateways, accommodating trade flows worldwide.

All the flights are operated via ABC's cargo hub in Moscow Sheremetyevo airport, which features up-to-date equipment and guarantees seamless connection throughout the airline's expanded international network within a 48-hour delivery time – including handling – all managed by highly skilled and qualified ground-handling personnel.

ABC's fleet consists of 18 Boeing 747 freighters, and is one of the youngest and most modern in the airline industry.

Operating in the market since 2004, ABC is committed to catering to the needs of its customers worldwide with high-quality services. The excellent operating advantages of ABC's freighter fleet, the performance of its highly skilled personnel, and constant improvements to its internal processes enable the airline to carry all types of air cargo in full compliance with global industry standards, including those requiring observance of special handling conditions, such as temperature-sensitive products. The company is constantly reviewing its existing service offers in order to realign them with both market and customer expectations.

## abc pharma – a part of the mission to heal

ABC is the best partner when it comes to an in-depth knowledge of the healthcare and pharmaceutical industry. ABC has developed a special abc pharma product as well as verticals within the company comprising dedicated and qualified staff at all levels – sales, customer service, operations and procurement – helping it to reinforce the handling procedures and control processes required during all stages of transportation. Creation of special services is proof of ABC's commitment to every single detail before and during transportation, especially for pharmaceutical goods that require special attention.

*"ABC's cargo hub features up-to-date equipment and guarantees seamless connection throughout the airline's expanded international network within a 48-hour delivery time."*

Benefits and special solutions of abc pharma include:

- exact temperature monitoring from acceptance to delivery
- special packaging solutions and thermal blankets for palletised shipments
- abc pharma Active and abc pharma Passive solutions – the first is for time and temperature-sensitive pharmaceutical products that need to be shipped in active containers (including dry ice technologies) and the second is for prepackaged pharmaceutical products
- dedicated, skilled staff trained in handling healthcare products
- full compliance with IATA TCR and CEIV certifications
- Envirotainer QEP-accredited stations within ABC network
- customer service support, online track and trace option for all shipments
- Boeing 747-8 and 747-400 with three compartments enabling different temperature settings from 4°C to 29°C
- fast temperature pull down times after take-off
- temperature-controlled facilities at the majority of stations throughout the ABC network
- high-tech pharma hub at Moscow Sheremetyevo International Airport with effective connections to deliver cargo worldwide
- tailor-made logistics solutions based on your individual requirements
- sophisticated, cohesive and forward-thinking approach based on peer learning and networking through industry-related initiatives: these are Pharma.Aero, Pharma Gateway Amsterdam (PGA) and others
- 24/7/365 Control Tower (CT) operation to monitor and manage transportation of special cargo consignments
- adoption of the latest digital technologies (Sky Fresh for automated notifications, temperature data loggers to monitor consignment conditions and more).

## Continuous improvements guarantee the best logistics solutions

From vaccines, laboratory equipment and MRI/MRT machines to blood samples and beyond – ABC, will always find the best logistics solutions to cater your needs and expectations.

ABC aims to continuously improve its service quality, embracing all the company's key components – equipment, personnel, technologies, internal processes and procedures – with implementation of the recent developments and cooperation with partners, sharing its values in terms of high quality standards. ●

**For further information**

www.airbridgecargo.com


# We love
# **to make it happen.**

abc | pharma

- Efficient fleet of B747 freighters
- Active and passive pharma solutions
- Exact cargo temperature monitoring from acceptance to delivery
- CEIV and QEP certifed stations
- Certified and highly-skilled personnel
- Dedicated customer service support
- Online track & trace

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CARGOIQ IOSA Registered Operator IATA | Member CEIV PHARMA QEP Envirotainer

www.airbridgecargo.com

## Glass versus plastic

Accu-Glass's products have many advantages over conventional plastic.

Many advances in manufacturing technology have brought forth new products made from glass, which may have significant advantages over conventional plastics.

Glass is a clean and inexpensive material that is easily manufactured for single-use applications that are frequently required in the medical field. Some of its benefits include:

- can be shaped, cut, polished and marked
- is clean, clear, strong and can be sterilised
- is inexpensive, making it perfect for disposable medical or clinical laboratory applications.

Choosing glass over plastic may be a way to avoid undesirable chemical reactions and unwanted alterations in the properties of the fluid collection or storage method. A wide range of custom shapes, containers and collection devices are available in glass. Glass offers a non-leachable interface between liquid (such as fluids, drugs or chemicals) and container (such as syringes, capillary tubes or ampoules).

Disposable devices are commonplace in medical and electrical industries. Glass devices offer the advantage of being chemically inert, non-leaching and stable at a wider range of temperatures than plastic. Leachables from plastic have the potential to chemically alter the substance with which they interface, leading to undesirable results.

Accu-Glass's precision glass manufacturing process is capable of holding tolerances as low as ±1µ. This lends itself to processes and applications requiring highly controlled volumes, flow rates and physical barriers. Large quantities of glass parts may be produced with a known size tolerance at a time and cost-effective rate.

**Further information**
Accu-Glass
www.accu-glass.com

## Advantech medical equipment builders

Advantech product portfolio includes a range of medical computing systems.

Advantech has been delivering IoT products for over 30 years. To best serve its outsourcing customers, Medical DMS – a dedicated team – was created to provide professional customisation services for industrial-grade computing systems. Advantech specialises in the design and manufacture of high-quality industrial hardware and tailored software that fulfil exact needs for sectors such as gaming, healthcare, portable devices, retail and embedded systems.

DMS offers not only collaborative design, flexible manufacturing and European support, but also a service that gives customers a dramatic market advantage. Embracing the value of altruism, the company is as a long-term partner that helps customers maintain prosperity, now and in the future. The mission of Advantech Medical DMS is to become the strategic partner of the leading healthcare providers. Advantech provides a wide range of customised medical-certified computing solutions. Its product portfolio includes medical computing systems, medical panel PCs/AIOs, medical tablet PCs and fitness computing consoles. With strong customisation capability and experience in medical-grade systems, Medical DMS not only delivers qualified medical computing products to its customers but also acts as the strategic and innovative partner for medical customers.

Reasons to choose Advantech for your next project include:

- complete and integrated back-end infrastructure to streamline design-in processes
- expert engineering, project management and design capabilities for efficient product development
- broad customisation scope for diverse needs in vertical markets
- global design, service and manufacturing centres
- reliable and long-lasting design solutions
- one-stop shopping and a faster time to market
- trusted business model with global partner
- technical feasibility study
- new product developments (CPU cards, chassis and systems)
- design verifications
- changes management
- EOL or LTB management
- product life-cycle management
- refined design, manufacturing and quality processes to meet the medical customer's requirements
- medical product safety and EMC certifications.

**Further information**
Advantech Europe
select.advantech.com/dms

## Custom-manufactured radiopaque clad wires

Anomet's clad composite wires offer an alternative to typical medical wires.

Anomet Products has introduced custom-manufactured clad composite wire – an effective alternative to solid precious-metal wires with marker bands – to improve the visibility of implantable devices. This clad wire is a proven alternative to wires typically used in medical disciplines, such as:

- cardiac rhythm management (pacing and defibrillation)
- neurostimulation
- vascular therapy (stents, catheters and guidewires)
- biosensors
- monitors.

Anomet radiopaque clad wires allow original equipment manufacturers (OEMs) to specify the degree of visibility they desire under fluoroscopy by selecting the radiopaque alloys and cladding thickness best suited to their products. Easier to see than solid wires with marker bands, they are offered in sizes between 0.05mm and 1.52mm (outside diameter) for use with stents, guide wires and related devices.

