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VOLUME 14, ISSUE 6

# Pharmaceutical MANUFACTURING

THE DRUG INDUSTRY'S VOICE FOR MANUFACTURING EXCELLENCE

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*PLUS...*



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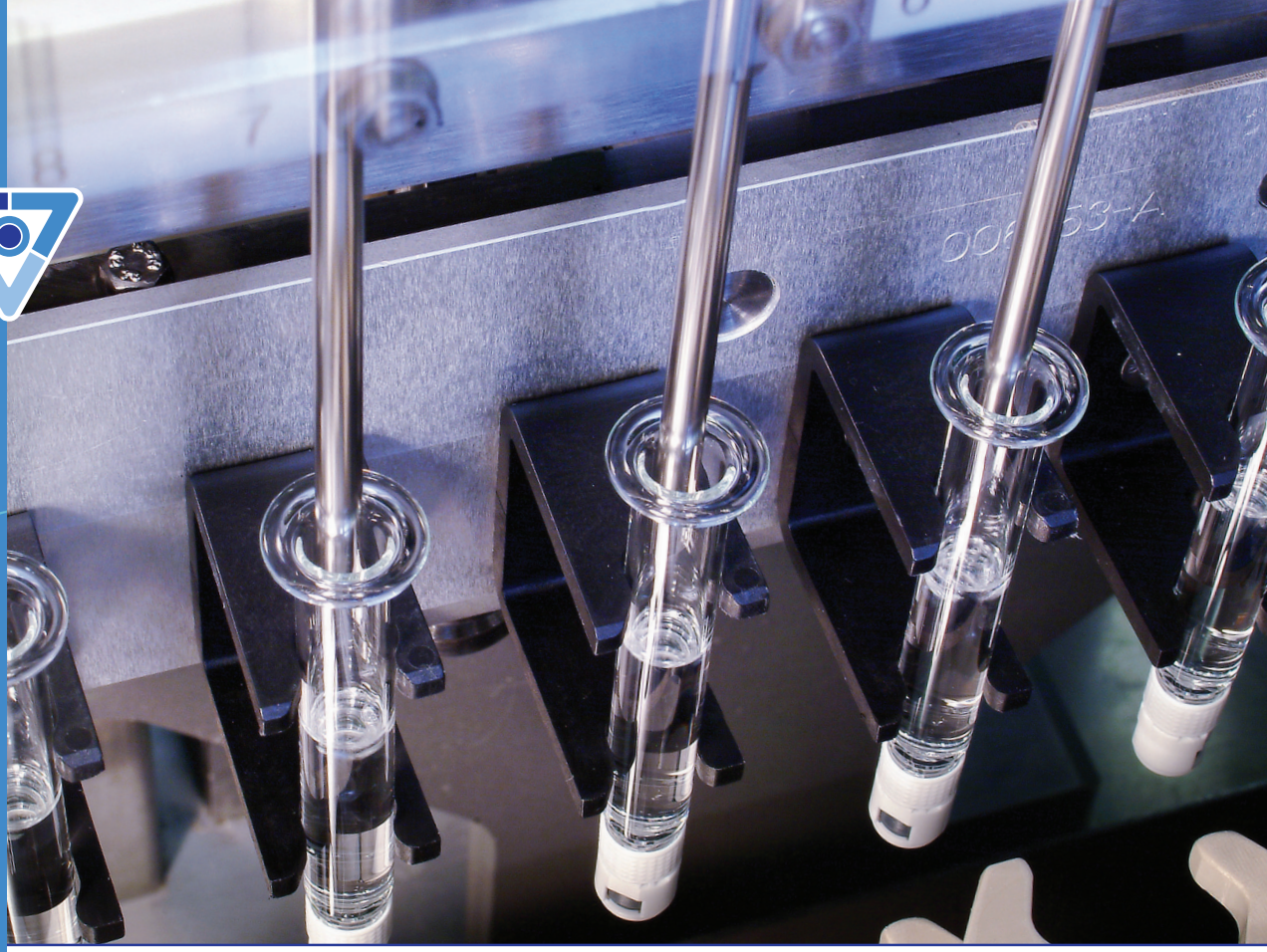

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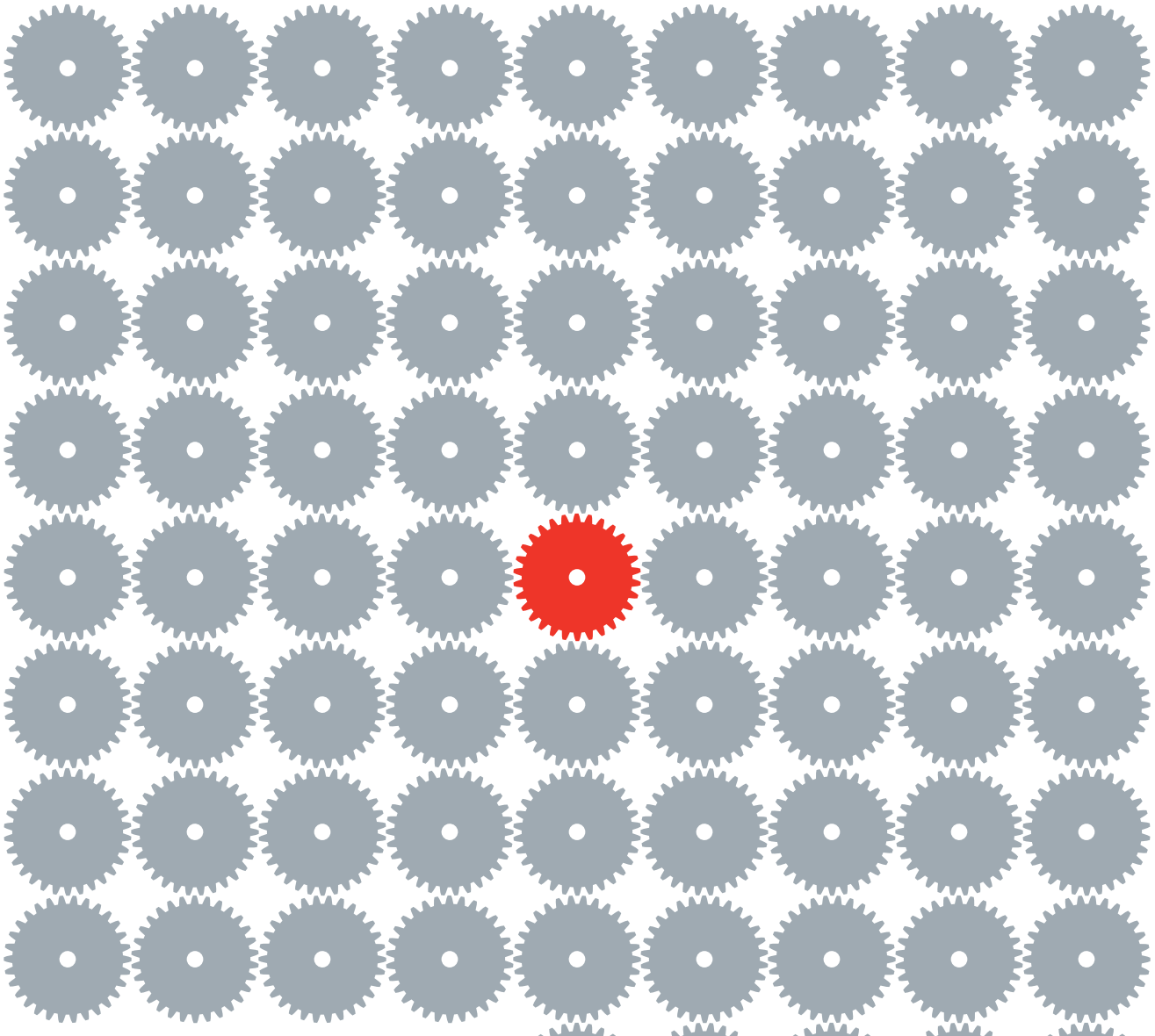

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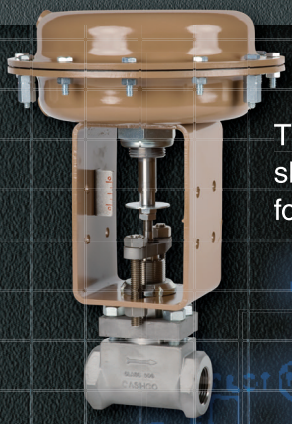

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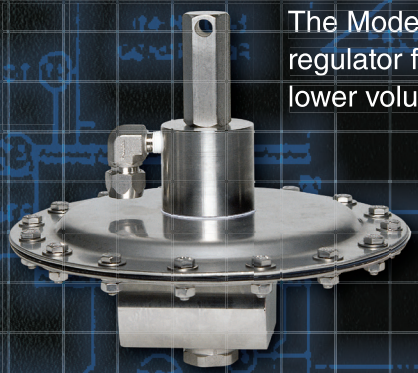
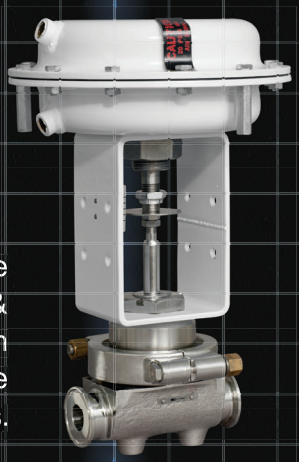


The Model 1088 is a perfect blanketing regulator for small batch tanks with lower volume requirements.



The Model SCV-S & SCV-30 are constructed for clean steam & process fluids respectively. Now with the compact C-27, these models are perfect for OEM skid installations.

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# New Ideas Welcome Here

Advancing Pharma's craft is both art and science; innovation drives them both

**IT'S ALL-STAR** season here at *Pharmaceutical Manufacturing,* and at game time we're excited to bring you what we think is a winning roster of technologies from the industry's most respected and talented suppliers.

Personally, I enjoy editing the All-Star Innovators issue. There are many reasons why, but this issue always resonates with me because it focuses on technology —something I've been fascinated with since assembling my first plastic model airplane at age six, a Spitfire I recall. Sentimentality aside, members of the amazing global technocracy we like to call the Pharmaceutical Manufacturing industry have always recognized how important and central applied industrial technologies are to the industry's mission and ultimate goal, delivering better health by manufacturing safe, effective quality medicines.

The Pharma global industrial complex certainly has its warts, but it's becoming apparent that the most successful pharmaceutical manufacturers are supporting their innovation and competitiveness by paying close attention to the technical advances and solutions the vendor community brings to the industry. To Pharma's big leagues, Branded Pharma, Generic Pharma, Contract Pharma and Bio Pharma, much of what is advancing the art, craft and science pharmaceutical manufacture comes from technology suppliers competing for their chance at bat.

Successfully applying technology is everything in this arena and in her column (page 9), digital editor Karen Langhauser talks about the Industrial Internet of Things (IIoT to all you acronym fans out there) and how this emerging area of technological innovation has great potential to drive the next wave of operational excellence across Pharma's manufacturing landscape.

A quick flip through the All-Star Innovators issue will confirm that it is intensely focused on applied technology. In fact, it's practically obsessed with it. UpFront has an item on Janssen instituting continuous manufacturing into its operations; not only are they doing it, they are publicizing the capability — that's innovative on several fronts. We've got a contribution from Rockwell on managing global engineering projects efficiently and our own contributing editor and PAT guru Emil Ciurzak went mining for innovation at PittCon and found several process analytical technologies worth a close "scan" on page 26. In Technology Up Close, I cover Festo's innovative approach to automating and controlling modular water processing plant modules with Craig Correa, that company's process control expert. From concept to application, Festo's Lego approach brings the benefits of modularity to process automation system integration to add capacity without the headaches associated with scaling up processes to meet demand and other competitive and operational imperatives.

We dig deeper into automation's role in delivering better control and outcomes for the world's largest maker of custom oligo products, a key building block for molecular research on page 34. This case study details how Beckhoff Automation helped IDT streamline a solid phase synthesis process and deliver solid gains operationally and financially.

**THIS YEAR'S ALL-STAR INNOVATORS** ARE READY TO HELP DRUG MAKERS **BRING HOME THE WINS.**

The All-Star Innovators the *Pharmaceutical Manufacturing* team has chosen for this year's roster were introduced over the last 12 months. These players, through outstanding effort and resulting performance and other operational gains are being recognized for their technical innovation. From robots ideal for tricky maneuvers within sterile containment, to hand-held PAT scanners, and a steam trap that takes full advantage of steam's potential energy and in doing so came up with a design that eliminates all moving parts!

### NEW IDEAS WANTED AND NEEDED

New ideas are always welcome on the pages of *Pharmaceutical Manufacturing* and our goal is to bring to light the best ones from the brightest minds across the commercial manufacturing landscape. For Pharma's biggest teams there's virtually no room for anything but operational excellence, and this year's All-Star Innovators are ready to help drug makers bring home the wins.

**STEVEN E. KUEHN, EDITOR IN CHIEF**
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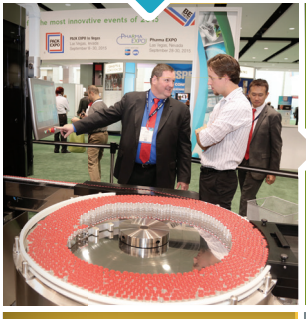





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# IIoT: Buzzwords Have Feelings, Too

BY KAREN LANGHAUSER, DIGITAL CONTENT MANAGER

**BUZZWORDS GET** a bad rap. This is mostly due to operator error. Sometimes really valid concepts get haphazardly tossed around so frequently by people who don't fully understand them that the actual concept starts getting muddled. But this shouldn't always devalue the initial idea.

The "Internet of Things" is a good example. There are so many articles casually using the acronym "IoT" that it has become difficult to find a basic discussion of the concept.

In its most simplistic form, the IoT is a network of physical devices embedded with sensors and electronics, where all the devices speak to each other using the existing Internet infrastructure. The INDUSTRIAL Internet of Things (IIoT) is simply the Internet of Things when applied to the industrial sector (oh hey, that's you guys).

With some touting it as the "4th Industrial Revolution," clearly the IIoT is quite complex and, as I'm not a tech expert, I won't add to the confusing amount of chatter. That being said, the IIoT's applicability to pharmaceutical manufacturing is undeniable, even to the non-technical observer.

Having a network of connected devices in pharma manufacturing facilities means remote access to equipment, proactive maintenance of equipment based on actual logs and analytics, real-time plant floor visibility, the ability to recognize and respond to compliance issues immediately, and the ability to monitor and control serialization. The resulting analytics from these connected devices can be used to improve business and manufacturing efficiency, reduce risk and essentially disrupt aging business models.

As with all technological advancements, there are always associated risks and challenges. Security and data privacy are definitely huge concerns in pharma. Additionally, the industry will be tasked with finding the right software and systems to organize and analyze the huge amount of data that will become available.

