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Industry Voice

Heard it on DCAT Street: Pharma leadership talks strategy at one of the industry's oldest gatherings

By Steven E. Kuehn, Editor in Chief

IF BEHAVIOR often speaks volumes, then the pharmaceutical industry is saying a lot lately in the way that it is responding to the social and economic forces that affect its markets and the potential commercial success of the drugs they develop and deliver around the world. It's the Pharma industry's voice, articulating its direction, its strategies and its aspirations using a familiar, but sophisticated commercial vocabulary learned over its long history.

Certainly the "Industry" speaks with many tongues, but its ongoing dialogue was recently articulated by thought leaders meeting and presenting at DCAT Week 2015. Celebrating its 125th year, the Drug, Chemical & Associated Technologies Association meeting may likely be one of the industry's longest running events, attracting the leadership of Pharma's top companies including CMOs and technology suppliers. *Pharmaceutical*

Manufacturing was there, lobbying in the truest sense of the word at the famous Waldorf Astoria hotel in New York. While there, we took the opportunity to query some of Pharma's most dynamic companies on what's driving their strategic plans in the near term.

Who's listening? Patheon's CEO Jim Mullen is and very carefully, noting that the supply chain is growing more complex and that Pharma companies are outsourcing more work, but with companies with broader capabilities. "They're trying to shrink the network of suppliers they're using. They have a growing slice of products that require some kind of specialty capability. On the small molecule side, the estimate is [that] maybe a third of the pipelines out there that have solubility absorption issues. What does that mean? They need more specialty formulation technologies to solve these problems," says Mullen. What is Patheon doing in response? "We keep building our technology base," he says, citing the recent Agere Pharmaceuticals acquisition which in his words was "exactly aimed at that problem" of helping Patheon make drugs with better absorption rates for its customers.

Talking injectables, Mullen mentions that it's been a challenging market to find high quality CMOs with reasonable capacity and flexibility to get the job done noting it's a market that's been really stretched over the last years: "Look at all the biologics coming along and biosimilars; there's a lot of pressure in the injectable space."

Indeed, and Graham Reynolds, vice president, Marketing and Communications, Delivery Systems for West Pharmaceuticals agrees. "There are a couple of major trends that I think are really driving West's strategy. "First is the general growth in biologic drugs and in particular the newer molecules that are being developed [which] have their own challenges." Reynolds explains some of those therapies may need to be self-administered by patients and this creates challenges of how to make them effective, safe, and as painless as possible for the patient. Reynolds notes that many newer injectable drugs tend to require higher dose volumes. "So what traditionally would be injected in a one mL syringe," explains Reynolds, "now these newer molecules — because of the complexity — suddenly you have to deliver two mL or three mL or even more to make an effective dose." That's driving the development of newer delivery technologies, he says, "that will not only contain that volume of drug but deliver it in an appropriate time." Reynolds says the evolution of plastic primary containers, syringes, etc., is certainly a driver adding that West understands some of the newer biologics are more sophisticated and that some molecules can interact with glass, thus prompting drug owners to explore the alternatives.

David Mayers, president, pharma services, for Canada-based WellSpring Pharmaceuticals, also hears the industry loud and clear when it comes to injectable medications, the rise of biologics and niche compounds. "From a CMO perspective," says Mayers, "we're seeing a lot of smaller orphan drugs, and we are doing a lot of work in orphan drugs — IMS validated that … with data from earlier in the [DCAT] conference. We find it is becoming much more the norm. The concept of these smaller organizations taking up a few products — we're seeing a lot of change too," explains Mayers. So from a CMO perspective, he notes, the industry is seeing a surge, in opportunity, because basically a number of companies are now either merging or switching and selling three or four of their products to somebody else.