Featuring platinum-iridium, tantalum and tantalum-tungsten alloys, as well as similar alloys metallurgically bonded to high-strength wires, such as 316LVM stainless steel, nitinol and MP35N with cladding thickness of 2% or higher, Anomet

radiopaque clad wires have a smooth, consistent finish. They are supplied on spools and manufactured to precise OEM specifications.

Anomet is well known as a leader in innovative composite metal products. Founded in 1976, it specialises in the manufacture of custom-clad metal composites featuring a true metallurgical bond. The company is dedicated to developing new products using advanced metallurgical technology, resulting in long-lasting, reliable, cost-effective materials. With material costs today representing 90% of the overall cost of products, Anomet specialises in helping to reduce costs, while improving material properties and quality.

Producing clad wire, rod, bars, ribbon and plates, Anomet Products offers a wide range of metal alloy compositions that are available with virtually any ratio or thickness. The major industries the company serves include aerospace, automotive, appliance, corrosion protection, defence, electrochemical, electronic, industrial, medical, and oil and gas.

**Further information**
Anomet Products
www.anometproducts.com

## Precise quality control

Quality control is a crucial aspect of any manufacturing processes to ensure customers are receiving exactly what they're looking for. Apple Rubber takes proper care in providing customers with precise, high-quality products through rigorous product and material testing, broad ranges of experience, superior design knowledge and state-of-the-art mould making. In order to meet quality standards, everything

Apple Rubber takes the proper measures to ensure high-quality products and processes that meet and exceed expectations.

must be tested – from raw materials to finished products. Apple Rubber has a refined testing process that includes vision-measuring machine dimensioning, durometer, tensile, density and FTIR testing. These tests are a confirmation for the manufacturer and customers that the parts leaving the facility are exceptional and meet set specifications.

Apple Rubber operates state-of-the-art custom moulding in-house, allowing them to produce the highest-quality moulds at the lowest cost and with the shortest lead times. To ensure quality control, it uses sophisticated CAD and CAM software to efficiently design and manage the fabrication and machining of custom rubber moulds. The quality of the moulds is verified with contact, optical and laser measuring equipment. A high-quality product starts with a high-quality mould.

Cleanroom facilities offer heightened quality assurance, allowing manufacturers to completely produce and package products that cannot risk contamination, such as medical devices and electronic components. Apple Rubber's Class 10,000, ISO 7-certified cleanroom facilities feature cleanroom processing, LSR moulding and full-lot traceability.

Through advanced technology, rigorous testing and certified quality control systems (ISO 9001 and AS9100), Apple Rubber can assure precise quality control for every product.

**Further information**
Apple Rubber
www.applerubber.com

## From concept to solution

Backer Calesco's heating products, together with its control devices, offer complete solutions.

Backer Calesco develops new products and solutions in close cooperation with its customers, transforming client requests into working solutions. The process is successfully achieved through a combination of the company's broad experience, advanced design tools and efficient production capabilities.

Backer Calesco supports many segments of the life sciences and medical industries, offering a variety of heating options. By understanding that new tools and equipment are integral parts of advancing the industry to make new scientific discoveries, and recognising the importance of technological advancements, Backer Calesco is able to develop and design heating solutions that work in the medical field. Its expertise regarding heating products allows it to produce heaters that can meet individual heating specifications, and among Backer Calesco's customers are globally recognised companies. Typical applications include:

- surgical tables and beds
- sterilisation equipment
- research equipment for laboratories
- autoclaves
- DNA analysis
- respirators
- incubators.

In conjunction with Backer Calesco's foil heating elements, it is usually necessary to arrange some form of control to ensure that the desired temperature is maintained. A foil element has a tiny mass and is quickly heated, so accurate temperature control is needed. This can be achieved in many different ways, depending on customers' needs. Backer Calesco can confidently design and fit thermal-management systems (such as rigid/flex PCB controllers), a negative temperature coefficient, thermostats, temperature fuses and sensors directly to elements, in accordance with customer specifications. This helps to ensure reliable control.

**Further information**
Backer Calesco
www.backercalesco.com

## Innovation partner for med-tech applications

Cendres+Métaux manufactures high-precision implantable components

Sophisticated solutions in the field of medical device implants often require a range of skills that a single company can hardly master alone. Such developments require close cooperation with partners who offer complementary competencies. Cendres+Métaux, a Swiss manufacturer of high-precision implantable components, has specialised in

offering related skills and services to further the market success of its customers.

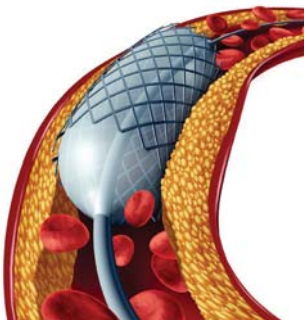
Cendres+Métaux is a valued engineering partner for numerous manufacturers of medical devices, ranging from maxillodental implants to cardiac pacemakers, joint respiration vascular prostheses up to highly sophisticated devices such as permanently implanted hearing aids, or interface connectors for haemodialysis patients.

Medical technology developments require the interdisciplinary cooperation of partners with comparably high levels of competence in the field. An important prerequisite is an in-depth experience with the rules and prescriptions governing the activities related to the development and approval of medical technology products. In the early stages of such a project, an assessment of the basic feasibility of expectations and of the processes that might be suited to master the production of the desired device often plays a decisive role. This, in turn, means that a positive outcome of such a project is more likely the earlier in the development process the partners begin to cooperate. For such endeavours, Cendres+Métaux can contribute a host of very experienced specialist teams along the whole value chain. The number and extent of customer projects that the company has been able to foster until market maturity and successful commercialisation underscores its role as a competent and trustworthy partner for new development undertakings.

Cendres+Métaux masters the full range of manufacturing technologies in its sector, from basic production processing, such as casting, forming, turning, milling or injection moulding, through to surface treating, cleaning, assembly, packaging to supply chain and end-to-end order management.

**Futher information**
Cendres+Métaux
www.cmsa.ch

## Innovation required



Compounding Solutions develops innovative materials for manufacturers.

The medical device industry is trending towards minimally invasive surgical techniques, which requires the development of devices that are smaller and materials that are stronger. Devices for vascular and other such applications continue to reach deeper into the anatomy with more therapeutic technology, and medical device manufacturers are demanding polymeric tubing that boasts greater precision, tighter tolerances and increased functionality.

In catheter design, the designer must not only consider the functional requirements of the application but also be cognisant of the manufacturing process required to produce the device. The designer must identify the key performance requirements of the medical tubing, such as flexibility, lubricity, clarity, kink resistance, push strength, torque transfer characteristics, hoop strength, radiopacity and bondability. Generally, a single polymer material will not meet all of the performance requirements adequately. As a result, designs have become very complex, with different materials required in different areas of the catheter.

For example, for a typical balloon catheter the inner diameter needs to be very smooth and lubricious so that a guide wire can slide with minimal effort along the tortuous path of the anatomy to the treatment site. Though fluoropolymers are traditionally used as lubricious catheter liner materials, they present bonding and processing challenges. A proven alternative would be HDPE loaded with Compounding Solutions' Mobilize technology. Mobilize effectively reduces the coefficient of friction of the catheter inner layer. Polyolefins are also suggested as they are easier to process and bond with traditional equipment.

The healthcare industry demands that OEMs and suppliers produce devices engineered to diagnose and treat patients using innovative design, requiring state-of-the-art manufacturing and technology. In order to support the changing needs and requirements of medical device manufacturers, Compounding Solutions has developed innovative materials such as Mobilize, ReZilok and ReZilient.

**Further information**
Compounding Solutions
www.compoundingsolutions.net

## Accelerating product development

One of the challenges of providing custom manufacturing services is providing a high-quality product in as short a time span as possible. Speed to market wins.