Nonetheless, the potential seems almost endless. The Industrial Internet of Things is no longer a futuristic notion. Those that are embracing IIoT are realizing positive, near-term benefits and creating a competitive advantage in the market. There are resources out there to help you plan, execute and optimize your IIoT implementation. Shameless plug aside, Putman Media has one of the best coming up this October. Visit www.smartindustry.com and check out the Smart Industry Conference & Expo.

Perhaps *Wired* magazine put it best when it said, "Unlike consumer-based IoT that is trying to devise a way to make your world a better place by telling you when your washing machine needs service or letting you control all of your home's systems while you are away, the IIoT is working to make our collective world a better place by improving the monitoring, control and safety of everything around us."

For the first time in a long time, the Internet is abuzz with something that might actually eclipse the Internet in terms of impact on the world.

# How to Make Capsules Better

Capsule technology symposium reveals practical optimization strategies to improve operations

BY STEVEN E. KUEHN, EDITOR IN CHIEF, AND KATIE WEILER, MANAGING EDITOR

**QUALITY HARD** shell capsule manufacturing is still technically demanding and operations managers, many tasked with making millions of this dose form daily, still struggle with capsule processing quality issues. In early June, Techceuticals, Federal Equipment and Pfizer convened its second and likely annual Capsule Technology Symposium in Cleveland, Ohio, to help advance the science and craft associated with high-quality, high volume capsule production.

Michael Tousey, CEO of Techceuticals, chaired the event that put experts from Bosch, CapsCanada, Capsugel, Glatt and MG America in front of a diverse group of operations managers and other line staff seeking enlightening advice on how to optimize capsule processes, troubleshoot quality issues and get to share what the industry thinks are best practices.

According to Techceuticals, the purpose of the 2015 symposium was to create a dynamic document that details efficient, effective responses to the common defects. "Every company has their 'go to' capsule guru," says Tousey. "This person dashes in and addresses the situation, leaving before anyone can understand what they did, and why." The Symposium's objective, says Tousey, is to be able to continually train individuals to grow and develop with an understanding that all products don't react the same way. "The team (not the individual) must be able to identify the characteristics of powders and how they react to the process, environment, machinery," says Tousey, "and possess the technical ability to interpret them. Most companies do not have a troubleshooter's guide to solving common capsule defects." Tousey says the document resulting from this symposium will become that guide, in part, he says, because of the contributions of the expert panel and interaction with participants, most involved in day-to-day capsule-making operations.

Over the course of the two-day seminar, speakers from the participating sponsors worked to help reveal best operational practices from most, if not all, aspects of capsule production including formulation, blending and wet and dry granulization, to identifying and fixing the many defects that stem from issues related to the condition, set up and configuration of capsule filling machines, as well as how the shells and their material condition affect quality.


Techceutical's CEO Mike Tousey covers capsule defects and their causes at the company's recent capsule trouble-shooting symposium.

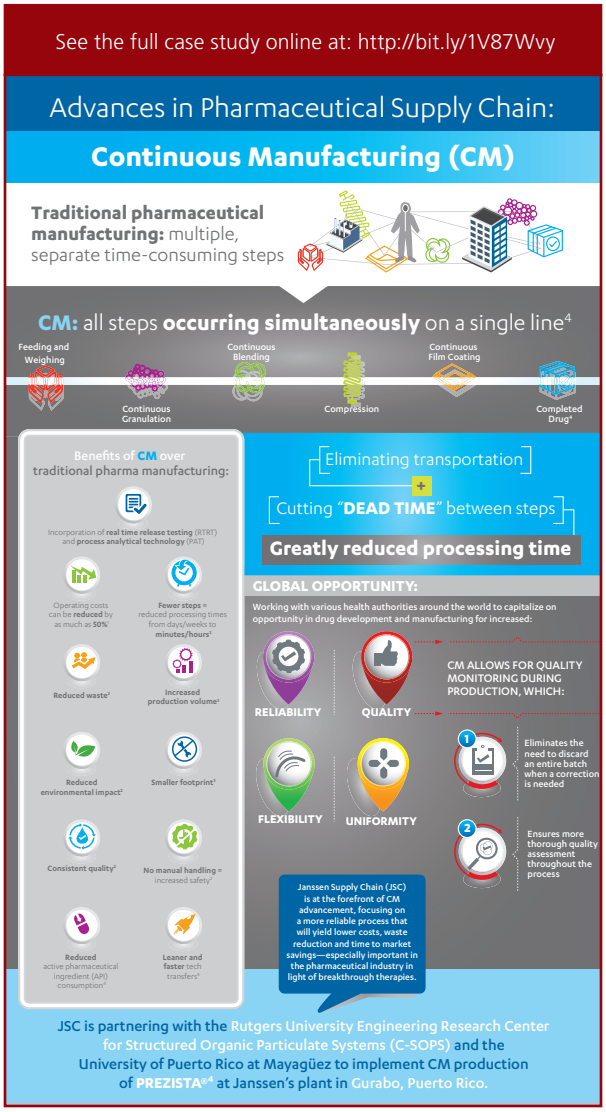
By in large, defects and difficulties associated with capsule manufacture manifest themselves in myriad ways, but usually can be traced to relatively obvious defects or wear/maintenance issues with the machines or the more tricky issues associated with formulization and incumbent processes like mixing, blending and granulization. Because capsule issues often have multiple sources, root cause analysis can often produce false leads. The symposium's panelists and presenters spent considerable time on how to peel back the layers of the onion so operators can determine the most likely cause (or causes) of a defect and ways to approach troubleshooting and resolving the issue.

Ultimately the goal of the symposia is to create a resolution handbook that covers common capsule defects, root causes and suggested remedies. Meant to be a live document, the handbook will always be a work-in-progress, but one that most operations types managing day-to-day capsule production would be smart to obtain. Techceuticals offers a number of training opportunities for professionals in the tablet and capsule production industry. For more on upcoming symposia, check the Techceuticals website http://www.techceuticals.com/.

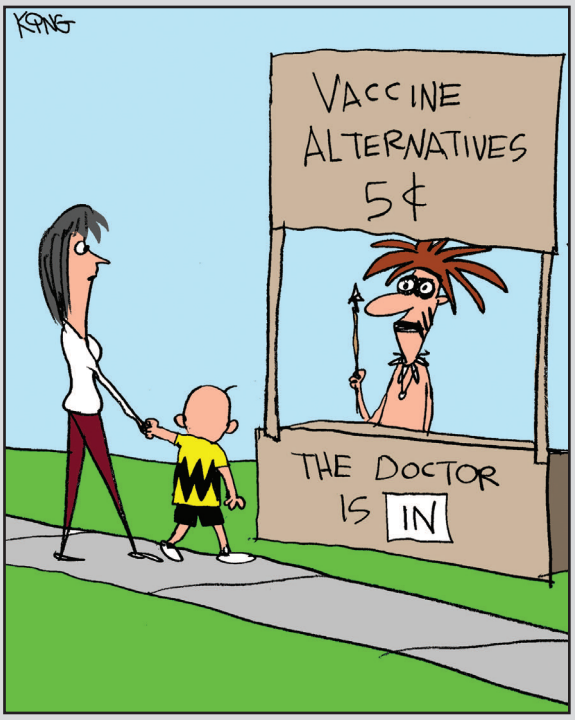
# JANSSEN AIMS TO "CM" PREZISTA AT ITS GURABO, PUERTO RICO, PLANT

Janssen Supply Chain, part of Janssen Pharmaceuticals, Inc., and a pharmaceutical company of Johnson & Johnson, announced recently that it plans to move operations toward continuous manufacturing (CM) and configure its Gurabo, Puerto Rico, plant to manufacture the drug Prezista continuously. According to Janssen Supply Chain, [the company] "is at the forefront of CM advancement, focusing on a more reliable process that will yield lower costs, waste reduction and time to market savings — especially important in the pharmaceutical industry in light of breakthrough therapies."

The announcement, which came in the form of a highly accessible, visually engaging infographic (below), says JSC is partnering with Rutgers University Engineering Research Center for Structured Organic Particulate Systems (C-SOPS a leading academic proponent of CM) and the University of Puerto Rico to institute CM processing at the site. Overall, says Janssen with the integration of CM, "Janssen and J&J aim to manufacture 70 percent of 'highest volume' products using CM within eight years, increase yield by reducing waste 33 percent and reduce manufacturing and testing cycle times by 80 percent. Janssen says CM can reduce operating costs by as much as 50 percent and provide increased production volume while requiring less API and reducing waste.




## FUNNY PHARM




"Our remedy has no preservatives, additives, dyes, GMOs or GMP."

— Tara Bronson

*Funny Pharm comics, drawn by professional cartoonist Jerry King, appear on PharmaManufacturing.com. Readers submit suggested captions. Above is March's cartoon and winning caption.*

# PLM Formulations for Chemicals

The roots of product lifecycle management and how PLM can help chemical companies today

BY TONY CHRISTIAN, DIRECTOR, CAMBASHI

**PRODUCT LIFECYCLE** Management (PLM) originated in the automotive industry, and as a breed of IT application it is still mainly associated with discrete manufacturing. Having started with the scope of product data management for the development phase of a product lifecycle, the reach of the technology has evolved to cover the full product lifecycle — and close the loop by supporting the exploitation of field experience to drive front end innovation (for example, Oracle seeks to reinforce this by referring to 'Product Value Chain Management').

The PLM technologies designed for discrete manufacturing industries deliver enormous benefit in product development scenarios involving high numbers of parts with their relationships defined by a well-structured bill of material (BOM) and especially where there are a variety of different individuals/organizations contributing to the development, manufacture, sale and support of the product. As a result, the PLM market has grown to approaching $3 billion in software revenues and much larger if you count the services and support ecosystem.

Having said that, although progress in recent years has been substantial, the adoption of PLM in chemicals has been rather more tentative — with good reason.

## PLM IN THE CHEMICALS INDUSTRY

PLM's initial foray into the process industries came from several directions. First, there were the understandable efforts to bend, twist and augment the functionality of the systems that had proved highly capable for discrete manufacturing. At a high enough level, this would be fine — the chemicals industry formulation simply replacing the automotive BOM (although while a car has more than 30,000 components parts, it's unlikely that a chemical formulation will have 30,000 ingredients). And after all, PLM is brilliant information management technology with workflow and information flow capabilities built in. However, the requirements of the chemicals industry have proved quite a barrier to moving discrete manufacturing technologies across.

Contemporary discrete-manufacturing PLM technologies knit together the data from the various applications used in product development — CAD, CAE, CAM. Some of the top PLM vendors (Autodesk, Dassault, PTC, Siemens) are companies that provide those 'data creation' solutions too. There is a "kind of" equivalence in the chemicals industry in terms of the range of applications involved in product development (for example, tools to support the development of formulations, lab data management, DoE and so on) but there are key differences as far as achieving the same breadth of coverage with PLM.

Chief among these are the fact that development of formulae for chemicals products involves a variety of scientific processes and the product data includes production process parameters; packaging is often an integral part of the 'product' and must draw on all manner of product attributes; and the product-related information to be managed involves a combination of structured and unstructured data that is a real challenge for traditional discrete market PLM technologies.

**EARLY ERP SYSTEMS ARE RATHER LIKE CONCRETE — YOU CAN HAVE IT ANY SHAPE THE FIRST TIME, BUT IT'S HARD TO CHANGE.**

PLM offered chemical producers another solution initially, an extension of the business (ERP) system vendors' product information management capabilities. However, the same limitations still apply and the approach seemed to embody a tacit acceptance of the limitations of PLM —given the goal to manage product information alongside other specialist applications — while providing an overall glue for the application set as well as an index to all the data wherever it's held. Vendors offering applications for specific aspects of the chemicals product lifecycle created a third approach which sought to build these out to provide broader workflow and information management capabilities.

However, chemical companies did not want to wait until there was a total all-embracing solution for chemicals (indeed, they would still be waiting!). As a result, it's perhaps most appropriate to talk about the product lifecycle information management picture in chemicals today in terms of PLM "environments" rather than "systems" because, even within individual companies, achieving a comprehensive PLM capability

has usually involved phased deployment of different applications for specific areas of the product lifecycle and a build-up of integrations to knit them together.

So, given the hurdles that we have identified above, can PLM deliver the huge benefits identified in the sidebar below for the chemicals industry? While there are several aspects that are important to competitive position and for which individual companies can develop their own strategies, there is one, compliance with industry regulations, that is not an option, it's a "table stake." The data needed to meet regulatory requirements varies from region to region or even from one part of a country to another and both the descriptions of the requirements and the information to be supplied comes in a variety of formats. So the document management capabilities of the PLM solution must be highly flexible in that respect alone. In addition, compliance must be monitored throughout the product lifecycle, all the way for initial development to retirement, given that regulations change all the time. A good example of the regulatory demands on the industry is the REACH (Registration, Evaluation, Authorization and Registration of Chemicals) safety standard that requires manufacturers and importers in Europe to register chemicals of which more than one tonne are used annually by supplying information such as chemical formulations, uses, volumes used and safety test results.

The industry still makes wide use of document-management-type systems for gathering and maintaining this type of information, but it's not surprising that it's an area that PLM's information management capabilities can address very well, with its traditional strengths in centralizing document storage, version control and information dissemination. Consequently, many chemicals companies have led their PLM strategies with regulatory compliance as the core requirement. Of course the danger is that a rich PLM system can end up as a glorified document management system focused solely on this aspect of product information requirements.

So while PLM provides strong document management capabilities, what else can it do towards delivering the type of benefit enjoyed by the discrete manufacturing industries? Well, today's systems have come a long way. The data-handling capabilities can accommodate the variety and dynamism of the information requirements in the chemicals industry. The drivers for this variety and high pace of change are numerous. Many customers in the chemicals industry are other manufacturers that have their own application and require specific product data. Raw materials prices are volatile, and for many it is an ongoing mission to seek alternatives that can be factored into a formula. Packaging and labeling requirements vary enormously from territory to territory, and development of the packaging is in itself often a complex technical development issue, given the need to meet safety requirements and provide a sufficiently long shelf life.

By taking a pragmatic view of the balance between what should be included within the scope of the PLM system itself and where PLM should provide integration glue with specialized applications information and workflow management solutions have evolved that can indeed support collaboration across the lifecycle.

There are a number of vendors that have achieved strong chemicals PLM capabilities — the approach following on naturally from their starting point. So the PLM vendors that have traditionally led the way in discrete manufacturing have acquired relevant technologies to enhance the capabilities of their PLM systems for process industry applications (Dassault with Enginuity, Accelrys; Oracle with Agile, Prodika; Infor with Optiva; Siemens with Simatic), or by continuing to build out from their original chemical industry-focused applications (Selerant, Sopheon).