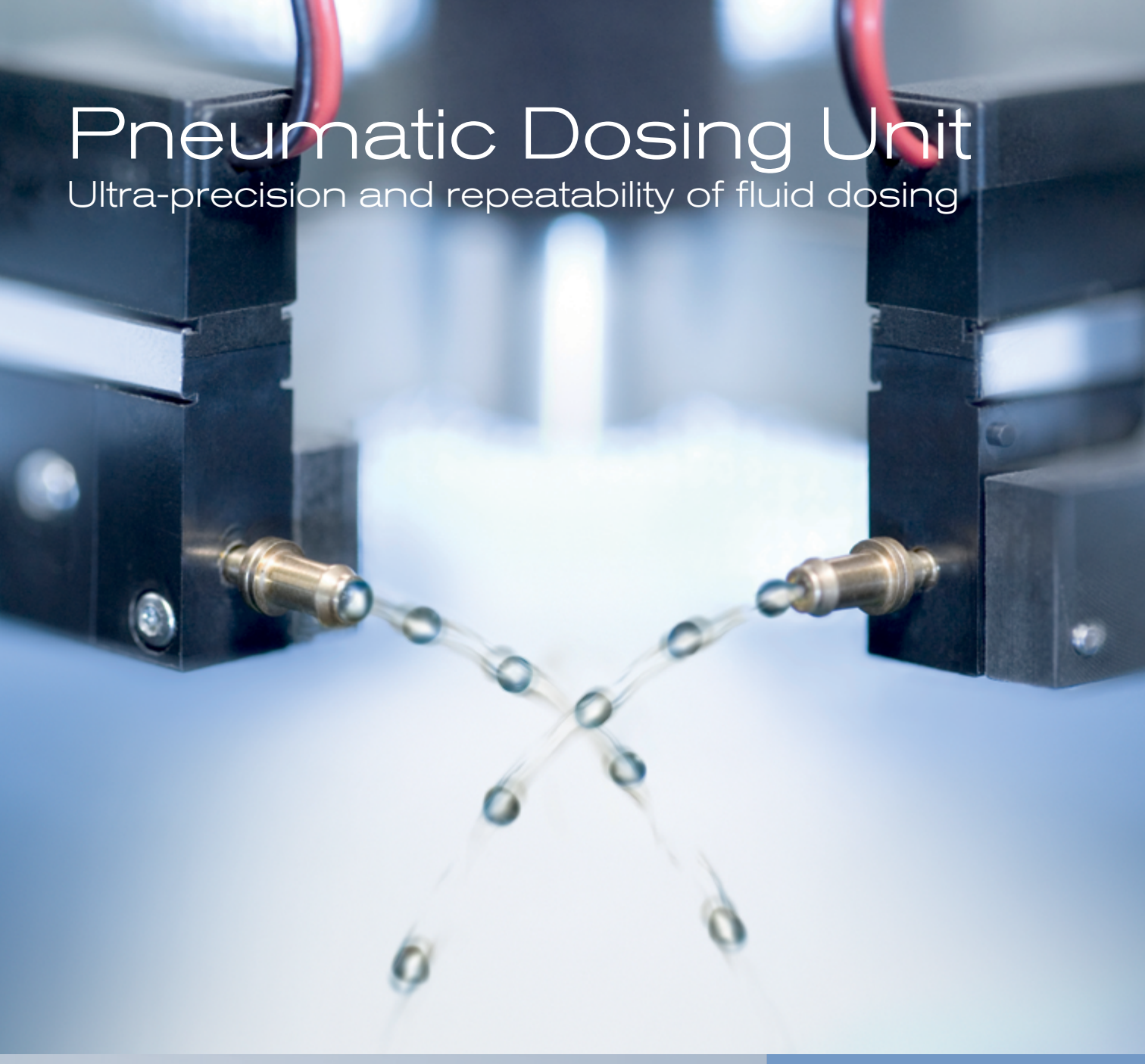
CMOs and other Pharma contract services companies are adapting to answer the needs of larger Pharma. Mullen says to compete and excel Patheon needs to field everybody including companies with orphan drug indications, which tend to be smaller scale with smaller batch size runs.

West's Reynolds explains "Pharma is always balancing risk against the reward of innovation, agreeing that the industry is striving to improve, working to understand the challenges of patient compliance and how they can better integrate supply chain partners into the drug development process."

"I think some [Pharma companies] are doing a much better job of figuring out who to work with and who not to," says Mullen, explaining that traditionally acquiring CMO support was managed as a procurement strategy, based on financials and available capacity among other things, and that "The pendulum has swung a little too far," in that direction. "Procurement is important, but the technical aspects [involved in engaging a potential CMO partner] are equally important, and we need to have the technical experts on both sides coming together and sharing things."