The phase-gated product development cycle goes:

- concept
- initial design
- proof of concept
- detailed design
- prototyping
- soft tooling
- production tooling
- product roll-out.

The proof of concept, prototype and soft tooling phases are typically staged as serial path functions, each with a design feedback loop. Using 3D-printed moulds allows Currier Plastics to combine these three phases into a single one, which means a significant reduction in the product development cycle.

The lead time to print a 3D mould is virtually as short as 3D printing a part, and in some cases it can be less than 24 hours from design to mould print. Some secondary operations may be required, but these are minimal and typically only add a few hours to the phase before the moulds can be run in an injection or blow-moulding press.

Design iterations can quickly be realised, improving final part performance and avoiding costly production tool rework. 3D moulds can be tested prior to releasing the design for hard tooling, and because the parts are made with the actual engineering-grade material, they can be tested for compliance, including

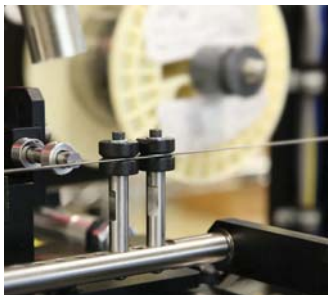
The lead time to print a 3D mould is virtually as short as 3D printing a part.

functional assemblies, chemical compatibility and stability, pressure and leak tests, life-cycle tests and more.

Currier's moulding expertise includes blow moulding and injection moulding. The company is ISO 13485:2016-certified and FDA registered with a Class 8-certified cleanroom at its New York manufacturing site. It offers design, blow moulding and injection moulding all from one team.

**Further information**
Currier Plastics
www.currierplastics.com

## Down to the wire



CWT offers micro-coiling services for wire used in medical device parts.

In a world where wireless dominates discussions about technological advancement, the lowly wire is easily forgotten. However, in the medical device industry, it is an essential component in the development and manufacturing of life-saving equipment.

US-based Custom Wire Technologies (CWT) is a leading medical device original equipment manufacturer (OEM) with experience in diagnostic and interventional guidewires. As the company's name suggests, it is equipped to customise its wire products for a variety of applications, such as guidewire coils and assemblies, Kirschner wires and profile ground-custom tubing.

Many of CWT's clients are OEMs providing innovative solutions to their customers, and they are continually searching for new tools to improve minimally invasive procedures. With this demand in mind, CWT also provides services such as coiling (custom coils, continuous coils and reinforcement coils), wire forming for medical device parts or subassemblies, grinding, fine-wire assemblies, laser and plasma welding, and custom compression springs.

While wire technology's uses are vast, it is not a rapidly evolving industry. Rather, it is the design and application of the wire and tubing in medical products that continue to change. In spite of this, CWT's team of designers continue to push the boundaries of conventional wire processing.

CWT provides flexibility with its micro-laser welding machines, which are capable of rotary and stationary welding. The latter option is typical for custom prototypes and small orders, but automated rotary welding is used in larger production runs to ensure quality, consistency and quick turnaround times.

Another of the company's capabilities is its printing prowess. With 360° rotational printing, it can provide marking indicators and product logos on a variety of medical devices and components. CWT boasts an ISO Class 7 cleanroom for assemblies and packaging to ensure products meet the cleanliness requirements demanded by customers.

**Further information**
Custom Wire Technologies
www.customwiretech.com

## Quality rubber products

Da/Pro Rubber manufactures custom products including diaphragms, seals, connectors, custom shapes, rubber-to-metal parts and more.

Da/Pro Rubber's products meet demanding standards.

Its facilities are located in Oklahoma, California and Massachusetts in the US, as well as Singapore, and it has ISO 9001-certified facilities and a Class 10,000 cleanroom. Known for high-precision, close-tolerance moulding services, Da/Pro Rubber can manufacture LIM/LSR products to these same demanding standards.

The compression and transfer moulding consists of proprietary processes developed by Da/Pro Rubber. The presses are designed to adjust for compound or part-configuration variables. The moulding process is computer controlled and monitored to maintain consistent moulding conditions, assuring the duplication of the product throughout the moulding cycles.

When it comes to material development and qualification, Da/Pro staff chemists are available to develop organic, inorganic or silicone compounds to satisfy specific customer requirements. The physical properties of all rubber compounds that are critical to the function of the moulded product are monitored in the Da/Pro Rubber laboratory.

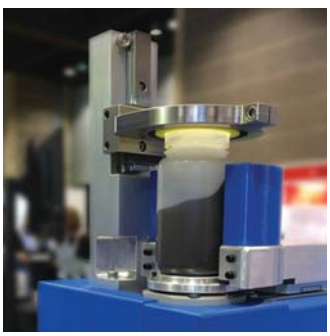
Da/Pro has a complete in-house engineering department to assist with the mouldability of components. The company's CAD/CAM capabilities guarantee effective precision tooling at competitive prices.

To ensure product consistency, quality is monitored throughout each process using a system based on ISO 9001 standards, and advanced statistical process control is used to monitor material properties and mixing, moulding operations and final product conformance to specification.

The final proof of the success of these efforts is the part itself. To ensure quality, all parts are visually inspected to check that they conform to design criteria. In addition, leak and deflection testing for diaphragms and insulation testing for connector inserts may be specified. Whatever the customer's moulding needs, Da/Pro has the expertise, experience and world-class service necessary to find a solution.

**Further information**
Da/Pro Rubber
www.daprorubber.com

## Solving resuspension with advanced technology



Dexter has an ISO 13485 certification for medical device quality systems.

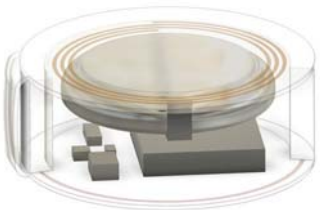
The challenge of using magnetic beads in assays for the life science and IVD (in vitro diagnostics) fields is maintaining a consistent bead concentration, and finding a verification process that measures successful separation and resuspension. The use of magnetic beads to isolate DNA, RNA, proteins and other biomolecules for particle separation is a common practice among many healthcare professionals.

Dexter Magnetic Technologies' engineers have developed magnetic bead-resuspension technology to automatically keep the bead solution homogenous in a variety of vessel configurations, allowing bead concentrations to be quantitatively verified. A magnetic field is created to increase bead agitation that causes the magnetic beads to remain in suspension in the reagent container. Continuous verification guarantees that the beads are properly suspended.

The device is ideal for automated liquid-handling systems, and can be easily modified to accommodate a variety of reagent containers used throughout the life sciences and IVD fields.

**Further information**
Dexter Magnetic Technologies
www.dextermag.com

## Ultra-small NFC sensor modules



Miniaturised NFC sensor module.

DYCONEX has developed a novel approach that delivers miniaturised, hermetic, biostable and highly reliable smart-sensor modules as small as 6mm in diameter and 2.5mm in height.

The tiny modules are based on liquid-crystal polymer (LCP), a thermoplastic dielectric material with very-low water absorption (less than 0.04%), high chemical stability and low thermal expansion. LCP is best suited as both a substrate material and an encapsulate. LCP's permeability for water and gases is the lowest among all polymeric materials. With proper design considerations, LCP packages can achieve a sufficient hermeticity for exposures in harsh environments.

Processing techniques for LCP substrates are the same as for other substrate materials. Resolution of lines, spaces and vias are comparable and multilayer structures can be built-up. Part of the metal layers can be used to form a coil for near-field communication (NFC). LCP is transparent to electromagnetic fields, providing excellent readability for standard RFID tag readers.

The substrates can be assembled with standard SMT processes. Furthermore, embedding of active and passive components within the multilayer system is possible.