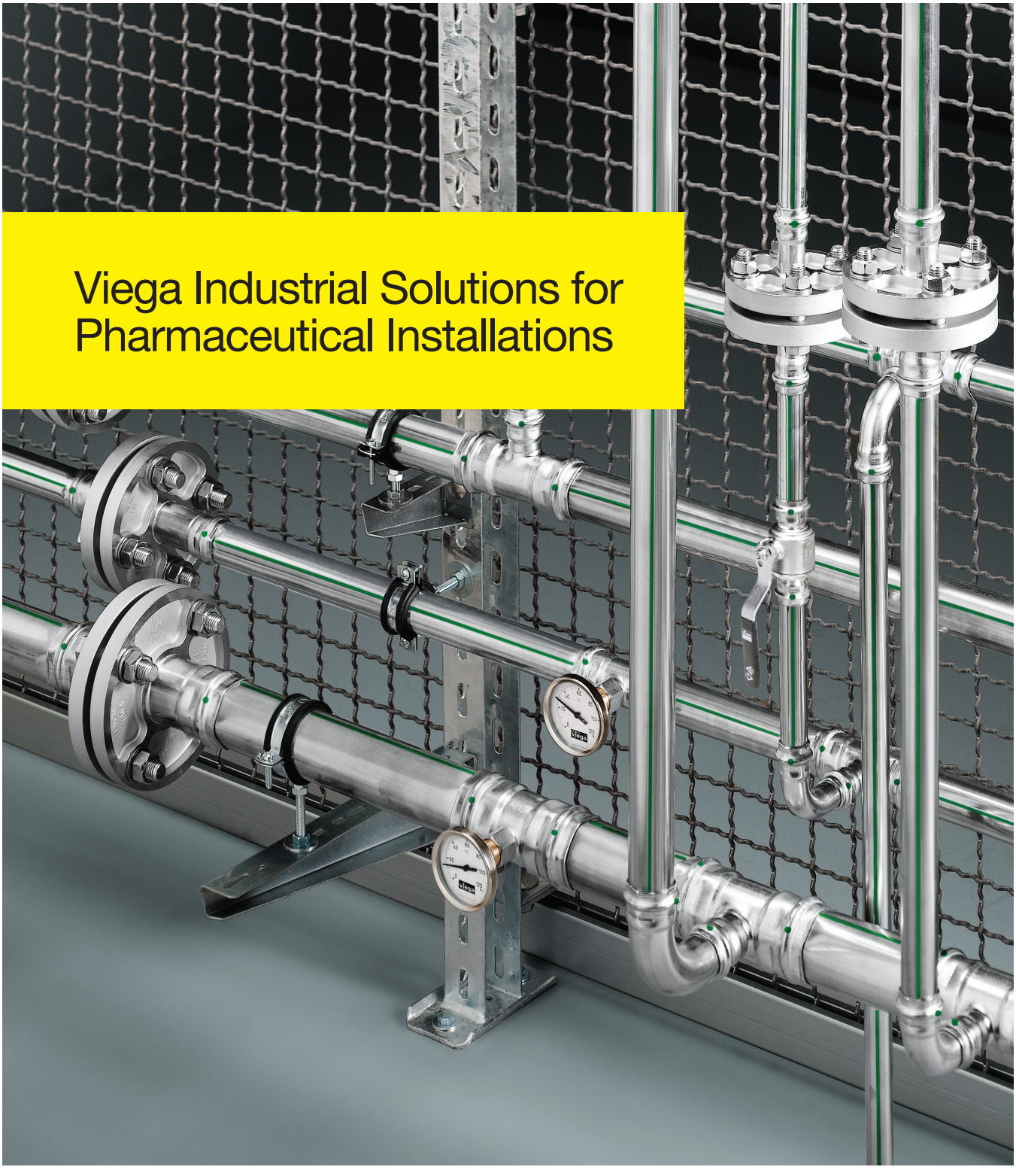
Due to the limitations of early solutions, the industry has a legacy of customized systems, stand-alone applications and integrations that, like the early ERP systems, are rather like concrete — you can have it any shape the first time, but it's hard to change. However, the combination of growing process industry PLM capabilities and the cost and accessibility advantages offered by the new cloud-based IT infrastructures are likely to make a change to a more off-the-shelf approach much more attractive.

## WHAT PLM CAN DO FOR CHEMICAL FIRMS

For discrete manufacturers, classic PLM benefits include:

- Integration of "data creation" systems leading to a reduction in the complexity of managing product development processes through effective collaboration.
- Controlled sharing of information throughout the value chain — integration of information across the product development, manufacturing, supply, support and retirement processes.
- Better decisions on optimization of the innovation project portfolio — including information drawn from field performance of products held in ERP systems.
- Ease of collating and organizing information associated with industry regulations.

# Viega Industrial Solutions for Pharmaceutical Installations



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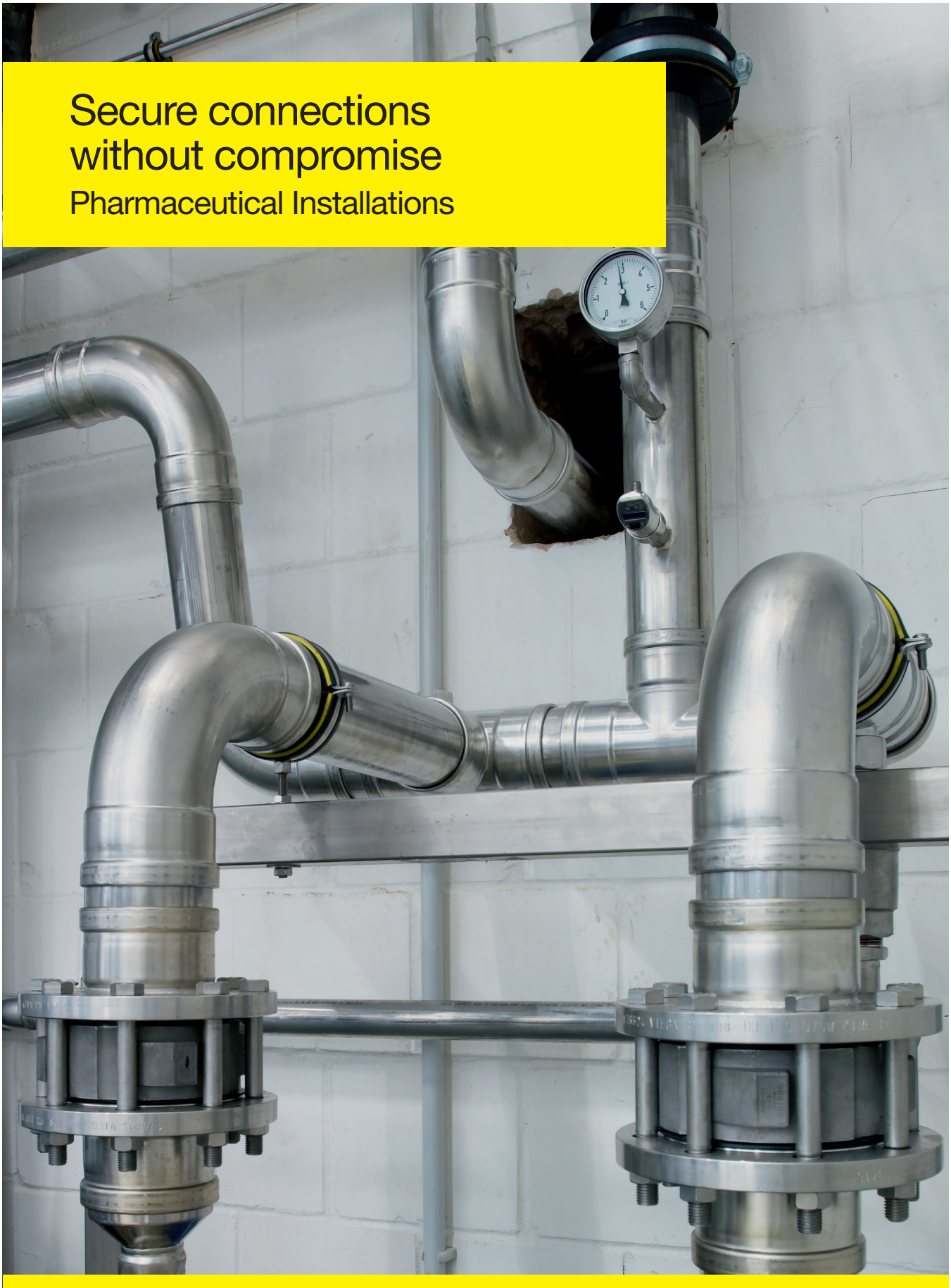
## Pharmaceutical Installations



# Viega systems are clean solutions

When pipe joining systems must provide clean, consistent performance, Viega press systems offer guaranteed reliability and efficiency whether the installation is potable water or process piping. Viega ProPress systems are well suited for pharmaceutical applications because installers don't need materials like solder or cutting oils, which can contaminate the entire system.

Available in stainless steel, Viega ProPress systems provide clean, flameless connections that can withstand high temperatures, pressures and corrosive cleaning materials. Viega ProPress systems are also available in copper. Viega MegaPress carbon steel fittings provide fast, clean connections for black iron.

Viega solutions are backed by written warranties and may be installed in the following systems:

| | |
|---|---|
| Acetylene | Instrument air |
| Ammonia | Isopropyl alcohol |
| Argon | Low-pressure steam |
| Carbon dioxide | Nitrogen |
| Caustic vent piping | Oxygen |
| Chilled water | Potable water |
| Condensing water | Process water |
| Fire protection | RO/DI water |
| Gray water | Steam condensate |
| Hydrogen | Vacuum |
| Hydronic heating | Wax |

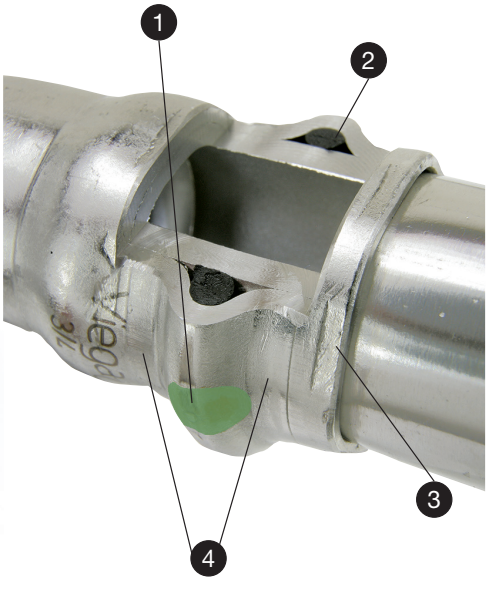
"With Viega ProPress for stainless, you can go into areas that don't allow hot work, even if it's a hostile environment. That's very important, especially in biotech suites."

**- Mike Feldman, Vice President, Hart Engineering, Cumberland, RI**

# Safe, secure solutions minimize shutdowns

Viega press fitting systems offer the only guaranteed method in the industry to detect unpressed fittings. The Viega Smart Connect feature allows installers to easily identify unpressed connections during pressure testing.

The patented Viega Smart Connect feature is built directly into the press fitting itself, which consistently allows water or air to leak past the sealing element of an unpressed fitting. Connection identification methods based within the sealing element found in other manufacturers' fittings aren't always reliable because sealing elements can be damaged or improperly installed, which can result in a false positive pressure test.




**1** The Viega Smart Connect feature helps installers ensure that they have pressed all connections.

**2** Viega offers three different sealing elements suitable for nearly any application: EPDM, HNBR and FKM.

**3** Viega's distinctive hexagonal pressing pattern connects fitting and pipe to provide a strong mechanical connection.

**4** Cylindrical pipe guides help installers ensure that the fitting is properly aligned on the pipe.

### Viega ProPress and Viega MegaPress systems operating parameters

| | Stainless | Copper | Carbon Steel |
|---|---|---|---|
| Operating pressure | 200 psi | 200 psi | 200 psi |
| Test pressure | 600 psi max. | 600 psi max. | 600 psi max. |
| Low-pressure steam | 15 psi max. | 15 psi max. | 15 psi max. |
| Vacuum | 29.2" Hg at 68°F max. | 29.2" Hg at 68°F max. | 29.2" Hg at 68°F max. |
| EPDM operating temperature | 0°F to 250°F | 0°F to 250°F | 0°F to 250°F |
| FKM operating temperature | 0°F to 284°F | 0°F to 284°F | FKM seals not available |

Consult Viega on parameters, selection of material and sealing element choices.

# Solutions that exceed your expectations

Viega ProPress and Viega MegaPress fittings have been tested to the strictest standards in North America. Viega ProPress in copper and in two grades of stainless steel, 304 and 316, is suitable for nearly any application, from potable water in commercial projects to corrosive chemicals in industrial projects. Viega MegaPress is the only press fitting system for black iron pipe that can be installed in both water and gas applications, residential, commercial or industrial.

# Approvals and Certificates for North America

ASTM A240
ASTM A312
ASTM A403
ASTM A554

ASME B16.51
ASME B31.1
ASME B31.3
ASME B31.9

American Bureau of Shipping

NSF-61 Annex-G Zero Lead Components

CRN – Canadian Registration Number

CLASS 6812 01

CLASS 3305 11
3305 91
3305 99

UL 213

CLASS 1920

Contact your local Viega district manager for details on local approvals.