The LCP substrates can be connected and sealed without the need for any adhesives, a benefit of their thermoplastic properties.

LCP is a homogenous material and can be easily machined with UV lasers with a precision down to the micrometre scale. Cavities and openings for recessed components can be integrated.

PBS and sulphuric acid soak tests with an embedded, moisture-sensitive test chip have demonstrated long-term stability (over 14 months) in aggressive environments.

LCP allows miniaturised smart sensor modules used in medical, food processing, pharmaceutical, chemical or industrial applications.

**Further information**
DYCONEX
www.mst.com/dyconex

## Precise pressure control for fluid delivery

Fluigent is well known for its high-quality and innovative fluid delivery systems based on pressure actuation. Using pressure to drive liquid flow provides unmatched flow stability and fast response times to any changes. Such systems also enable easy handling of disposable reservoirs of different sizes to adapt any requirement. Since its inception in 2006, Fluigent innovations have advanced pressure actuation technology to become the standard for microfluidic-based devices. The company is now expanding its OEM offering.

Fluigent's reputation for quality is evident in the PX pressure controller.

Fluigent has recently introduced the new PX pressure controller for integrated fluid handling in OEM systems. This series of miniaturised systems combines the excellent performance of the patented, field-proven Fastab technology for optimal flow control with the robustness required in demanding industrial environments at an affordable price.

The PX module is a CE and RoHS-compliant single controller available in three pressure ranges: PX-1 at 0–1,000mbar, PX-2 at 0–2,000mbar and PX-V at -600–0mbar (vacuum). It has been designed to maximise versatility with its dual-interface USB and RS232 ports, and is delivered with a full software package (SDK) to ease integration into Windows or Linux-based software platforms.

The company's reputation for quality (Fluigent is certified ISO 9001 since 2010), customer satisfaction and flexibility make it the company of choice for microfluidic OEM instrumentation.

**Further information**
Fluigent
contact@fluigent.com
www.fluigent.com/oem

## Award-winning implant syringes

Gaplast's innovative syringe application system has garnered much praise.

Implantation syringes are used for the application of medication (for instance, in cancer therapy) when the treatment is necessary over a long period of time. The medication is delivered in the form of a rod-shaped tablet placed subcutaneously. This procedure is often very painful and usually requires a local anaesthetic. There is also the chance that the medication can either be pushed deeper into the tissue than necessary or not deep enough, resulting in the tablet sticking out of the tissue.

Thanks to Gaplast's innovative syringe application system, this is no longer the case. The function of the implant syringe ensures that the drug is reliably placed in the puncture channel and not pushed deeper into the tissue, enabling safe and precise injection of the medication into the subcutaneous tissue. This has, of course, greatly

increased the comfort for the patient and a local anaesthetic is no longer necessary.

The reliable and simple application is also of particular benefit to the doctor. In fact, the syringe received the German Packaging 'Functionality and convenience' award due to its "innovative combination of medical packaging and syringe applicator".

**Further information**
Gaplast
www.gaplast.de

## New changeover valve with four channels

All of GeePlus's products can be found on its new website.

The new PT24-2CO pinch valves from Geeplus have a new changeover design with two NO and two NC channels.

Available in a wide range of operating voltages, the PV24 can be supplied with different springs in order to develop the required force to close the NC channels when the device is de-energised. Ideally suited to use with tubing that has a diameter of up to 3mm and wall thicknesses ranging 0.5–1mm, the pinch valve has a tubing clamp that secures the tubing in place during operation.

To replace the tubes, the specially designed clamp can be lifted, rotated through 90° to clear the tubing channels and raise the pinch bar to the mid-position, and then new tubing can be inserted.

Reversing the procedure closes the clamp over all four tubes and retains them securely in position during use.

This, and many other exciting new products designed for use by the medical equipment manufacturing industry, can be seen on the new Geeplus website.

**Further information**
GeePlus
www.geeplus.com

## Adaptable and reliable luer valves

The MLVs are currently available in four configurations.

Halkey-Roberts Robertsite Male Luer Valves (MLVs) are ideal for flushing and drainage applications, IV solutions and home healthcare. They incorporate proven valve technology, are high flow, and eliminate dripping and leakage when disconnected, with no clamping required.

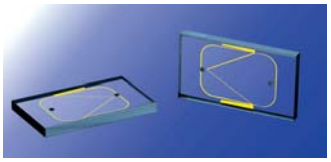
The MLVs are currently available in four configurations: female luer lock, a 0.125in barb, a 4mm tube port and a 6.6mm tube port. They are designed to attach directly to tubing.

The MLV with female luer lock can be attached directly to a syringe or male luer connector. All four valves can be used to access a mating female luer connector or luer-activated valve.

The MLVs are made of a clear polycarbonate body, a clear silicone valve stem, and a clear polypropylene luer and retainer. All materials are gamma-resistant, ISO 10993-compliant, DEHP-free and are made without natural rubber latex. The luer is also ISO 594-2 compatible.

**Further information**
Halkey-Roberts
www.halkeyroberts.com

## Cost-effective glass components



IMT produces customised high-precision, low-cost glass components.

Glass remains the material of choice for many biophotonic and microfluidic applications. It is inert to most chemicals, has unsurpassed well-defined optical properties, and has good temperature and pressure stability. However, glass components also have a reputation for being prohibitively expensive to manufacture, which means that using them as a consumable or semi-consumable in high-quantity applications is not cost-effective. In several cases, it appears to be the cost of the consumable glass components that prevents a new analytic method or technology from entering the mainstream.

Realising the market potential of high-precision but low-cost glass components, IMT of Switzerland is applying the foundry concept to the production of glass components for life sciences, such as microchannels, through-holes, electrodes and waveguides.

By combining the development and production of glass components for many companies at one site and applying manufacturing technologies from the semiconductor industry – and thereby reaching attractive economies of scale – IMT can offer customised glass components at competitive prices.

IMT has over 50 years' experience as a supplier of custom-made glass components for a wide range of optical and sensor applications including delineated optics, reticles, gratings, mirrors and filters. The company's core expertise is the coating and structuring of thin films using microlithography.

Its production environment – which includes 1,300m$^2$ of cleanrooms and a fully automated process line for 200mm glass wafers – is well suited to the mass production of lab-on-a-chip glass components, flow cells containing microchannels, and metallic and dielectric microstructures, in combination with waveguides and gratings.

**Further information**
IMT
www.imtag.ch

## Non-invasive free-entry fluid flow monitoring

Introtek's IntroFlow flow-detection devices incorporate the latest ultrasonic technology.

Introtek's IntroFlow non-invasive flow detection devices incorporate the latest ultrasonic technology for flow measurement. The non-invasive concept provides a platform for non-contact measurement where safety, hygiene and cleaning are of concern. This free-entry sensor is designed for easy tube installation and

can be accommodated for various tube sizes.

Fully integrated electronics yield the smallest footprint, with a simple interface to medical and industrial applications.

The standard configuration outputs a voltage frequency that is proportional to liquid-flow velocity. Absent tube and air detection are fault outputs for added value. Features of the devices include:

- non-invasive ultrasonic
- integrated electronics
- dry coupled
- compact, free-entry design
- low cost
- fast output-response time
- low power consumption
- high EMI and RFI noise immunity.

The options for the devices include a wide range of tubing sizes (custom prototypes), custom configurations and options available upon request. The applications for the devices include medical technology, the biopharmaceutical industry, liquid dispensing, and fluid-handling and process technology.

**Further information**
Introtek
www.introtek.com

## French leader in sterilisation services

IONISOS has the facilities for ionising radiations and EO.

IONISOS is a leading service provider for treatment using ionising radiations and ethylene oxide (EO). It has nine plants in Europe. There are three gamma plants in France, based in Sablé, Dagneux and Pouzauges. The company also owns a fourth gamma plant in Tallinn, Estonia. IONISOS has three ebeam plants in Europe: one in Chaumesnil, France; another in Taracon, Spain; and a third cross-linking plant in Bautzen, Germany. It has two EO plants in France, at Gien and Civrieux.

Additionally, IONISOS is a service provider for sterilisation, decontamination of medical devices, implants, packaging for drugs, raw materials, drugs, API, cosmetics and cross-linking polymer applications.

**Further information**
IONISOS
www.ionisos.com

## Motion control and counterbalancing through precision spring products

John Evans' Sons serves many of the world's largest medical companies.

John Evans' Sons is 'America's oldest springmaker'. Founded in 1850, the company manufactures precision springs, wire forms, mechanical assemblies and stampings. It is a leading manufacturer for the medical-equipment industry and has provided spring assemblies for many of the world's largest medical corporations.

Evans' quality assurance procedures have been surveyed and approved by more than 300 of the world's largest corporations. By employing ISO 13485:2003 and ISO 9001:2008, in conjunction with cutting-edge inspection and calibration systems, it can ensure that customers' most exacting requirements are met.

The engineering group consists of skilled professionals with broad experience in the design and development of all types of springs. The group is backed by an unusually high level of expertise – due to having more than 160 years in business – and the latest in spring manufacturing equipment.

The company provides three different types of spring:

- Constant-force springs provide a smooth range of motion and a constant load in the extending or retracting direction. This spring design has no inertia to overcome when considering the initial-position starting forces. Constant-force springs are compact and mount easily to existing hardware.
- Spiral torsion springs allow rotation in two directions and a 'return to centre' capability. Spiral torsion springs are normally used in applications requiring less than 360° rotation. They are generally used to obtain a large amount of torque with a small amount of rotation.
- Helical spring or wire forms and custom spring assemblies can be designed to meet challenging space and mounting configurations. The company is experienced with many stainless and alloy materials used in critical medical applications.

John Evans' Sons is eager to discuss the design requirements and spring challenges in clients' various design and prototype phases. Many choices of springs and reels are stock items that can be shipped quickly to aid in product evaluations.

**Further information**
John Evans' Sons
www.springcompany.com

## Interconnection expert

Keystone manufactures products suitable for a huge range of applications.

For more than 71 years, Keystone Electronics has been manufacturing quality interconnect components and hardware for original equipment designers and engineers worldwide. Be it portable ultrasound devices, defibrillators, implantable pacemakers or mobile electrosurgical instruments, Keystone's precision capabilities reach the highest standards.

While its full line of catalogue-M65 products meet most standard requirements, modifications and custom fabrications are manufactured to meet special needs. Keystone's engineering team uses manufacturing equipment, including progressive dies, four-slide stamping, wire-forming, in-die tapping and high-speed blanking, along with automated machining, to produce tight tolerance standards and custom products:

- **Battery clips, contacts and holders:** cylindrical, coin-cell, 9V, lithium-battery, steel, aluminium and plastic holders; battery contacts and component clips; and battery straps.
- **Fuse clips and holders:** auto fuses; subminiature; midget fuses; cylindrical glass 2ag, 3ag and 5ag; and 5mm-style fuses.

- **Terminals and test points:** PC quick-fit; male and female; solderless; PC test points and screw terminals; and SMT/THM test points.
- **Spacers and standoffs:** nylon, brass, aluminium and ceramic materials; and clear hole, swage or force-fit, hinged and threaded styles in imperial and metric threads.
- **Panel hardware:** handles; mounting screws; fan and finger guards; LED spacer mount and lens caps; knobs and instrumentation cases.
- **Pins, plugs, jacks and sockets:** USB and firewire plugs and sockets; banana, audio and phono plugs; binding posts; test and micro jacks; micro and push-in pins; and modular Rj45 jacks.
- **PC board and multipurpose hardware:** computer, threaded and mounting brackets; PCB accessories; clamps; ties; grommets; bushings; bumpers; washers; eyelets; rivets; tool kits and turret terminals.
- **Terminal board and strips:** scored and turret terminal boards; and terminal strips.

Keystone is ISO 9001:2015-certified by DNV Certifications under the RAB and RvA accreditations, and compliant with RoHS and REACH directives. It is headquartered in the US with offices in Canada, Europe, Australia and Asia.

**Further information**
Keystone Electronics
www.keyelco.com

## Helping companies to evolve

Innovative solutions in the medical device industry often contain software. For this purpose, medical device

Developing medical device software calls for a specialised approach.

manufacturers frequently hire software development companies to create this component. However, software development companies are not always familiar with the regulatory requirements for medical device software, especially when it comes to the maintenance requirements in the post-market phase.

A sole software developer is often not prepared to support a medical device manufacturer throughout the whole life cycle of the medical device containing its software. To avoid the failure of such projects and frustration on both sides, software development companies need to become software development partners. They need to understand the needs of medical device companies and be prepared for long-lasting relationships.

The following key rules should be considered by software development companies when developing software that is a for a medical device or is intended to be part of a medical device:

- Employ considerate software developers who wish to think about a robust software architecture before they start programming, and who document their decisions and source code.
- Think about regulatory requirements and risks related to the software system from the beginning. They are important inputs to your software design and architecture.
- Do not view the project as an isolated development project. You need to consider interrelations with experts from a medical background, regulatory experts, and various other stakeholders who provide support during development and once the software system is used live.
- Do not underestimate the maintenance effort once the medical device software is live. Changing medical device software requires a sound impact analysis and should be understood as a project itself.

**Further information**
Knoell
www.knoell.com/en/business-units/medical-devices

## Medical-standard welding

The Leister Basic S is essential for effectively welding plastic components.

The new Basic S from Leister is the perfect integrable plastic laser-welding system for the medical industry. Incorporating a unique, state-of-the-art cooling system that was developed in-house, the Basic S is set to redefine the market. The permanent cooling of the laser ensures the precise and repeatable welding of plastic components.

To ensure products can be welded in accordance with stringent medical industry requirements, the Basic S is coupled with powerful software that can record and output all welding-process data and parameters in a single file. Newly developed management profiles divide users into operator, expert and service categories. This critical feature secures parameters from alteration and accidental loss. All parameter changes are recorded and saved in a log. This feature makes it possible to track who accessed information, and where and when data for process modifications were initiated.

A newly developed web-based human-machine interface (HMI) makes integrating the Basic S quick and intuitive. Digital, as well as analogue signals, are clearly displayed graphically and in real time. This new functionality makes it possible to detect which signals are on and off in the Basic S system at all times. Process parameters can be set using the web HMI or directly with the LCD display on the front of the system.

The Basic S can be operated with the innovative, modular Leister laser optics. In contrast to the BT line, premium AT optics offer fibre connection monitoring, laser power measurement and pyrometer functionality. In April, the new Leister Basic S was presented for the first time at MedTec Europe 2018 in Germany.

**Further information**
Leister
www.leister.com

## Custom solenoid valves improve medical device performance and design

With over 20 years' experience in manufacturing medical application solenoids, LISK has grown its expertise and knowledge of customer requirements, and created strong partnerships with its clients. The company's solenoids help its medical device manufacturing partners to use energy more

LISK solenoid valves are manufactured for use in dialysis and anaesthesia equipment, ventilators and respirators.

efficiently, and build more compact and portable equipment. LISK's expert solutions are used in dialysis equipment, and for the critical control of fluid and ventilation applications. In-house design customisation enables the company to optimise its compact, low-energy proportional control solutions.

Key features of the solenoid valves include:

- proportional flow control
- long-life-cycle-tested product
- custom preset and adjustments enabled
- low noise operation
- interface can be changed to customer application.