Viega ProPress and Viega MegaPress fitting systems are also compliant with the following:

ICC International Plumbing Code

PHCC National Standard Plumbing Code

UPC Uniform Plumbing Code

UMC Uniform Mechanical Code

| Types of Service | System Operating Conditions | | | ProPress 304 Stainless | ProPress 316 Stainless | | ProPress | ProPressG | MegaPress | MegaPressG |
|---|---|---|---|---|---|---|---|---|---|---|
| | Comments | Pressure | Temperature | FKM | EPDM | FKM | EPDM | HNBR | EPDM | HNBR |
| **Fluids/Water** | | | | | | | | | | |
| Hot and Cold Potable Water | | 200 PSI | 32°F-250°F | | √ | | √ | | | |
| Rainwater/ Gray Water | | 200 PSI | Note *4 | | √ | √ | √ | √ | √ | √ |
| Fire Sprinkler | | 175 PSI | Note *4 | √ | | | √ | | √ | |
| Chilled Water | Ethylene Glycol / Propylene Glycol | 200 PSI | Note *4 | √ | √ | √ | √ | | √ | |
| Hydronic Heating | Ethylene Glycol / Propylene Glycol | 200 PSI | Note *4 | √ | √ | √ | √ | | √ | |
| Cooling Water | Up to 50% Ethylene Glycol or Propylene Glycol solution | 200 PSI | Note *4 | √ | √ | √ | √ | | √ | |
| Deionized Water | | 200 PSI | 158°F | | √ | | | | | |
| Low-Pressure Steam | | Up to 15 PSI | 248°F | √ | √ | √ | √ | | √ | |
| Isopropyl Alcohol | | 200 PSI | 75°F | | √ | | | | | |
| Latex Paint | | 200 PSI | 32°F-250°F | | √ | | | | | |
| Methyl Ethyl Ketone | | 200 PSI | 230°F | | √ | | | | | |
| Nitric Acid | 10% | 200 PSI | 73°F | √ | √ | √ | | | | |
| Phosphoric Acid | 25% | 200 PSI | Ambient | | √ | | | | | |
| Paraffin Wax | | 200 PSI | 100°F | √ | | √ | | | | |
| **Fuel, Oil and Lubricant** | | | | | | | | | | |
| Heating Fuel Oil | | 125 PSI | Note *4 | √ | | √ | | √ | | √ |
| Diesel Fuel | | 125 PSI | -40°F-180°F | √ | | | | √ | | √ |
| Ethanol | Pure Grain Alcohol | 200 PSI | Note *4 | | √ | | √ | | | |
| Liquid Propane | Compliant with CSA LC4 | 125 PSI | -40°F-180°F | | | | | √ | | √ |
| Liquid Butane | Compliant with CSA LC4 | 125 PSI | -40°F-180°F | | | | | √ | | √ |
| Kerosene | | Note *4 | 68°F | √ | | √ | | √ | | √ |
| Lube Oil | Petroleum Based | 200 PSI | Note *4 | √ | | √ | | √ | | √ |
| **Gases** | | | | | | | | | | |
| Compressed Air | Less than 25mg/$m^3$ oil content | 200 PSI | Note *4 | √ | √ | √ | √ | √ | √ | √ |
| Compressed Air | More than 25mg/$m^3$ oil content | 200 PSI | -40°F-180°F | √ | | √ | | √ | | √ |
| Natural Gas | Compliant with CSA LC4 | 125 PSI | -40°F-180°F | | | | | √ | | √ |
| Oxygen - $O_2$ (nonmedical) | Keep oil and fat free / non-liquid $O_2$ | 140 PSI | Up to 140°F | | √ | | √ | √ | √ | √ |
| Nitrogen - $N_2$ | | 200 PSI | Note *4 | √ | √ | √ | √ | √ | √ | √ |
| Carbon Dioxide - $CO_2$ | Dry | 200 PSI | Note *4 | | | √ | √ | √ | √ | √ |
| Ammonia | Anhydrous | 200 PSI | 122°F | √ | | √ | | | | √ |
| Acetylene | | 200 PSI | 86°F | √ | √ | √ | | | | |
| Argon | Welding Use | 200 PSI | Ambient | | √ | | √ | √ | √ | √ |
| Hydrogen - $H_2$ | | 125 PSI | 0°F-250°F | | √ | | √ | √ | √ | √ |
| Vacuum | | 29.2 in Hg | Note *4 | √ | √ | √ | √ | √ | √ | √ |

1. All systems are recommended to be clearly labeled with the fluid or gas being conveyed. For further information please consult Viega Technical Services.

2. All Viega systems must be used with the manufacturer's recommended sealing element. Contact your local Viega representative or Viega Technical Services for application temperature, pressure and concentration limits.

3. System pressure and temperature ranges depend on sealing element.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The term Viega does not apply to a specific company within the various separate and distinct companies comprising the Viega group of companies. The term Viega as used in this publication refers to the Viega brand itself or generally to the Viega group of companies. References to activities in North America specifically refer to activities of Viega LLC.

# Pharma's all-star tech athletes have the gear to win the big game

By Steven E. Kuehn, Editor in Chief

**EVOLUTIONARY OR** revolutionary, technical innovation is supporting new gains in pharmaceutical manufacturing and processing efficiency. That is, the technologies are available to help achieve these gains, but only if these players get a chance to get out of the bullpen and have their turn at bat. Let's be honest, it's been a long time since Pharma's leadership in manufacturing excellence was accepted as fact, but there are plenty of drug manufacturers out there (as well as their design, engineering and technology suppliers) who beg to differ.

But it's a new year and another season entirely, one spanning an incredibly dynamic, complex global marketplace. The pace of change and the market's dynamics are prompting fresh capital investment in equipment and facilities, especially in the Bio and Contract Pharma sectors. Pressure on global players to improve quality is intensive. Excluding Japan, Asia's Generic Pharma business is spending more than ever to gain compliance and subsequent relief from regulators. All of Pharma's big teams want to play in this World Series, but to do it successfully they have to be competitive; and increasingly, to be competitive manufacturing operations have to be fit, flexible and agile enough to meet the market's challenges while beating other teams playing the field.

Pursuing competitive agility through operational excellence is a winning strategy most of Pharma's manufacturing-oriented leadership will recognize. The means to achieve competitive agility is increasingly coming from the Pharma industry's technology and system suppliers. Many companies are delivering technical innovation to support drug development and innovation. These innovators deserve to be recognized. What follows are this year's All-Star Innovators, technologies and systems introduced within the last 12 months that, based on their relative applicational and technical merits, were selected by *Pharmaceutical Manufacturing*'s editors and reviewers to be on this year's All-Star Innovators Roster. Just like in the big leagues, products and companies (players and teams) were featured on their own baseball card, complete with performance and other stats. What follows are excerpts from those cards, but to view them in their entirety, visit *PharmaManufacturing.com* and click on the "All-Star Innovators" logo. For now, though, take a look at who made this year's roster; there's bound to be something able to help make your process or operational task a winner for your organization.

# Analytical and Monitoring Devices

**AMETEK Crystal Engineering**'s HPC40 Series hand-held calibrator leads off, ready for on-the-run calibration tasks around the plant. Because the HPC40 Series is the world's first mA loop calibrator that is fully temperature compensated from -20° to 50°C, it can deliver the same accuracy whether measuring pressure, current, voltage or temperature. The HPC40 can typically replace several gauges or calibrators and offers a full-color display paired with a new user interface that offers a shallow menu structure allowing tasks to be performed quickly and intuitively.

To help users gain a better understanding of biologic formulations earlier, **Malvern Instrument**'s Zetasizer Helix combines Raman spectroscopy with Zetasizer dynamic light scattering (DLS) technology to conduct highly detailed protein aggregation mechanism studies. According to Malvern Instruments, a key priority for the industry is obtaining a greater understanding and control over the formulation process, a need exacerbated by the increasing adoption of QbD. By allowing users to fully scope protein behavior within a formulation, the device provides insight at the molecular level as to which variables trigger, for example, oligomerization and aggregation, this supporting a QbD approach.

**Primex Wireless** offers a pervasive, flexible wireless solution with its OneVue Intelligent Monitoring Platform. The platform, says Primex, is unique in that the data generated by sensors is tied to the room, physical equipment (such as refrigerators) or inventory (such as pharmaceuticals) being monitored, rather than to the sensor. As a result, OneVue delivers comprehensive, historical data trails for compliance audits, preventative maintenance, benchmarking, cost comparisons and more — all without requiring users to merge records each time a sensor is changed or assets are moved.

Like the bat is to baseball, so is **Thermo Fisher Scientific**'s Gemini handheld FTIR and Raman analyzer; that is, it's essential, portable and goes where the game is. According to Thermo Fisher, Gemini analyzers require minimal training and are easy to use. The innovative design combines FTIR and Raman spectroscopy in a single, lightweight but rugged handheld instrument that delivers lab-quality analysis on demand. For those substances identifiable by Raman and FTIR, the scanner provides comprehensive analysis, delivering more actionable information to the operator. Switching between analysis techniques is fast and easy using the tactical keypad or touchscreen.

Unified to simplify chromatographic separation and analysis, the Nexara UC from **Shimadzu Corp.** eliminates the need for complicated sample pre-treatment and enables highly reliable and stable analysis of delicate samples that are prone to oxidation or dissociation if exposed to air. Fully automated, Shimadzu's system can sequentially analyze up to 48 samples via automatic extraction and chromatographic separation combined with high-sensitivity detection of targets by mass spectrometry. According to Shimadzu, the automated extraction and chromatography is achieved using a mobile phase of supercritical fluidic carbon dioxide (that exhibits the solubility of liquids and diffusivity of gases) into which alcohol and other such organic solvents are added.




# Automation, Control and Sensing

**Denso Robotics**' VS-050 Six Axis Aseptic Robot Possesses ISO 5 cleanroom rating and specially designed coverings for applications where biocontamination control is required. Pharmaceutical, medical and life sciences sectors, says Denso, can benefit from the unit's high speed and features like a protective outer coating, and sealed joints allow the VS-050 to be safely sterilized with hydrogen peroxide or UV light. The smooth, rounded exterior of the robot has no external screws, to keep dirt, dust or other contaminants from adhering to its surface. Wires are internally embedded up to the flange and the control-cable connector is located on the bottom of the robot, further streamlining the arm and facilitating cleaning.

The CMSX Closed Loop Controller from **Festo** delivers proportional closed-loop control, energy savings, safety at nearly half the price. The positioner was designed from the ground up, according to the company, to answer the shortcomings of today's closed loop proportional position controllers for quarter turn actuators, namely in the areas of cost, energy consumption and safety. Made from a technical polymer, the housing makes it ideal for indoor and outdoor applications. Most positioners, says Festo, cannot match the control, feedback and simple set up of the CMSX, which meets the IP65 standard for dust and water protection as well as the ISO 5211 mounting standard.

Knowing exactly what's going on with a batch during bioprocessing is important and **Stratophase**'s Ranger Solo sensor technology provides the data one needs to control feeding effectively. (*Editor's note: Although Ranger Solo was introduced more than a year ago, we missed the opportunity to report on it last year as planned so we brought it up from the minors.*) Ranger Solo technology is targeted at single use systems and offers the same functionality as the company's Ranger Probe. Ranger Solo can be integrated into all bioprocessing systems enabling bioprocess managers to automate their feeding regimes by observing the metabolic rate of their process in real time. In addition, Ranger can be used to rapidly determine, identify and react to key process characteristics, such as maximum metabolic rate and process completion.

**GF Piping Systems**' Pressure Regulating Valve Family is well-suited to high-purity piping system duty. Its elastomer-free piston and modular design, in addition to its elastomer-free capability provided by the proprietary piston design, high-purity operation is further enhanced via the valve's threaded bonnet, which has no exposed metal bolts. The central housing nut does away with re-torqueing for easier operation and compact design enables installation in limited space. Other outstanding characteristics include its modular system that allows the user to easily adjust the set pressure range and quickly go from reducing to retaining (or vice versa) by simply switching the cartridge.

# Bio Processing

Ready to bring enhanced single-use efficiencies to fluid transfer, **AdvantaPure, NewAge Industries'** AdvantaPass combines single-use tubing, connectors and seals with permanent, wall-mounted, stainless-steel components to eliminate cleaning validations associated with clean room protocols. AdvantaPass is the first system of its kind to offer complete isolation between manufacturing environments when transferring multiple lines of fluid through a single wall portal. The technology offers a practical, safe, secure and easy way to move large volumes of liquids from one room to another while maintaining separate atmospheres and minimizing cross-contamination risks.

**3M Purification** has introduced a new class of clarifying products designed to help biopharmaceutical manufacturers achieve high product purity early in the manufacturing process. According to 3M, its Emphaze AEX Hybrid Purifier offers improved efficiency and process economics and can deliver the highest possible level of product protein purity early in biopharmaceutical downstream process. By targeting the removal of particularly problematic impurities from entering the protein A column earlier, says 3M, a profound impact on the entire downstream process can be realized.

Need a bigger bat for commercial scale bioprocessing? The Mobius 2000 Liter Single-Use Bioreactor from **EMD Millipore** might be just what is needed to hit that home run. Sporting the industry's first bottom-loading drawer, EMD Millipore says this enables the easiest Flexware assembly installation on the market. A patent-pending baffle design offers the mixing performance of a stainless-steel bioreactor with no cleaning required. A 5:1 turndown ratio provides the most flexible seeding and growth strategy.

With 2000-liter bioreactors up stream, clarification needs to be at similar scale to avoid bottlenecks. To get past such constraints, Sartorius Stedim Biotech introduced **Sartoclear Dynamics** clarification line. Used in combination with precipitation, this technology, says the company, transforms harvesting from a two-stage process into a single-stage operation saving valuable footprint and time. Sartoclear Dynamics consists of prefilled single-use bags containing ultra-pure diatomaceous earth (DE) in a choice of 0.5 kg to 10 kg. Sartorius says customers can expect cconsistent results, ease of use, tremendous speed and linear scalability from this Biopharma player.



# Process Hardware

Installing a Delta DSV Steam Trap from **Delta Steam Systems** can knock some 20 percent off one's boiler fuel bill says the company. The Delta DSV steam trap uses flash steam to create a back pressure inside the venturi. As the condensate is forced through the trap's orifice by the upstream pressure, the resultant pressure drop generates flash steam. This flash steam is about 1,000 times the volume of the condensate so the sudden expansion accelerates the condensate in the venturi. This sudden acceleration creates an equal and opposite force or back pressure inside the venturi, which restricts the flow of less dense steam through the orifice while allowing the denser condensate to be ejected. Delta Venturi Orifice steam traps have an expected lifespan in excess of 30 years. All steam traps are constructed from stainless steel and come with a 10-year mechanical and performance guarantee.

Secotec TF Refrigerated Dryers from **Kaeser Compressors Inc.** handle flows from 520 to 1060 cfm. Kaeser says its new design pushes the boundaries of compressed air refrigerated dryer performance thanks to its game-changing thermal storage system. The dryers' internal design also makes it possible to reduce pressure loss across the dryer to 2.2 psi (compared to 2.9 and higher for conventional models). These dryers include Sigma Control Smart, a micro-processor based controller which controls the thermal storage process. It also has an alarm and service message memory, as well as remote on/off control capability. An optional Ethernet interface for connecting to a master control system is also available.


## Solid Dose Processing

Fit for high-output OSD processing lines, the GKF 2600 Capsule Filling Machine from **Bosch Packaging Technology** offers high output and configuration flexibility. Capable of filling 156,000 capsules an hour, Bosch's high-performance machine doses powders, pellet, tablets and liquids, as well as combinations, precisely and reliably. The machine, says Bosch, is equipped with new filling technologies for different products, an optimized drive concept, significantly enhanced sensor technology for process control, as well as a demand-oriented containment concept.

The XT600 High Speed Double Rotary Press from **KORSCH America Inc.** is specifically geared toward the high volume production of single and bi-layer tablets. Its exchangeable turret, says Korsch, offers the flexibility to produce a tablet of virtually any size and shape with the highest efficiency. The XT600 offers an extremely space-efficient design with a small footprint and ample access for cleaning, changeover, and turret exchange. The unit features a 60 kN or 100 kN compression column for precompression and main compression, plus proven compression dwell bar. Korsch is offering a completely new HMI environment which includes a smart-touch 19-inch HMI display providing an intuitive operating experience. The control capability is supplemented by a comprehensive array of multi-media online help, which features pictures, videos, drawings, and access to machine manuals to support the machine operation, maintenance and troubleshooting.