**Further information**
LISK
www.gwlisk.ie

## More than just FDA regulatory assistance

mdi Consultants has been in the regulatory business for over 40 years and has the expertise to provide exceptional professional aid in:

- US FDA compliance, regulatory strategy development and clinical trial development/ management, as well as QSR/CGMP compliance
- assist with MDSAP implementation and certification preparation
- on-site audits – mock FDA audits by lead auditors that are ex-FDA investigators
- PMA/ANDA/NDA/510(k) application submission services – mdi has a 100% success rate after more than 3,000 510(k) applications
- crisis intervention – 483 and W/L responses and third-party inspections
- electronic drug listing and registration with FDA
- device listing and registration
- US agent services for foreign companies
- assistance with e-MDR
- assist with the UDI for medical devices
- FDA labelling guide reviews for food products, and dietary and nutritional supplements

**Further information**
mdi Consultants
info@mdiconsultants.com
www.mdiconsultants.com

## Developing high-quality springs

Ming Tai Industrial is an expert in producing medical device springs.

Ming Tai Industrial is a professional manufacturer of steel strip springs for medical device applications, including constant force springs, constant torque springs, constant force springs for carbon brush, power springs and prestressed power springs, variable force springs and spring-strip tubes.

As of today, Ming Tai has helped lots of medical device manufacturers to successfully develop new products. All innovative products include a pen-type drug injector, highly adjustable monitor-and-keyboard-integrated medical workstation, highly adjustable patient bed trapeze, highly adjustable patient bedside table, Bowden cable for endoscopes and draw-wire encoder for MRT machines. The performance of Ming Tai's steel strip springs and the company's manufacturing service have gained much praise and appreciation from customers.

Ming Tai is capable of providing customers with technical support during the development procedure and prototype, through to trial runs, mass production, spring mounting and assembly. Each manufacturing procedure, including steel strip slitting, heat treatment, edge trimming and forming process, is a consistent production and completed in-house to ensure the highest quality is achieved.

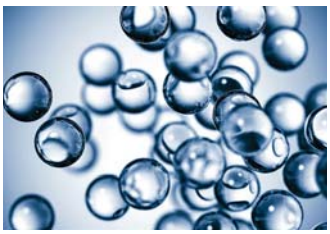
Ming Tai also has precision instruments to do force, torque and product-life testing to ensure quality. Ming Tai is certificated with ISO 9001:2008 and RoHs. There are a number of different spring design possibilities for a given application, and Ming Tai suggests consultation with one of its engineers early in the design phase.

Ming Tai is pleased to create an optimised solution for any spring demand. Custom designs are available as well.

**Further information**
Ming Tai Industrial
www.powerspring.com.tw

## Medical-grade custom glass manufacturing

Mo-Sci specialises in manufacturing technical glass materials such as glass powders, microspheres, and ingots specifically designed and manufactured for the medical industry. Mo-Sci materials, like bioactive glass and precision glass microspheres, can be found in numerous medical devices on the market today. The company has melting capabilities for temperatures up to 1,600°C and quantities from a few kilograms up to several thousand kilograms annually. Its unique in-house capabilities allow it to melt larger quantities in a variety of crucible types. Customers look to Mo-Sci when they need high-purity implant or medical-grade glass materials, or custom glass compositions specific to their application needs. Other service capabilities offered include glass analytics, coatings, spheroidisation and glass development.



Mo-Sci produces technical glass materials for medical devices.

Mo-Sci also serves the aerospace, energy, automotive and defence industries among others. MO-SCI is ISO 9001 and AS9100-certified.

**Further information**
Mo-Sci
www.mo-sci.com

## Protect patients and brands

Recent controversy surrounding the safety of medical devices has made it clear that the industry needs to put quality and safety first.

Medical device recalls cost the industry $2.5–5 billion a year, and companies associated with a recall can expect an average 10% drop in share price.

Lost revenue and increased spending on public relations and crisis communications are inevitable additions to the cost

OPTEL offers turnkey vision inspection solutions that protect patients and brands.

of doing business without a solid brand-protection strategy. Companies with products that represent potential health and safety risks, such as medical implants, often face especially high costs, both financial and reputational.

The bottom line is patients need to know and trust in the quality, integrity and, above all, safety of medical implants and other sensitive medical devices – and brands need to protect themselves.

How can medical device companies make sure their products are safe, were carefully handled and stored, are not counterfeited and do not contain any noxious substance? The answer lies in vision inspection and supply chain traceability.

OPTEL, a global leader in both fields, provides efficient, cost-effective solutions to precisely inspect medical devices on the production and packaging lines.

Leveraging three decades of proven expertise, OPTEL develops world-class vision inspection solutions that ensure the quality and integrity of the product and its packaging, improve the performance of lines and stations, and also minimise risk.

The company's turnkey, scalable solutions provide inspection of seals, packaging, printing and labels, component presence in trays and kits, serialisation, and tracking and tracing capabilities – everything medical device manufacturers need to secure their supply chain and put patients' minds at ease.

**Further information**
OPTEL Group
www.optelgroup.com/medical-devices

## Innovative synergies and packaging solutions

Phase 3 produces high-quality and secure medical device packaging.

Phase 3 Plastics designs and manufactures thermoformed plastic packaging solutions for medical, healthcare, electronic and defence industry clients. The company adopts a synergistic approach with clients to achieve high-standard packaging solutions throughout the thermoformed plastics market.

Its philosophy is to provide clients with solutions that will help them to improve performance, integrity, security and economy. This is done through research and innovation, with a strong focus on design. Phase 3 Plastics' products also meet the BS EN ISO 2001:2015 standards, which ensure the following:

- packaging designed for performance, security and economy
- device transit protection and security features
- J-Class 10,000 cleanroom manufacturing facilities with fully automated manufacturing processes.

Phase 3 Plastics' product range includes:

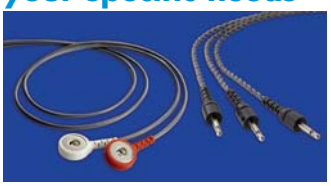
- blister packs or double blister packs
- insert trays and handling systems
- testing trays and protective profiles.

The materials the company uses include amorphous polyethylene terephthalate, polyethylene terephthalate, high-impact polystyrene, polycarbonate and acrylonitrile butadiene styrene.

Extensive market experience ensures that the designs of Phase 3 Plastics' products provide the right combination of performance and economy of scale for successful solutions. The company is always on hand to assess the packaging requirements of its customers.

**Further information**
Phase 3 Plastics
www.phase3plastics.co.uk

## Custom cables for your specific needs



Plastics One is at the cutting edge of medical moulding.

Plastics One has been partnering directly with original equipment manufacturers worldwide since 1949, working together to provide solutions for industry needs.

The company specialises in the design, moulding, and assembly of components and electronics for the medical device industry. Each product is designed with tight tolerances to fit even the smallest device, including parts that are assembled under a microscope.

Plastics One's manufacturing experience is reflected in excellent quality over complete product lines, including:

- patient-monitoring cables
- medical cables and electrodes for EEG, ECG, EKG and EMG studies
- medical cables for sleep studies
- custom medical cables and touch-proof connectors for various medical devices
- cables for EMS, rescue, police and media communications
- cables and connectors for custom applications.

Plastics One's facility encompasses 100,000ft² and boasts an in-house design department that uses 3D software and a fully equipped mould-making shop, with the latest in plastic injection-moulding technology. Plastics One also employs a dedicated research and development team that is constantly searching for cutting-edge methods and products. This allows the company to produce quality products from concept to creation and design, and to build its own customised machines, as well as retrofit existing machines to meet specialised needs.