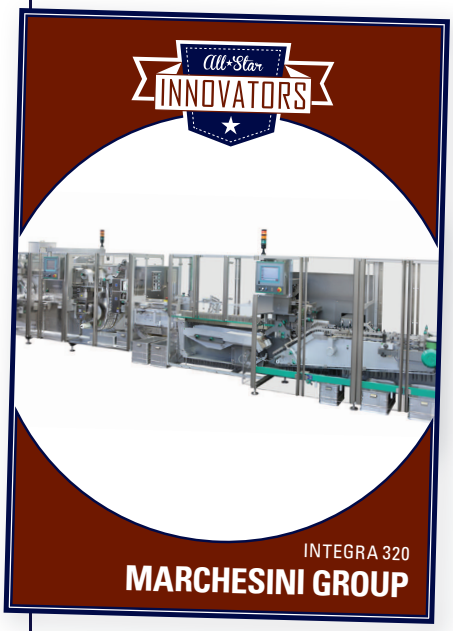
## Information Technologies

**Waters'** NuGenesis Lab Management System is a powerful alternative to a traditional Laboratory Information Management System (LIMS), with advances, says Waters, that enable deeper insight into scientific challenges, accelerated decision-making, better business results and compliance with government regulations. Offering a user-centric platform that encompasses a Scientific Data Management System (SDMS), Electronic Laboratory Notebook (ELN) and Laboratory Execution System (LES), the system offers an optional, secure web-client for sample submissions and results management, and a complete stability protocol management and testing solution to facilitate a consistent regimented workflow across lab operations. Waters says NuGenesis enables science-driven chemical, environmental, food and pharmaceutical companies to connect and communicate across their laboratory operations, maximizing consistency and efficiency across products, labs and countries.

## Packaging and Handling

**Marchesini Group**'s Integra 320 integrates primary and secondary packaging process for faster set up and production tempo. Innovative and ergonomic, Marchesini says the 320 is designed to be installed in rooms of different classes to save time and expense. The integrated robotized blister line offers a mix of innovation and the best of Italian packaging technology, says the company. A new pitch-control system, cartoning section, and carton-opening and product-insertion system has boosted performance to up to 320 blisters and more than 260 cartons a minute. All this, says Marchesini, is incorporated in a very small footprint, thanks to the integration of the blister thermoforming and carton packaging phases in a compact line.

Robots are great efficiency drivers, but only if they can handle what's being manipulated without damaging it — especially if the item is fragile or delicate. The principal behind **Parker**'s Piezo Gripper's piezo electric technology is the fact that it measures changes in pressure, acceleration, strain or force and converts those inputs into an electrical charge suitable for the safe handling of products of any size, configuration or delicacy. Piezo is Greek for '"press" or "squeeze." With the appropriate combination of proximity and position and distance sensors, a piezo-equipped robot can be suited to a wide variety of material handling applications, especially in Pharma packaging's big leagues.





## See More Online

Read more online at www.pharmamanufacturing.com/all-star-innovators/

By Andy Weatherhead, Manager, Global Engineering, Rockwell Automation

# OPTIMIZING GLOBAL ENGINEERING EFFICIENCY

Across major geographies, under-budget projects are the exception rather than the rule

**GLOBALIZATION AND** disruptive technological advancements, such as virtualization, cloud and big data, are continually altering the industrial landscape. To succeed, innovative companies must re-envision where and how they do business so the right resources are applied regardless of their location. In the past decade, concepts like virtual teaming and multi-office execution began to play major roles in the operating strategies of engineering, procurement and construction (EPC) and global engineering firms. Offshoring is no longer isolated to manufacturing, data processing and call-center positions, as a growing number of firms move engineering, design and development work overseas as well.

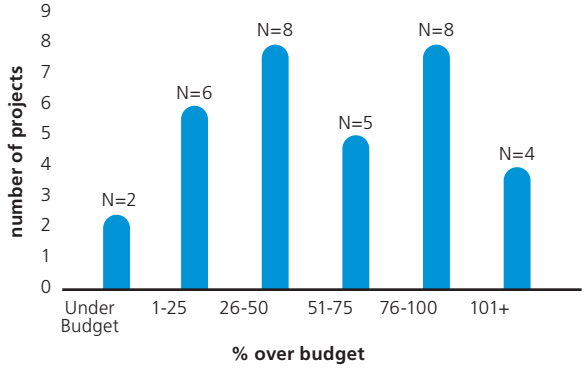
## IN PURSUIT OF COSTS TO CUT

Cost reduction is a primary driver for these moves and a top concern for both facility owners and EPC contractors, given today's complex global environment. To further minimize costs, many owners also are tightening requirements for EPC contractors — they want firms to assume more risk while meeting tighter project schedules.

On top of cost pressures, the increasing difficulty of finding qualified engineering personnel looms large for owners and EPC firms. After all, even the most advanced virtual teams and multi-office capabilities cannot succeed without the right people in place.

The skills shortage has received significant visibility in developed regions, such as North America and Western Europe. This deficit is driven by trends, such as downsizing, EPCs refocusing on core competencies other than automation, and the increasing wave of retiring baby boomers. The growing skills scarcity even extends to newly advanced economies, such as China. While that nation graduates large numbers of engineering students annually, too few highly trained and qualified personnel are available to fill the requirements of process industries.

**NUMBER OF PROJECTS WITHIN COST OVERRUN CATEGORIES**




Source: "Insights and Trends: Current Portfolio, Program, and Project Management Practices." 2012. PricewaterhouseCoopers LLP

Figure 1

## DELIVERING SOLUTIONS AROUND THE WORLD

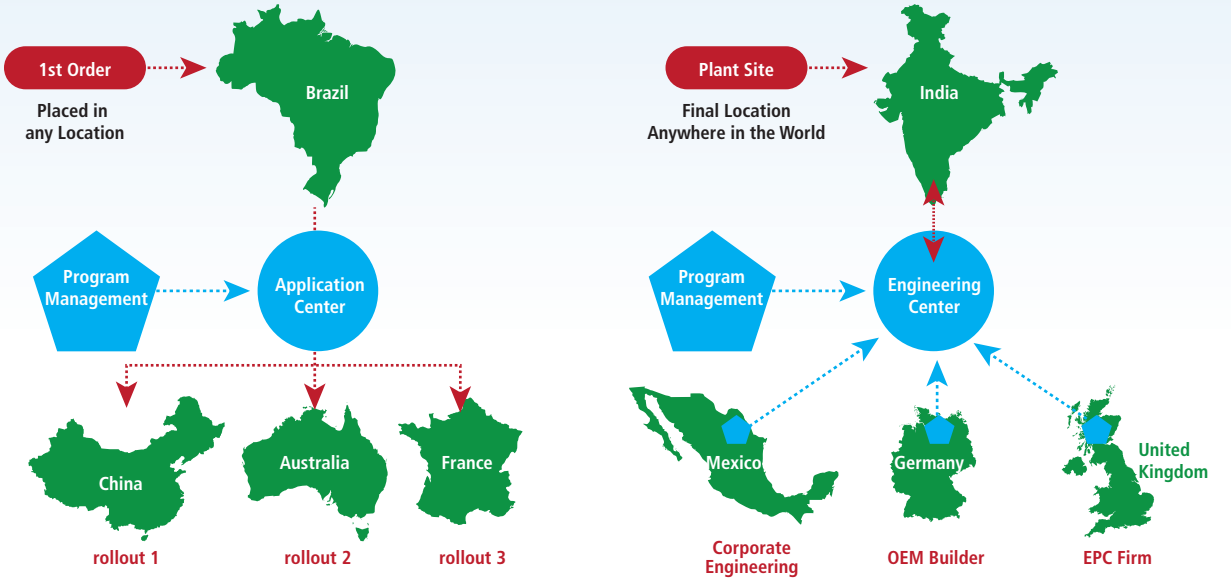



Figure 2

Companies are implementing multiple strategies to simultaneously reach cost-reduction goals for capital projects, while finding experienced and qualified personnel to execute projects, and operate and maintain their plants, including :

- Teaming with automation suppliers to provide this knowledge and fill the skills gap.
- Sourcing engineering services globally.
- Tapping global virtual engineering teams for around-the-clock engineering support.
- Locating services close to the project location or equipment and vendor locations.

The global nature of many of these strategies means that execution will necessitate collaboration from locations with varying levels of IT infrastructure, different engineering tools and best practices, diverse engineering backgrounds, and varied industry domain expertise — not to mention cultural and communication differences. The reality is that most companies do not have the proper tools and infrastructure in place to effectively address these complexities.

Overcoming these project challenges overwhelms some manufacturers. The 2012 PricewaterhouseCoopers (Global Project Management Survey) found that "poor estimates/missed deadlines" was the greatest factor contributing to poor project performance. Additionally, research found many of these projects exceed budgets by at least 50 percent.

Investing in front-end engineering and design can help companies overcome project cost overruns, as well as help develop a detailed project scope, budget and timeline to reduce risk and uncertainty during a project's design and commissioning phases. Trusted third-party service providers can help companies navigate complexities related to global project execution through the entire project lifecycle. Rockwell Automation, for example, relies upon a unified, flexible work environment comprised of a standard delivery toolset embedded with domain expertise, rigorous project methodology and detailed governance processes. Regardless of a company's access to qualified talent or location, this approach helps minimize risk and drive efficiency and consistency into projects.

### GO HOLISTIC

Industry libraries: a core element of effective execution. Companies embarking on global projects face a myriad challenges related to schedules, start-up time, cost, productivity, quality and safety. Overcoming these challenges can be difficult. In their quest to deliver consistent project outcomes, many engineering companies rely on industry libraries containing engineering content. These standard software modules of industry functionality are critical for standardizing complex designs in a repeatable way. Industry libraries are just one element to successful

project execution — a holistic approach also includes project methodology and governance processes.

With most large organizations that deliver automation solutions, engineers are designing and implementing solutions for multiple customers around the world on turnkey projects that require the coordination and management of the scope from multiple vendors, and for the same customer at multiple locations around the world. (See Figure 2)

In the past, it was standard practice for two developers to design the same software module in different ways. The process can be simplified if the developers instead agree upon the fundamental function and desired output. Then the code is consolidated into a standard, repeatable solution that can be stored and re-used in the future. The library grows as multiple, repeatable functions are defined and stored.

Creating libraries of content drives efficiency in engineering because developers can reproduce code automatically rather than starting from scratch or re-testing the same code multiple times. In addition, global engineering teams can tap into industry-specific domain expertise, regardless of who is executing the project. This efficiency and access to expertise drives repeatability, scalability and a higher quality standard.

The process and quality standards involved in creating a robust library are critical to success. When a re-usable piece of content is identified, multiple domain experts must help define fundamental requirements and contribute their domain expertise to understanding broader requirements as well. Additionally, all library content should undergo a rigorous lifecycle-management process. Content is continually refined and updated with each project, which means end-users not only benefit from schedule improvement inherent in using a library approach, but also receive better quality and a reduced risk profile.

PODs provide flexible manufacturing environments for both new and traditional therapeutics.

Project Methodology: Creating a Common Work Environment. A well-defined project methodology is critical to consistently and efficiently develop a robust library, and apply it to customer-specific applications. For Rockwell Automation, a common, flexible work environment serves as the foundation and a single point for engineering data.

The traditional approach to engineering involves gathering inputs from a customer, writing a functional specification, designing, writing application code, testing and commissioning. Multiple sets of data are maintained throughout various stages of the project. When new or updated data comes in, it is generally only applied to the current deliverable, which has a ripple effect, and can erode quality and affect timelines.

By using a common work environment, there is a single source of data used to create and update customer requirements, which improves consistency of output, improves data quality and minimizes risk. Standardized engineering content from industry libraries is available within the tool. A collaborative environment allows engineers — including contracted engineering resources — to access this content and work concurrently. Plus, a common database for the project is updated automatically.

Global teams can design and develop the control strategy and work independently to increase delivery speed. For example, an engineer at a pharmaceutical plant in Mexico designs and debugs a bioreactor unit's operation controls, as an engineer in India works on the site's process control platform. All the while, a hardware engineer is working on hardware design, testing and procurement to support the deployment of the application. The company's lead engineer then takes the results from all sites, and can integrate them remotely with minimal effort. This approach creates a consistent output based on industry best practices and domain expertise, and drives standardization across teams, locations and knowledge levels.

Engineering outcomes can vary from project to project, and

industry libraries can include a variety of content — such as process control code, visualization information, documentation and testing — all scalable across geographies. Using a common work environment also helps automate the capture of project requirements more accurately, regardless of the outcomes. Data, such as configurations and alarm limits, is gathered electronically and automatically input into the work environment accessed by engineers throughout the project. End-users save time and money because the engineering content being applied to their project already has been tested on multiple projects and refined along the way.

## CONSISTENTLY MANAGING QUALITY

Rockwell Automation's approach to global project execution is supported by delivery standards and processes governed by a quality management system (QMS) that helps minimize risk by driving quality through the project process. This system regulates how project deliverables are defined and specifies the procedure for executing them.

Every engineer is required to follow the QMS and processes in place when executing work to help embed consistency across all projects. This includes following defined work instructions for key process steps, using templates for engineering deliverables, and using defined work packages when transferring work to regional centers for customization. To further reduce risk, project teams participate in quality gate reviews and internal audits of active projects.

THE QMS HELPS REDUCE ANY INCONSISTENCIES IN PROJECT DELIVERY AND REDUCES PROJECT RISK VIA QUALITY GATE REVIEWS AND RISK ASSESSMENTS.

The QMS helps reduce any inconsistencies in project delivery, helps ensure a standard deliverable that fully meets the end-user's expectation, and reduces project risk via quality gate reviews and risk assessments. To use a consumer example, if a customer is buying a car, both parties will naturally expect a vehicle that will move them from Point A to Point B. However, there are many questions related to how this will happen. Will they have control over shifting? Will there be air conditioning? Will the windows roll down automatically? These questions need to be answered ahead of time — and the functionality of each individual "extra" needs to be clearly defined.

The QMS helps eliminate any gray area. For example, if the buyer wants air conditioning, there is no need for the buyer and the dealer to discuss how air conditioning is defined. They both know what to expect, and there is a standard deliverable.

## THE HOLISTIC APPROACH IN ACTION

Industry challenges related to regulatory compliance and speed were particularly important in a recent project executed by Rockwell Automation for G-CON, a builder of biotherapeutics-manufacturing facilities. The holistic approach to project execution helped overcome these challenges.

Traditionally, drug manufacturers have built inflexible and expensive production facilities that take three to seven years to complete and even longer to validate for production. With the advent of single-use technologies and process improvements, a paradigm shift is occurring, making such large-scale facilities a thing of the past. Instead, modular, scalable, flexible manufacturing solutions are the industry's goal. G-CON created the POD platform to respond to this need.

G-CON and Rockwell Automation collaborated to develop a severely compressed schedule that called for many steps to occur simultaneously. The POD concept was key to making this tight schedule a reality. While the shell of the facility was under construction, the downstream process PODs were built and commissioned at G-CON's neighboring manufacturing facility.

The Rockwell Automation life sciences toolkit of engineering content made rapid development of "smart" systems within the POD possible. Additionally, they were able to train G-CON's engineers on how to use the toolkit, allowing them to take advantage of pre-validated code. The common work environment made it possible to codevelop new applications and products remotely from multiple locations. The Rockwell Automation QMS mandates that all documentation aligns with GMP guidelines for the life sciences industry. The team was able to reduce testing time and validation costs, further impacting the ability to deliver the project on budget and within a tight timeline.

## CONFRONTING REALITY

Many manufacturers today are confronting the reality that they lack the proper tools, personnel and infrastructure necessary to successfully navigate the complexities inherent in global project execution. Finding the right help and enlisting firms that subscribe to a holistic methodology will help manage risk while breathing efficiency and consistency into far-flung projects — regardless of their geography.

Instrument and PAT vendors are continually innovating, and 2015 is no different

# ADVANCES IN PROCESS ANALYTICAL TECHNOLOGIES

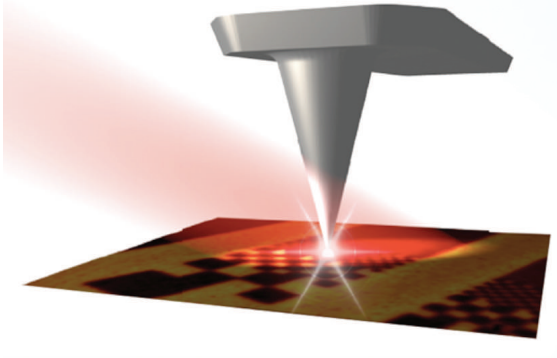
By Emil W. Ciurczak, Contributing Editor

**PROCESS ANALYTICAL** Technology (PAT) and instrument vendors are continually advancing the usability, reliability, accuracy and efficacy of their technologies, and the first half of 2015 is no different. Companies in this sector introduced technological advancements and other innovations to better support lab and QA/QC operations.

When it comes to demonstrating new analytical equipment to the industry, PittCon has traditionally been a primary launching point for introducing PAT systems and innovations to the industry. Several vendors brought out new systems or introduced significant new features at the conference (Editor's note: More PAT innovation can be found in "All-Star Innovators 2015" on page 14).

## SPECTROSCOPY

In the world of PAT/QbD, spectroscopy occupies a leading role. One instrument that should interest physical chemistry and spectroscopy-minded pharma professionals is the nano-FTIR (below) from **Neaspec GmbH** (www.neaspec.com). This combination of AFM (Atomic Force Microscopy) and IR may be somewhat specialized, but is unique in what it can do.




A focused IR LASER illuminates a standard metal-coated AFM probing tip. The tip generates a nano-focus at its apex that is 103 times smaller than the diffraction limited IR LASER spot. The nano-focus is used to probe the sample, with IR imaging and spectroscopy performed by recording the scattered light during a surface scan. Their background suppression allows spatial resolution of 10 nm throughout the IR spectrum. There may not be thousands of applications in Pharma, but where small particle discrimination is needed, this is a technique worth exploring.

**Spectroclick** (www.spectroclick.com) shared an interesting, compact spectrometer (photo above). While it is "merely" a visible spectrometer, its methodology is unique. It is a portable instrument making use of consumer-grade megapixel camera technology to generate absorption spectra from 430 nm to 720 nm with intensity dynamic range comparable to instruments with more expensive detectors. Using stacked gratings technology to produce

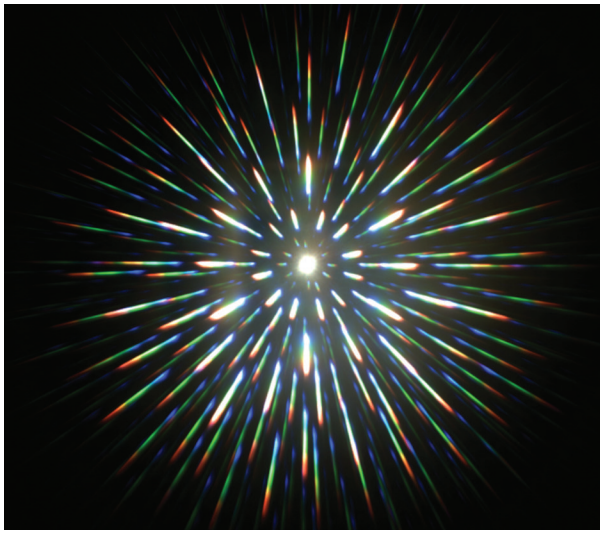


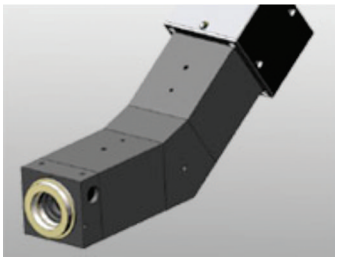
Figure 1. Scatter-spectrum effect of Spectroclick instrument.

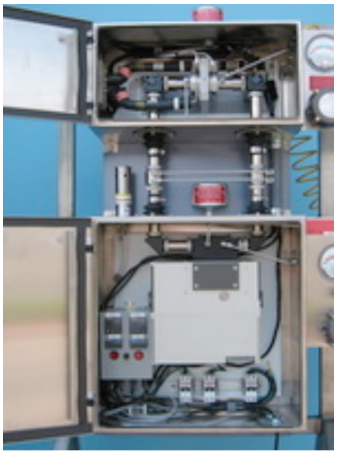
SpectroBurst™ data (see Figure 1), they trade intensity dynamic range and wavelength resolution without moving parts … and graphic display is unusual enough to be noted. Associated software leads users through the steps of a determination so that no advanced training is required.

**Cobalt Light Systems** (www.cobaltlight.com) introduced a powerful Raman system (photo below) for raw materials identification (RMID). While both NIR and Raman instruments have been used in the past to measure RMs (often through plastic liners), this new portable (not hand-held) instrument can measure RMIDs through paper sacks, glass and opaque plastic containers. The Spatially Offset Raman Spectroscopy (SORS) simply focuses the light on the far side of the container, minimizing absorption of the radiation by the container. The demonstration was impressive.


A small, rugged system (photo top, right) for transmission imaging was developed by **InnoSpec GmbH** (www.inno-spec.de). Working in two ranges (950-1700nm or 1200-2200nm) with a 320 x 256 pixel InGaAs (thermoelectrically cooled) detector, the instrument can achieve a spatial resolution of < 35µm. The image size is 7.68 mm (spectral) by 9.6 mm (spatial); the instrument (400 x 184 x 180 mm) weighs 7 kg, and runs on a 24V battery.

Falling into both the hardware and software categories is the MA-5000 Series Application-Specific Spectroscopic Sensor by **Symbion Systems Inc.** (www.goaxiom.com), a division of Axiom. The hardware components of the MA-5000 Sensors (photo bottom, right) combine robustness with low power consumption, which enables models to operate using rechargeable batteries. Specific engines are chosen to optimize performance for each application, for liquid, gas-phase, or solids analysis.





Spectral ranges range from UV to NIR; each sensor includes a miniature on-board computer equipped with the appropriate range of Symbion Systems software. Typically they include the Symbion RTM rapid-deployment package and Symbion QT Chemometrics. Secure web-based communications provide for cloud-based data storage as well as remote monitoring in real time via a smart phone or tablet. This software allows analysts and technicians to perform QbD or merely PAT (via on-line process monitoring). Symbion RTM employs multithreaded data processing to facilitate rapid deployment of analyzers capable of 30 or more analytical outputs per second.

## SOFTWARE TOOLS

Although the focus so far has been hardware, vendors are offering some nice additions to the software "toolbox" and are worth mentioning. For the third time in five years, **RuRo** (www.RuRo.com) brought the innovation to PittCon. While there are a number of LIMS systems on the floor, RuRo's Limfinity system uses an interesting approach. Instead of offering a number of software packages for each application (each needing to be shown 21CFR11 compliant), their approach is a single platform that can be configured for each application (billing forms, test samples, patients' information, sequencing instrumentation, or any other item to be managed/controlled).

## MISCELLANEOUS

A number of vendors have introduced non-spectroscopic tools worth highlighting. As far as a delightfully simple idea is concerned, **Hanna Instruments** (www.hannainst.com) showed a stand-alone (WiFi/Bluetooth-based) pH electrode, named edgeblu. The WiFi range is 10 meters and they can be monitored by the base supplied or a wireless device (smart-pad) with the proper app installed. Envision a number of these placed into fermentation or API synthesis tanks and monitored by either a roaming station or a centrally located monitor (which then can relay data to an office), and imagine the operational benefits the data points and related transparency will bring and you might understand how effective deploying this tech might be for your organization.

**Excellims** (www.excellims.com) has added a high-performance ion mobility (HPIMS) spectrometer to its inventory, the IA3100 HPLC-HPIMS system. When coupled with an HPLC, the HPIMS acts as a mass spectrometric detector. A small fraction of the eluate from the LC is directed to the IMS, ionized with an electrospray ionizer, and sent through the IMS chamber. The mass/shape sensitivity of the IMS can "see" differences not apparent in a LC column.



For example, any isomers that co-elute from an LC column (e.g., Leucine and Isoleucine or Melezitose and Raffinose) can easily be separated. UV transparent compounds (e.g., Fructose and Glucose, both with a MW of 180) are also well separated on the instrument. And, as with any IMS instrument, no vacuum pump is used; a low velocity of ambient air is directed against the ions to effect separation. The effect of LC and IMS data is to easily produce two-dimensional information/schemes.

**Sirius** (www.sirius-analytical.com) showed their new Insight Particle Size and Shape Analyzer. The Sirius Insight is a particle size analyzer that utilizes two measurement methods: Laser Obscuration Time (LOT) and digital video imaging. This approach enables the measurement of particle size using the LOT technique and provides a large number of particle shape parameters through dynamic image analysis.

LOT is independent of optical properties and makes no assumptions about the particles being measured (e.g. shape or refractive index). This makes it suitable for making size measurements on samples which are either single compounds or mixtures of compounds. Not being a volume-based measurement, it can be used for poly-dispersed samples or minor size fractions. LOT is a time-domain measurement, making it suitable for solids concentration measurements. Its dual-channel detection does two things: the video channel enables determination of various particle shape parameters, enabling material behavior to be correlated with particle properties other than size.

**Oselsa Inc.** (www.oselsa.com) makes an interesting tool: a Random Pattern Projector (RPP). The RPP is a divergent dot matrix pattern of NxM pixels with a ratio of bright and dark pixels of about 15% (each bright pixel is surrounded by a minimum of 8 dark ones, with none of the bright pixels touching). The distribution is pseudo-random, yet symmetric with respect to the center. Recommended uses are 3d stereo vision, gesture recognition, volume measurement, bin picking, depth sensing and palletizing. I suggested that it would also produce a working pattern for arranging fibers in a bundle to assure over-all light distribution for (spectroscopic) sampling.

**Skyray Instrument Co.** (www.skyrayinstrument.com) was showing two hand-held x-ray fluorescence (XRF) instruments. Low cost and easily used, while designed for metallurgical work, there are occasions where "spots or particles" are found in products and a rapid analysis of them is required. It may be used to detect/measure elements from Sulfur to Uranium (76 Element Total) with a precision of 0.05% - .1% STD. It only weighs 1.35Kg and can be used with line current or batteries.

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# MODULAR APPROACH TO WATER PROCESSING CONTROL &AUTOMATION

"Lego" inspired control concept from Festo creates a better fitting, economical method to automate this critical utility

By Steven E. Kuehn, Editor in Chief

**ALMOST ANYONE** can recognize the practicality associated with the concept of modularity. To the many engineers who busy themselves designing, engineering and constructing complex pharma processing systems, the idea of managing such complexity by breaking it down into standardized subsystems and components is a well understood and pragmatic approach to system design. According to Festo, such is the case with automation and control. Modular systems, say Festo, speed up the design and configuration of automated processes, lower overall costs, and make a process like water filtration more flexible and therefore better at adapting to new operational requirements and responsive to market demands.

"This approach represents a fundamental shift in the design and engineering requirements for water filtration applications," says Craig Correia, head of Process Automation at Festo. "Flexibility is achieved through consistent modularization, i.e., dividing a complete plant into functional units. "These functional modules are combined to create the automated filtration system. Water filtration plants built on these functional elements can be extended almost indefinitely by adding modules, thus enabling immediate adaptation to market and filtration requirements."

According to Festo, the design and engineering of a given process is precisely tailored to the respective task, whether for producing a specific product in X units per time unit or to generate the throughput of a specific substance in X quantity per time unit. As a whole, the mechanical design of the plant is geared toward meeting specifications and assuring the required performance data over its projected lifecycle.

Correa explains that the corresponding automation is configured using management systems comprised of process-specific (control) components, operating and monitoring stations as well as engineering stations. The entire process is centrally controlled by a single management system.

## SPEED TO MARKET IMPERATIVE DRIVES DEMAND FOR FLEXIBILITY

Festo maintains that markets are increasingly demanding shorter product development cycles, particularly in the small and large molecule pharmaceutical industry segments. The result? Correa says it has prompted a fundamental shift in the design and engineering requirements for process plants of all types including water filtration. He explains the necessary flexibility is something that is

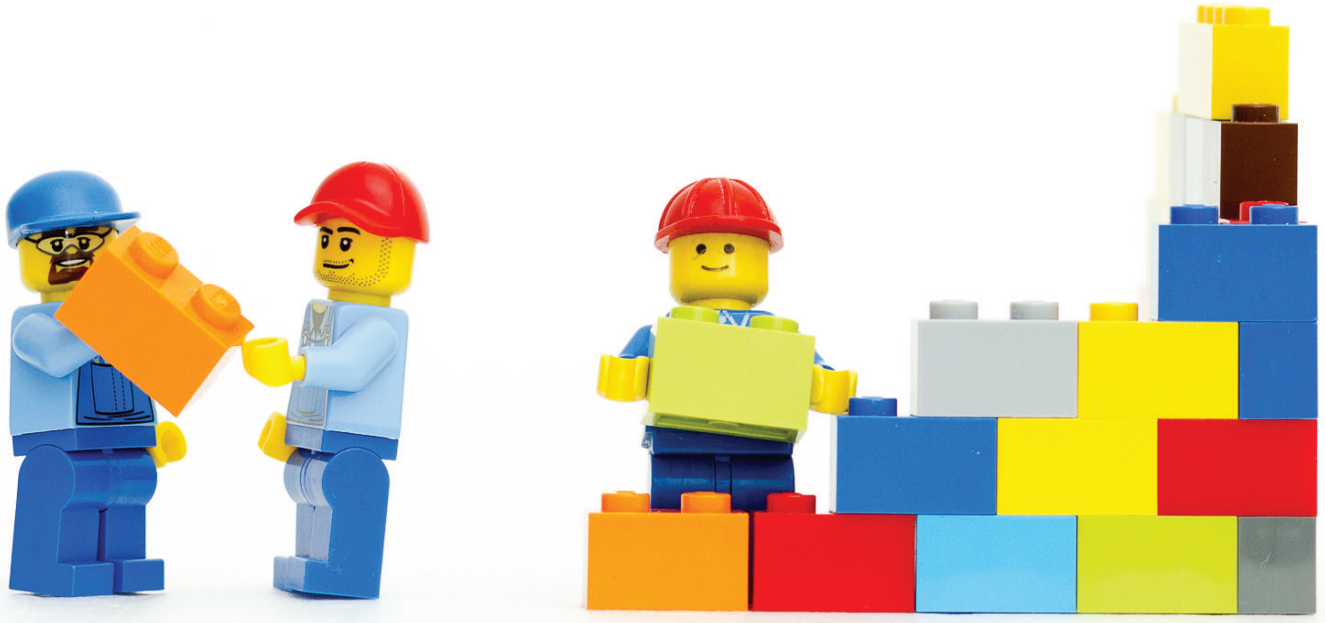


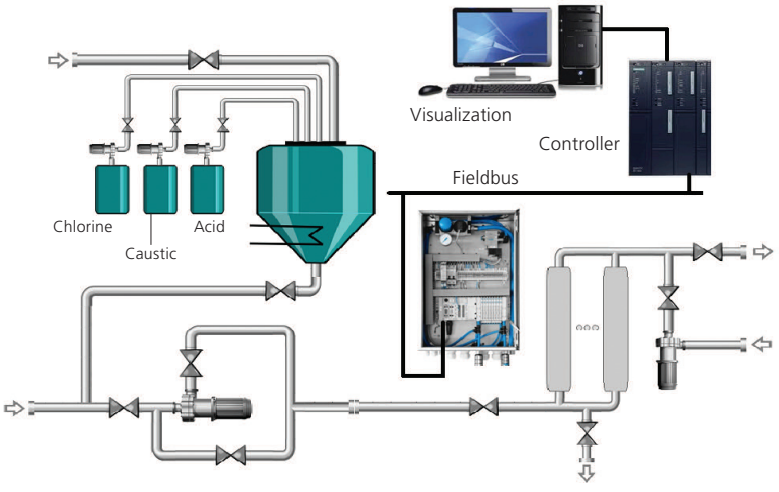
photo: simone mescolini / Shutterstock.com

available now and achieved through consistent modularization, that is dividing a complete plant into its functional units. "These production modules can be combined to produce specific process plants," says Correa, "which can be extended almost indefinitely by adding modules, thus enabling immediate adaptation to market and production requirements. Capacity is increased by numbering up instead of scaling up."