Plastics One realised a need for cleanroom manufacturing in the medical device industry and added a Class 10,000 cleanroom, in addition to the eight already in the facility.

The new 760ft² cleanroom is fully maintained and certified as required by ISO 7, and will be used for moulding, assembly and packaging parts for the medical device industry.

**Further information**
Plastics One
www.plastics1.com

## Precision saves lives

Protomatic is a prototype and production computer numerical

Design it, and Protomatic can make it from any material.

control (CNC) contract manufacturer specialising in orthopaedic, cardiovascular and medical devices. It 'always strives to enhance product quality, while also improving the quality of human lives'.

Gearing the company's manufacturing capabilities to the medical industry enables it to reduce development time, bringing about faster commercial launches. It has proved itself as a provider of quality orthopaedic devices, forming long-lasting partnerships with customers that require high-quality, precision medical products.

Protomatic manufactures orthopaedic tools, cardiovascular pump components and precision medical device components for diagnostic instruments, and is an ISO 9001:2015 and ISO 13485:2016-registered company. Its talented, dedicated staff take pride in the superior quality of its wares. Among the products created at Protomatic are:

- cardiovascular medical equipment components
- trocar devices
- tunellers and cannulas
- peristaltic pump components
- left ventricular assist device components
- surgical tools
- sampling components
- optical stages, lenses and filter holders.

Protomatic also offers CNC precision machining for all medical industries, including biomedical, dental, cardiovascular and orthopaedic. If a client designs it, Protomatic can make it with any material, including aluminium, titanium, medical-grade plastic and stainless steel.

**Further information**
Protomatic Medical
www.protomaticmedical.com

## An innovative oral delivery system

The Sympfiny system makes for easier treatment of children.

It is often difficult to orally administer the correct amount of medicine to children accurately and safely. Young patients refuse the medicines because many of them are bitter tasting. To solve this problem, a new way of administering drugs has been developed, known as multiparticulate drugs: tiny spheres, measuring 0.1–0.6mm, with a protective coating. The coating neutralises the taste of the active ingredient without impairing its effectiveness.

Together, HS Design from Gladstone, US, and the medical division of the Röchling Group have developed the new drug delivery system Sympfiny (registered trademark), specifically designed for this new way of administering drugs. It allows simple and reliable administration, and the exact dosage of the drug. This innovation makes the safe treatment of children considerably easier.

Sympfiny consists of a container for the drug, and an accurately fitting oral syringe for drawing and administering the multiparticulate drug. The oral syringe is connected to the container so that the drug can be precisely dosed, drawn and administered. A plastic part in the syringe allows the dosage to be set safely and transparently. This easy handling means the multiparticulate drugs can be administered as precisely and safely as liquid drugs. With the oral syringe, users can rely on a trusted and proven system that is standard with liquid drugs. Moreover, it is spill-proof, clog-resistant and has a chew-resitant outer shell.

The system can equally be used for dry powder or microsphere drug formulations.

The reusable syringe comes in two sizes and has selectable dose settings. The 1ml and 2ml variations have been tested for dose accuracy and satisfy the requirements of ISO 7886-1 2017. The system fits common bottle sizes and can be prefilled or filled at a pharmacy.

**Further information**
Röchling Medical
www.roechling.com/medical/pharmaceutics/sympfiny

## Over-moulded cable solutions for medical technology

SAB Bröckskes offers a comprehensive range of quality cable solutions.

Cable system manufacturer and cable specialist SAB Bröckskes offers high-quality cable solutions with high material diversity as a plug-and-play solution for system equipment, even for prototypes and small series.

Connection cables for medical devices and treatments are often subject to demanding requirements in daily use, be it through cleaning, disinfection or handling. A well-thought-out system solution is a key factor for reliability and completes the individual application.

The special cable manufacturer SAB is expanding its range of medical cables with a new plug-and-play solution with over-moulding, made of medical-grade silicone or thermoplastic elastomers as a consistent implementation of market requirements. In order to achieve a secure and smooth material connection between the electrical line and the plug, all the necessary components are fine-tuned to each other.

The results flow directly into production. This benefits the manufacturers of medical components as they can rely on the proven support of the biocompatible base material prototype and 0 series through manufacturing lengths starting at 100m.

"This can only be achieved through constant dialogue with customers," explains Marc Gerlatzek, SAB's medical product mananger. "We count on our material diversity, experience and constant investment in the machine park at our site in Viersen."

Possibilities for over-moulded plugs and nozzles are available for almost the complete cabling solution of the SABmed Line material family. Medical cables with the flexible and smooth SABmed T can be engineered and customer customised to produce thermoplastic and elastomeric materials with better haptics than conventional thermoplastics

If a medical cable with UL approval is needed then the material SABmed S UL is used. The base material can be offered as a platinum cross-linked variant, with an ultra-flexible sheath or with a non-

adhesive surface. New developments, such as autoclavable USB 3.0 cables, are already being designed by SAB Bröckskes with an outlook to possible over-moulding. Manufacturers of medical devices will be able to use this complete system solution as a tailor-made plug-and-play product from a single source, allowing greater design freedom in the development of devices.

SAB Bröckskes is a world-leading manufacturer of cables and wires, cable harnessing and temperature measuring techniques. More than 60 years of experience in cable manufacturing, as well as in temperature measuring techniques, has turned a one-man business into a company with almost 500 staff members.

The strength of SAB Bröckskes is not only the manufacturing of standard cables, but also the construction of special items. Every year, SAB manufactures more than 1,500 special cables on the requests of customers.

**Further information**
SAB Bröckskes
www.sab-cable.com

## A reliable, cost-effective and disposable connector system

Eclipta is suitable for disposable medical applications.

Smiths Interconnect's Eclipta ECL series features high-performance, edge-card technology designed to enable quick and reliable connections, while delivering the serviceability and affordability required by a broad range of critical medical devices. Eclipta's easy assembly and high-density design makes it the ideal connector system for disposable medical applications.

For electrophysiology catheter applications, Eclipta connectors bridge the gap between the catheter and the extension cable.

A standout feature of Eclipta is the fact that the printed circuit board (PCB) acts as the contact in the connector. Since the board is part of a disposable device, it eliminates the cost of using a contact system. In addition, its plug-and-play design provides effortless termination and virtually eliminates the potential contact damage associated with the termination process. An added benefit of incorporating the board inside the connector is the ability to add active-surface mount components, such as electrically erasable programmable read-only memory (EEPROM), to either side of the board.

Eclipta's storage/processing temperature range is -40°C to 135°C, which allows use with standard sterilisation protocols, including autoclave, ethylene oxide (EtO) and STERRAD. Its high-mating lifetime of up to 2,500 cycles increases the mean time between failures (MTBF), and the fingerproof contacts on the reusable side contribute to the safety of patients and medical personnel.

Eclipta has been developed to deliver benefits to healthcare providers, while addressing their real-world manufacturing process needs, as its component design facilitates easy assembly and increased labour efficiency. Additional benefits include the mass termination of catheter wires directly to the PCB in the disposable and reusable sides, scalability, customisation and the possibility to be reworked on the reusable side.

**Further information**
Smiths Interconnect
www.smithsinterconnect.com

## Quality guide wires

SP Medical offers a wide range of guide wires for use in angiography, cardiology, urology and gastroenterology.

SP Medical is a Danish company with more than 30 years of experience in the development, manufacture and sale of guide wires for the medical industry. Over the past 30 years, SP Medical has built up its knowledge of polytetrafluoroethylene-coated products and medical devices for leading suppliers, such as those that supply sterile-packed guide wires, or offer guide wires on an original equipment manufacturer basis.