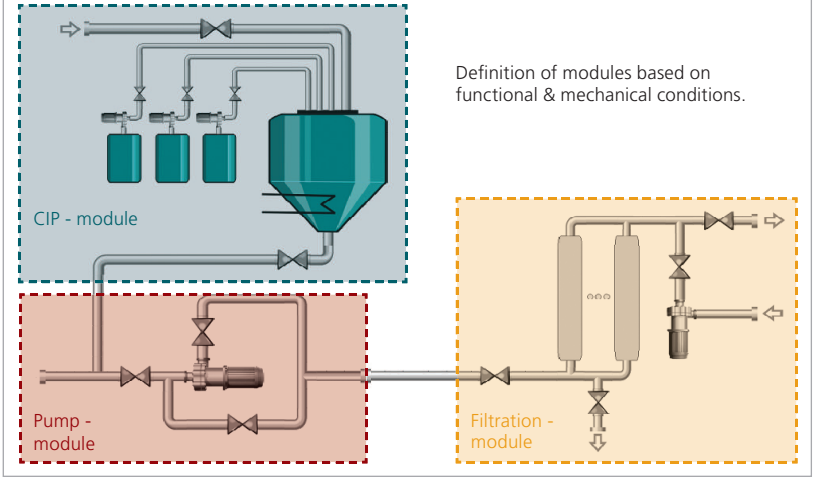
The ability to temporarily sideline production modules from the current production process, notes Correa, is another aspect of the concept's inherent flexibility that will have a positive impact on operations and managing maintenance, equipment change-outs and other similar tasks.

Most water filtration plant designs include pipes, pumps, valves, tanks, filter modules and sensors. Correa says the required components for actuating the field devices are installed in a control cabinet. Valve terminals, such as a remote I/O system with integrated pneumatic section, are connected to a central controller with visualization (management system) via a fieldbus. Plants of this type, he says, can be easily modularized by breaking down the process into subprocesses and defining a module for each subprocess with all the mechanical and

**WATER FILTRATION** / TRADITIONAL SOLUTION Figure 1




**WATER FILTRATION** / MODULARIZATION - STEP 1 Figure 2



automation components required for stand alone operation. For a water/waste water plant, key or critical modules would likely include its pumps, filtration modules and the clean-in-place system.

Builders find themselves engineering a skid based on a customer's spec," says Correa. "So each one is different. They might be able to cut and paste previous designs, like the control cabinet or skid layout, and just scale it. But this adds to lead time, and as a result adds cost." In an ideal world, explains Correa, builders would have a design that is scalable, not by changing the design, but by plugging a few modules in parallel. "Because even when they change the design," Carrea notes, "they have to purchase a fabricated frame, etc., which is unique. The concept here, which some OEMs are doing, is to create smaller solutions which can be mounted easily in parallel as more throughput is needed and have specific functions for each. When the spec specifies the volume and the filtration levels, they can expand both the capacity (parallel modules) and filtration types (modules in series)."

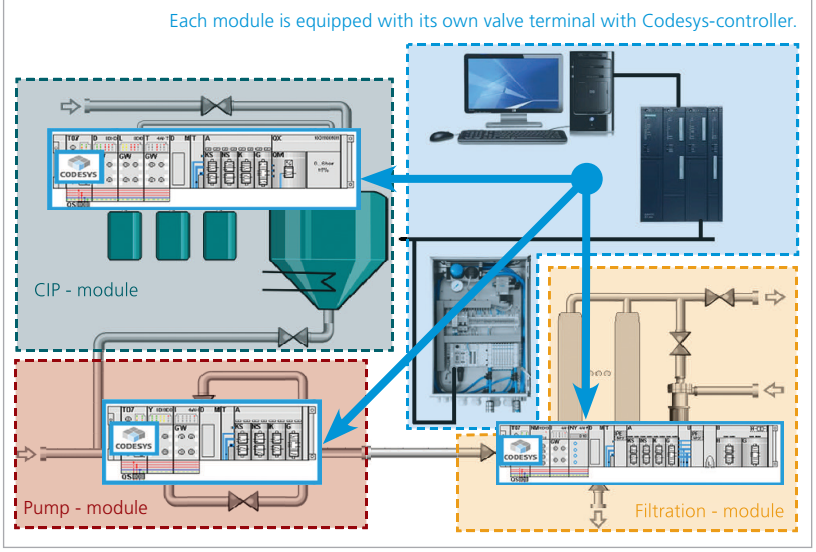
Figure 1 diagrams a typical design for a water filtration plant with valves, pumps, tanks, filter modules, sensors and pipes. Components required for actuating the field devices are installed in a control cabinet, and a valve terminal as a remote I/O system with integrated pneumatic section is connected to a central controller with visualization (management system) via a fieldbus.

Plants of this type can be easily modularized by breaking down the process into subprocesses and defining a module for each subprocess with all the mechanical and automation components required for standalone operation.

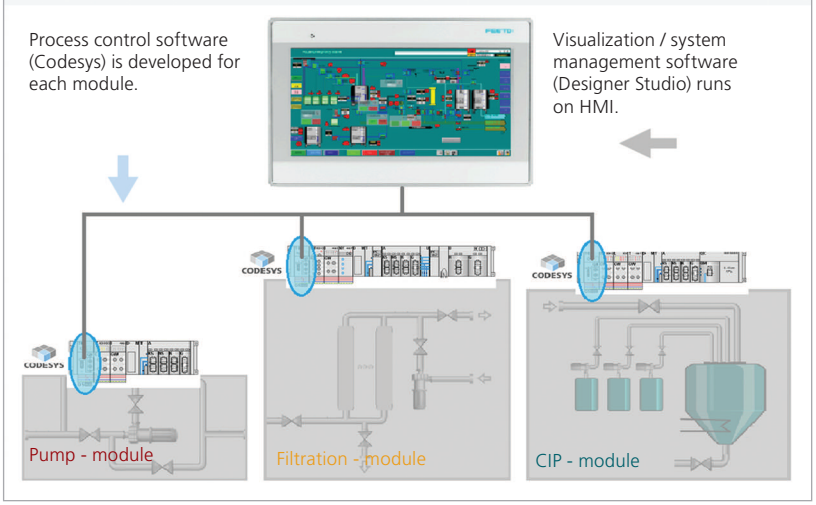
Correa says Festo's concept modularizes automation components: "The control cabinet components and the "central intelligence" (the application software for the process) are divided up so that the modules each have their own controllers, remote I/O components and pneumatic actuators." (See Figure 2)

Festo explains each module provides its specific functionality discretely at a data interface, that is, after the modules are interconnected to form a process plant, characteristics like operating mode, status, process measurements, alerts, etc., can be read/written in order to realize the functionality of the plant as a whole. (See Figure 3) "A process management system is required to coordinate the module functionalities in the complete system, that is, to manage the process," says Correa. "Unlike traditional management systems, this system has a greatly reduced range of functions since the process-specific control functions are realized in the standalone modules."

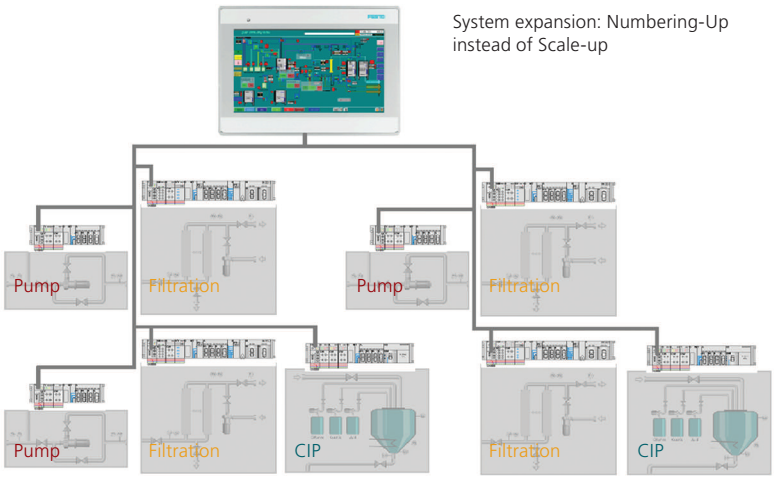
**WATER FILTRATION** / MODULARIZATION - STEP 2 Figure 3




**WATER FILTRATION** / MODULARIZATION - STEP 3 Figure 4



**WATER FILTRATION** / MODULARIZATION - STEP 4 Figure 5




System expansion: Numbering-Up instead of Scale-up

- Modular automation and control supports a plant engineer's pursuit of process modularity where any configuration to be assembled can be by adding modules of identical construction and function (See Figure 4), thus allowing a numbering up expansion strategy instead of scaling up (See Figure 5).

According to Festo, the modularization solution shown in Figure 5 has been consistently implemented for water filtration plants and can be applied similarly for processes and plants supporting pharmaceutical manufacturing operations. Festo explains that it is not just plant operators who are likely to benefit from modular automation's flexibility when it comes to adapting plant sizes to different production requirements, but will also benefit vendors and solutions providers who are striving to introduce the efficiency, flexibility and economy of modularity into the plant and process systems they engineer for their Pharma customers.

- Modules are precisely defined units with clear functionality.
- Modules are equipped with their specific application software, which reduces the respective software complexity.
- Modules are easy to change/extend in terms of their (clear) functionality.
- Modules can be manufactured in small series and fully tested prior to delivery.
- Customized complete systems are assembled from different modules of identical construction (numbering up).
- Modules are programmed using CODESYS (as per IEC 61131-3, no license costs), i.e., independence when selecting the automation hardware.

"In the context of 'Internet of Things'" and based on the NAMUR recommendation NE 148," concludes Correa, "modular automation will effect a fundamental shift in the design and engineering of process plants." Modularization will not be possible to the same extent for all industry segments or every process, Correa explains, "However, the technical design process for each plant should include a review and assessment of whether modular concepts can be applied so both the plant operator and plant manufacturer can benefit from the associated advantages."


By Josh Olson, Beckhoff Automation

# Designer Genes

## Integrated DNA Technologies Offer Made-to-Order DNA Oligos

PC-based control platform reduces cost by $4,500 per system; smaller machine footprint effectively doubles system throughput

**CONSUMERS HAVE** grown quite accustomed to having the ability to customize the products they buy, from clothing to cell phone cases, to interior lighting and more. This made-to-order trend is not limited to the consumer space, however. Even biotech research organizations are utilizing highly custom synthetic genetic material to advance discovery. This type of research represents the upper echelons of scientific progress in the pharmaceutical, agricultural, academic, and other life science markets. Genetic study analyzes the basic elements of life, allowing scientists to understand biological processes and make discoveries that protect our world.

Genetic research requires synthetic nucleic acids, DNA and RNA, unique to each application. Research scientists use custom-made DNA sequences of various lengths and with unique modifications to drive genetic discovery. These custom manufactured nucleic acid sequences, or oligonucleotides, are often referred to as "oligos."

Oligos are typically short, single-stranded, synthetic DNA or RNA molecules that provide the basic tools for molecular biology research and forensics. Oligos are chemically manufactured through a process called solid-phase synthesis.

The incredible variation inherent in research requires this type of customization, often with very specific composition and on a tight timeline. Integrated DNA Technologies, based in Coralville, Iowa, fills this niche in the market, providing these customized molecular biology products for diverse application areas. From manufacturing facilities in Iowa, California, Belgium and Singapore, IDT delivers custom oligos to a global customer base, offering the highest quality and broadest product selection to ever-expanding research markets.

A manual process in the past, synthesis is now automated, much as a result of advances in robotics, computer processing and monitoring. These efforts to make their manufacturing processes faster, more precise and more efficient led to IDT's creation of the M1 DNA Synthesizer, the company's newest oligo manufacturing machine. The M1 offers a streamlined, flexible platform for custom DNA synthesis, facilitating significantly faster changeover of materials in the process. In particular, the M1 makes it easier to offer customers a wider array of options, increasing support of non-standard products, as switching time for materials has been drastically reduced with the new design.

An important factor in the effectiveness and flexibility of the M1 is the use of PC-based control and EtherCAT solutions. A product platform from Beckhoff provides a solid technological foundation for this next-gen DNA Synthesizer.

Dan Brock, Senior Scientist at IDT, checks the status of the M1 DNA synthesizer.

## BUILDING A "BASE" FOR GENETIC RESEARCH

IDT is the largest manufacturer of custom oligo products in the world. For more than 25 years, the company has manufactured and supplied oligos for molecular biology research. Approximately 44,000 individual nucleic acid sequences leave company facilities each day, shipped worldwide to the company's 82,000-plus global customers. Each sequence is custom manufactured to the exact requirements of the customer, as Dan Brock, IDT Senior Scientist, explains: "Genetic research applications come with an inherent level of complexity in the types of oligos needed. Every one of the 44,000 sequences IDT manufactures each day is specifically tailored to the needs of the customer. Much like a snowflake, each DNA sequence we create is unique. We aspire to create each one with the highest level of quality, while efficiently getting them to our customers for their immediate use."

IDT has refined the process to an incredibly streamlined series of steps, enabling the company to receive orders as late as 1 p.m. local time and have the oligos in the hands of the customer the next morning. With this level of production volume and manufacturing speed, maintaining customer service and quality is of utmost importance. Owen Piette, Lead Automation Engineer, adds that "one of the biggest differentiators for IDT is that we do quality control on every oligo that we synthesize, which we refer to as "100 percent" QC. Our customers deserve this level of effort, and this is reflected in their experiences collaborating with IDT."

## THE ANSWER IS MOST CERTAINLY "YES"

When it comes to the size or composition of a customer-requested oligo, IDT does not like to say no. Customers have an almost limitless number of options to choose from when ordering their synthetic nucleic acids.

"We work hard to provide exactly what our customers want; we look forward to the unusual, the new, and the exciting," says Brock. "If someone wants a particular product, standard or not, we'll work it out and, in almost every single case, make it happen."

As customer demands continue to grow and change, IDT has remained up to the task, continuing to offer new and exciting products. For example, the company's landmark Ultramer synthesis platform allows IDT to manufacture the longest oligonucleotides available on the market. This ability to synthesize long oligos has facilitated groundbreaking products, equipping their customers to push the limits of research farther than ever before.

Speed and space constraints were key determining factors in specifying a new controls platform. IDT pitted


The M1 Synthesizer can run four separate DNA synthesis processes at the same time — a significant upgrade over the previous platform.

different control system options against one another and, when the dust settled, the Beckhoff Automation solutions was chosen. Piette explains: "The Beckhoff control system provided the right mix of price, performance and functionality for IDT's application. The mix of PC-based control and high-speed EtherCAT technology offers a robust, flexible control system solution."

Providing the processing power for the M1 is a CX2020 Embedded PC running Beckhoff's TwinCAT 3 control platform. "This control system significantly reduced hardware costs compared to the array of controls products used previously," says Piette. "We had four separate synthesizers, each with their own controller, but we were able to replace these with a single, PC-based system using the CX2020." With the Beckhoff solution, IDT was able to combine everything into a simple package, with ample room for expansion through additional I/O slices or PLC functions programmed into the software. In addition, the Windows operating system (OS) on the Embedded PC fit perfectly into the overall scheme of IDT operations.

"IDT has always embraced Microsoft OS and tools. A significant amount of our programming is done in .NET, making the IT-friendly Beckhoff system, particularly TwinCAT 3, a complementary and integrated solution," said Piette. "The company's long-standing support of the Windows system and computer science standards along with automation technologies has allowed us to easily design IDT systems on the Beckhoff platform." He added that the convergence of technologies enabled through the integration of Visual Studio in TwinCAT 3 provides a clean method for data transfer. "The incorporation of TwinCAT 3 into the widely used Visual Studio environment helps immensely when we integrate into MES systems — a key point for the data-driven nature of our customers' applications. We have a new recipe for every single synthesis, which creates huge amounts of data, so expert management of this information is integral to the success of the process."

An incredible amount of data is created by the numerous sensors in the M1, tracking every aspect of the synthesis reaction. These are necessary to help IDT scientists create nucleic acid products that conform to the exacting specifications necessary for the applications of their customers. The company constantly monitors chemicals and reagents, as well as the minute details of the reaction itself, making sure processes proceed exactly as they should. IDT found that the sub-millisecond response time of the EtherCAT industrial Ethernet system provided the necessary speed and high throughput for this type of monitoring. "The real-time throughput and high precision offered by Beckhoff's EL Series EtherCAT I/O terminals," says Ryan Witt, IDT System Engineer, "provides a previously unheard of level of monitoring functionality in our applications."

The M1 samples a wide range of Beckhoff EtherCAT Terminals from the EL and ES series, working together to provide a robust suite of I/O functionality. The 16-channel digital output terminal, for example, connects binary control signals from the controller to the actuators at the process level. Receiving and transmitting the signal at the other end is a group of digital input terminals, each offering electrically isolated signal transmission. EL3068 and EL4008 analog terminals provide additional coverage for field devices. In addition, connecting the barcode scanners used for logging and authorization is a quartet of EL6002 2-channel serial interfaces. "Overall, the EtherCAT I/O system represents a compact solution, reducing the necessary space for the networking equipment, as well as reducing required cabinet space," Witt elaborated. "As a result, IDT can squeeze four synthesizers into the space previously occupied by two."

Brock went on to discuss additional benefits, adding that they "can monitor the reaction much more closely, through all the steps of the reaction, and very accurately determine when and where any problems occur. It's almost like an EKG, where we can see the machine's heartbeat and determine any irregularities and proactively address them." Previously, IDT had to wait until the next day to be notified of issues with the machine. "Now with the real-time monitoring via EtherCAT, we don't have to wait until downstream quality control catches an error. This saves us hours in our processing time," Brock noted.

Because the process uses organic solvents, a multi-touch panel provided a solution for their application requirements. "The organic solvents we use in the synthesis process are not very plastic-friendly," says Brock. "In fact, we've gone through quite a few keyboards because of this issue. Everyone has analog-resistive touch displays, but they all have plastic fronts, so if you touch them with your glove, they just melt. The Beckhoff displays' high-quality glass construction, as well as unbeatable performance even while using gloves, offers the perfect solution for our environmental conditions."

## PC-BASED CONTROL STREAMLINES EXPANSION

Overall, integration of PC-based control and EtherCAT provided the right mix of price, performance and flexibility. "Versus the other options we considered," said Piette, "the powerful centralized control solution saved us around $4,500 per system, as we did not have to purchase a separate PC or PLC for each of the four synthesizers integrated into the M1.

"The exceptional expandability was a welcome benefit, allowing us to keep our options open for upgrades as necessary. In the future, when one of our scientists comes to me with a list of requested additions or improvements to the machine, the process will be much smoother. We will be able to implement changes in a matter of months, rather than starting from scratch and pushing the timeline out a year or more," says Piette.

The IDT M1 DNA Synthesizer is a leading-edge system for creating customizable synthetic oligonucleotides.

Form factor of the control hardware also plays into the success of the IDT integration of Beckhoff systems. "The space savings provided with the PC- and EtherCAT-based platform was immediately evident within the cabinet assembly time," Piette said. "These components pack an incredible level of functionality into a small form factor, reducing cost as well as assembly time. As clear evidence, we lowered the cabinet assembly time by 66 percent."

IDT plans to continue integrating Beckhoff technologies into their designs with projects in motion to build additional M1 synthesizers. IDT says it intends to include Beckhoff in future systems that the company believes will eventually account for as much as 60 percent of their business. As IDT keeps pushing the limits of custom DNA synthesis technology, pharmaceutical companies, the research industry and academia will certainly benefit from their commitment by receiving an answer for each unique request. By leveraging the power of PC-based control, IDT is well positioned to continue its evolution by introducing breakthrough technologies in genetic research.

# Tubing Provides Reliable Fluid Transfer

New designs offer flexibility, peristaltic pump and single-use compatibility, and connections that eliminate risks for leaks

BY KATIE WEILER, MANAGING EDITOR

## MOLDABLE BIOPHARMA TUBING

AdvantaFlex biopharmaceutical tubing is available with molded connections to form single-use manifold assemblies. This eliminates many barbed fitting connections and their risks for leaks and contamination. The tubing is sterile weldable and heat sealable, and molded bottle closures and stoppers are offered. AdvantaFlex contains no silicone oils or animal derived components and complies with USP Class VI, FDA, ISO and EP standards. Validation and extractables test portfolios are available, as well as validated sterility assurance.

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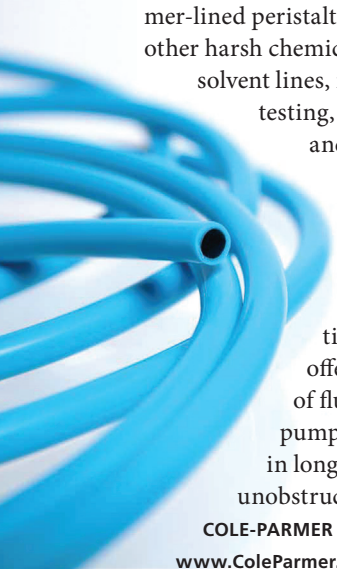
Masterflex Solve-Flex Pump Tubing from Cole-Parmer is designed for transferring corrosive fluids. The fluoropolymer-lined peristaltic pump tubing handles solvents and other harsh chemicals. The tubing can be used for organic solvent lines, ink and solvent production, diagnostic testing, specialty chemical processing, and ink and toner feed lines. It also provides an option for transferring essential oils in the food processing and pharmaceutical industry. The fluoropolymer-based liner is plasticizer-free, hydrophobic, and resists the absorption/adsorption of aqueous fluids. It also offers low spallation and assured purity of fluid. A flexible outer jacket extends the pumping life of the tubing. It is available in long continuous lengths, allowing for an unobstructed fluid path.



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## COMPATIBLE WITH PERISTALTIC PUMP OPERATIONS

Meissner says BioFlex TPE (thermoplastic elastomer) tubing offers next generation performance and the robust supply chain required for critical applications. The clear tubing is available in common sizes up to ½" inner diameter and will be available in larger diameters in the near future. BioFlex TPE tubing offers excellent sealing and welding performance, is compatible with peristaltic pumping operations, and has been optimized for integration into single-use systems. It has been extensively tested and offers robust performance over a wide range of operational conditions, including sub-zero applications.

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## USER FRIENDLY CLAMPS AND QUICK CONNECTS

Nordson MEDICAL has expanded its offering to include user-friendly clamps and quick connects that offer a secure connection. PharmaLok clamps feature a state-of-the-art design that simplifies the assembly process by making it effortless to securely attach sanitary fittings to bag ports and filters. All clamps operate at a maximum pressure of 80 psi. Single-use and easy-open clamp sizes include .5" to .75" and 1" to 1.5", and the tube clamp supports tubing sizes from .5" to 1.25". The tube clamp is also designed for use with silicone and TPE tubing. RQX Series quick connects feature a large locking button for easier handling and connection as well as a single barb open flow design. Available in polypropylene and polycar-

bonate materials, these connectors fit 3/8" and 1/2" tubing sizes.

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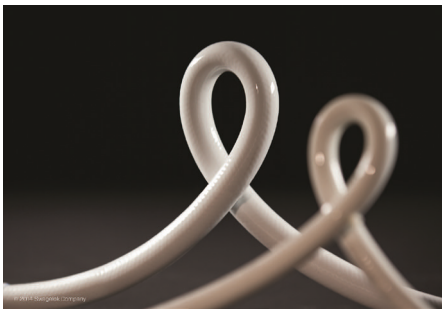
Swagelok says its U series hose offers the flexibility of a silicone hose, but with the hoop strength more typical of convoluted PTFE hose. The PFA core tube is reinforced with a silicone layer bonded directly to the



core and braid layer without adhesives or cements, providing high flexibility and outstanding kink resistance. 300 series stainless-steel braid reinforcement ensures pressure containment. Sizes are 1/2" through 2". Working pressures range to 300 psig. Temperature ratings are -65 to 400F. Stainless-steel end connections include sanitary, tube and pipe.

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EQUIPMENT & CUSTOM SERVICES

# The People Factor and Quality Control

We need to use our training/left-brain strengths to solve and improve the "people factor" inside our facilities

BY GERARD CREANER, CEO, GETRESKILLED

**WE ARE** an industry of scientists and engineers and we naturally define the problems we face in technical terms — and then get stuck solving them. We write new Standard Operating Procedures; we design new production processes; we specify and install new manufacturing equipment; we find ways of doing it all faster…the list goes on. Why, however, do we avoid looking at the People Factor, where 80% of the solutions to quality issues reside?

This is not unique. We are continually reminded that we are in the business of saving lives — we are in a life critical industry. It is a very serious business underpinned by very complex technologies where people's lives are at stake and so we convince ourselves of the primacy of technical solutions when looking to solve problems. But we are not alone. When considering the range of high-tech industries out there with huge regulatory compliance drivers, you don't have to look much further than NASA, which also falls into the category of a life-critical industry.

NASA was originally developed to put a man on the moon and get him back again. We can only begin to imagine the complexity of the problems they had to solve. Many of us saw Tom Hanks in Apollo 13, which, although a cinematic experience, gave viewers insight into NASA's incredible response capability during a crisis, when people's lives were at stake. In our industry we face our own crisis points with people's lives at stake. For example, drug shortages are currently leaving patients adrift, and quality issues have been identified as one of the root causes of this problem. Yet still it puzzles this author. Why are we still not looking at one critical area — the people who make the medicine?

NASA continually strives to be better, like we do for our patients, by pre-empting problems before they arise. Dr. Ed Hoffmann, NASA's Chief Knowledge Officer, when speaking at the Knowledge Management 2015 Conference in Dublin, Ireland, noted that 80% of the solutions to the issues that NASA faces are to be found in the People Factor. And when NASA speaks, from a true leadership position in both life critical and high-tech industries, we should listen and learn. According to Hoffman, even though NASA knows the rich vein where "people" solutions can be found, NASA finds it very difficult to mine this particularly rich seam of gold — and all because the engineers and scientists who make up their industry are not comfortable in what they consider the touchy-feely area of behavioral traits.

The pharmaceutical industry is no different. We're much happier defining the problems we face in technical terms and then facing the challenge of solving them. Sure, there are technical solutions to these problems, but we need to strike the right balance between solving 100% of the technical problems and 0% of the People Factor ones, just because the people factor solutions take us out of our "comfort zone."

An example of addressing the People Factor is the Behavioral Positioning System tool (BPS), which measures and strengthens the Quality Behavioral Traits of the workforce who come into direct contact with your manufacturing process. BPS combines an easy-to-use, online assessment tool that measures the quality conscientiousness profile of the manufacturing team, with GMP-specific video learning, that is delivered in short snippets of video which can be shown every day in the locker rooms, prior to operators coming on shift. The video learning uses the "why?" approach to tie quality activities with clear reasons for why those activities are so important, which has been shown to strengthen their quality performance reliability. BPS then goes one step further into the "touchy-feely" realm and ties real-life patient health challenges to the quality behavior as well.

**BPS ENTERS THE TOUCHY-FEELY REALM** AND TIES REAL PATIENT HEALTH CHALLENGES **TO THE QUALITY BEHAVIOR AS WELL.**

NASA and the pharmaceutical industry have some life-critical concerns in common. Going across the aisle to hear this world-renowned technical organization's recognition of our mutual limitations, as scientists, engineers, to problem-solving in the People Factor realm should feel alternately challenging and inspiring Let's use our training and left-brain strengths to face, solve and improve the "People Factor" inside our manufacturing facilities.

*BPS is a partnership between cut-e, a leader in design and implementation of online testing and questionnaires and GetReSkilled, a leader in online video-based capability building for production-line operators.*

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