It is SP Medical's goal to offer its customers a complete range of high-quality guide wires and special features, if required. The company focuses on core competency within the discipline of its guide-wire manufacturing process, so as to be able to offer optimal professional consultancy and development to all of its customers at all stages of their projects.

**Further information**
SP Medical
www.sp-medical.com

## Cross-roller ring for robots

With the new cross-roller ring RF, THK is expanding its already large, unrivalled range of cross-roller rings, with a particular suitability as rotary bearing for robots.

The cross-roller ring RF.

The cross-roller ring RF reduces the total weight of a construction, due to its unique design with a flange. It also allows direct mounting to the shaft and housing, making a housing flange unnecessary, which reduces the number of assembly steps and parts required.

THK's cross-roller rings are particularly powerful cylindrical roller bearings for momentary loads and loads from all directions, including those from the axial and radial directions. This is achieved by the crosswise arrangement of the cylindrical rollers, which roll in right-angle ground raceways.

THK offers the cross-roller ring RF with or without an inner flange. With an inner flange, the bearings are offered with inner diameters of 20–95mm, and without an inner flange that has inner diameters of 40–120mm.

**Further information**
THK
www.thk.com

## All the information in one place

The Organisation for Professionals in Regulatory Affairs (TOPRA) is the one-stop shop for EU training resources on medical devices, in vitro diagnostics and combination products. The company provides:

- essential overviews of medical device regulatory affairs for new recruits, and intensive introductory courses for those committed

to building a career in this speciality
- topic-focused continuing regulatory education and development courses, and masterclasses for senior professional as well as a highly respected master's qualification in medical device regulatory affairs
- small-scale roundtables to summits and international symposia where regulatory leaders and influencers network with regulators and policymakers.

TOPRA is the gateway to building an extensive European-focused network of medical device and IVD professionals from across the world.

Join TOPRA and the vibrant community of over 1,000 medical device professionals in the Medical Technologies Special Interest Network; take part in the members-only online community discussions; access free SPIN webinars on a wide range of topics, including vigilance changes, incident reporting and clinical evidence requirements. Read the latest legal news and developments in the monthly 'MedDev update' newsletter, and in-depth review articles in the peer-reviewed *Regulatory Rapporteur* journal.

The theme of this year's TOPRA Annual Symposium, 30 September to 2 October, is 'Europe at the forefront of global healthcare regulation – Driving innovation through convergent approaches in medicines, devices and veterinary regulatory affairs'.

TOPRA is the one-stop shop for a range of EU training resources.

Organised with the Health Products Regulatory Authority (HPRA) Ireland, the programme will cover topics such as the impact of technology, implementing new medical devices and in vitro diagnostic regulations. Delegates will have the chance to:
- benefit from an extensive EU-focused programme
- meet regulators from around the world
- network with innovators and opinion leaders in healthcare regulatory affairs
- share experiences with peers and discuss potential solutions to regulatory issues
- navigate the practical implications of disruptive technologies and a changing regulatory landscape.

**Further information**
TOPRA
www.topra.org

## High-quality electronic manufacturing and design


TRICOR Systems provides award-winning contract manufacturing.

TRICOR Systems, a US full-service contract manufacturer, is a US FDA-registered, ISO 9001:2015, AS9100D and ISO 13485:2016-certified electronic design and medical manufacturing facility. Founded in 1976, TRICOR has successfully provided high-quality products and services to the medical marketplace.

TRICOR possesses the expertise to design, develop, verify and manufacture Class I, II and III medical devices. It offers a wide variety of services, ranging from short-run prototypes and preproduction units to long-range production. Value-added services include experienced engineering staff to develop electromechanical and electro-optical equipment, from concept to full production; hardware and software design; packaging; qualification testing; and printed circuit board layout, from through-hole to surface-mount.

Whether a client is looking for a complete turnkey solution or is just supplementing its internal capabilities, TRICOR has the background and flexibility to meet every requirement. TRICOR offers customers the opportunity to confidently outsource project needs.

**Further information**
TRICOR Systems
www.tricor-systems.com

## Analytical chemistry – unknowns are unacceptable

In accordance with ISO 10993-1, 'Biological evaluation of medical devices – evaluation and testing within a risk management process', material characterisations should be considered for every device. Extractable and leachable studies are conducted to get a full characterisation of all chemicals, which is then used to create an accurate assessment of risk.

The expectation is that all chemicals are identified, so avoiding unknowns in chemistry reports is paramount. If unknown chemicals are listed in a report, be prepared for regulators to require you to complete the identification – complete material characterisation cannot exist with unknowns.

Regulators will look for extraction conditions that demonstrate a device has been challenged.

Full characterisation of all chemicals is required for an accurate assessment of risk, and it is WuXi AppTec's goal to identify all of the potential chemicals that could come out of your product. Using multiple analytical methods, WuXi AppTec's team of chemistry experts work tirelessly to understand your materials, processes and products to detect a full range of organic, semi-volatile and volatile chemicals, providing you with the data you need to make informed decisions and meet current regulatory requirements. Some benefits of using WuXi AppTec include:
- 80–85% of the time, the company is able to meet biocompatibility systemic endpoints with chemical characterisation and risk assessments.
- Unknowns can delay testing up to 27 weeks and can cost more than $75,000.
- WuXi AppTec has completed more than 4,500 material characterisations.

WuXi AppTec Laboratory Testing Division's medical device platform is the leader in complete identification – to WuXi AppTec, unknowns are unacceptable. Let its team design a chemistry programme tailored to meet your analytical needs.

**Further information**
WuXi AppTec Laboratory Testing Division Medical Devices Platform
medicaldevice.wuxiapptec.com

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# NSF INTERNATIONAL'S MEDICAL DEVICE eLEARNING

**Learn from our experts at your own pace**

## > Design Controls for Medical Devices and IVDs

NSF International's web-based virtual training course provides a basic understanding of Design Controls for medical devices and IVDs.

## > European Union Medical Device Regulation – EU MDR

This on-line course provides comprehensive instruction on the EU MDR. It walks students through every aspect of the regulation and identifying key topics and changes, including the new roles associated with EU MDR; standard requirements that must be met by all manufacturers regardless of class; and the requirements for conformity assessments. The module also provides pre and postmarket requirements of conformity assessment.

## > FDA Medical Device Reporting (MDR)

The U.S. Medical Device Reporting regulation (21 CFR Part 803) contains mandatory requirements for manufactures, importers and device user facilities to report certain device-related adverse events and product problems to the FDA. This course provides critical information to ensure mandatory reporters maintain compliance with the regulation.

## > FDA Presubmission (Q-Sub) Program – Requesting FDA Feedback

The presubmission or Q-Sub program is a voluntary mechanism to get FDA's feedback on specific questions necessary to guide product development and/or application preparation. This course provides instruction critical to prepare for a successful meeting with the FDA.

## > MDSAP and Regulatory Transitions – The Basics Virtual Training

This course provides the basic knowledge to prepare for the Medical Device Single Audit Program (MDSAP). It helps key personnel realize the urgency regarding MDSAP readiness and offers answers to vital questions direct from global Quality Systems expert, Kim Trautman, a former U.S. FDA official and key member of the original MDSAP development team. Learn about the MDSAP audit model, and grading nonconformancies, and regulatory transition timelines, to name just a few highlights of the course.

## > Medical Device Regulatory Requirements (5 course bundle)

Medical devices regulatory requirements for the United States, Japan, Australia, Brazil and Canada. A comprehensive overview of each countries' medical device regulatory framework, including both premarket and postmarket requirements.

Register today at **nsf.learnupon.com/store**
Use code **MDD20OFF** to receive 20% off all courses

Contact us at: **medicaldevices@nsf.org** or call **+1 202 822 1850**

**www.nsf.org**