Industry's talk of innovation is on Mayer's mind as well. "I find that in the pharmaceutical industry, we talk about the concept of innovation. We are an interesting animal in that we (Pharma) are more innovative than almost anyone else and less innovative than anybody else." But innovation just does not mean the same thing to the industry during this period of its history. "There isn't the new molecule — there's extension of things; there's new dosage forms, biosimilars, etc. But the other piece that's happening is we're becoming much more sophisticated and innovative in how we manage our companies."

As with these companies and others, they are listening carefully to what the Pharma industry's saying, digesting what's being "said" and turning it around to bring Pharma what it needs to remain competitive, while offering safe and affordable drugs.



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FLUID CONTROL SYSTEMS

Trends Impacting Pharma Equipment

Emphasis is now placed on the deployment of equipment and technologies that enable higher production yields and more rapid scale-up/commercialization

By Nigel Walker, managing director, That's Nice LLC

THE MAIN driver influencing all aspects of the pharmaceutical industry is the growing downward pressure on costs. Shifting markets, the end of the blockbuster era, government healthcare mandates, and the linkage of insurance reimbursement with medical outcomes are all affecting drug pricing around the world. In response, pharmaceutical companies are taking many different actions to reduce their costs and increase efficiency and productivity.

The recent rise in mergers/acquisitions in the pharma industry is one mechanism by which companies hope to reduce costs through synergies and access to new therapeutic classes and/or regional markets. Outsourcing of pharmaceutical manufacturing is on the rise, as is the use of third-party service providers for business activities traditionally considered core to sponsor companies, such as logistics. Interest in continuous processes is also intensifying, and emphasis is now placed on the deployment of equipment and technologies that enable higher production yields, the reduced need for purification and more rapid scale-up and commercialization.

As a result, equipment needs across the value chain are changing, from initial discovery efforts to the packaging of final products. Suppliers of research and development and production equipment, analytical instrumentation and packaging systems are responding with innovative

technologies that meet these needs. At the same time, the surplus equipment market has experienced strong growth due to the increased availability of high-quality equipment and the need of contract and generic manufacturers, and even branded drug companies, for low-cost equipment solutions.

SINGLE-USE TECHNOLOGY: COMMERCIAL-SCALE

Single-use, or disposable, technology is widely used in biopharmaceutical drug development, and more recently has begun to gain acceptance in biologics production at increasingly larger scales. This interest is driven by the advantages that disposable technologies provides in terms of decreased capital expenditures and operating costs due to the reduction of cleaning and sterilization steps and the need for validation. In addition, processes based on single-use equipment are more flexible, require shorter set-up times and have significantly reduced cross-contamination risk, all of which translates to a faster time to market and more robust and reliable production.

Numerous types of single-use bioreactors are employed for the production of the major types of biopharmaceutical products, including recombinant proteins and monoclonal antibodies. Different designs are also available for batch, fed-batch and perfusion reactions. While the initial focus was on the development of disposable technology for upstream processes, single-use formats are now available on the market for many downstream bioprocess steps, including filtration and chromatography. For instance, modular, disposable tangential flow filtration (TFF) systems can be readily integrated for the concentration of downstream biopharmaceutical process streams.

CONTINUOUS BIOPHARMA MANUFACTURING

In fact, many newer single-use systems are designed for use in continuous bioprocesses, and disposable technology is an enabler for the implementation of fully integrated continuous biopharmaceutical production. Continuous manufacturing is attractive because it leads to more consistent products and processes, which equates to the consumption of fewer resources (raw materials, energy, water) and less waste generation, for lower operating costs.

For upstream biopharmaceutical manufacturing, perfusion has become a well-established process that affords high quality biologic drug substances with high productivity. Other types of upstream equipment under development include continuous centrifuges, acoustic resonance devices and cell settlers. For continuous downstream bioprocessing, simulated moving bed chromatography and as mentioned above, TFF systems, are also available and being adopted by the industry. New flow-through absorbers are also being developed for integration with chromatography and virus filtrations steps. Advances in process analytical technology (PAT) systems are also crucial to the successful implementation of integrated continuous bioprocesses.

The benefits of continuous processing are not limited to biopharmaceutical production. In fact, the industry has recognized the value of flow-through chemistry for the production of active pharmaceutical ingredients (APIs) and continuous tableting for many years.

Although widespread adoption of continuous processing for small-molecule intermediates and APIs has not yet been achieved, most pharmaceutical companies and contract manufacturing organizations (CMOs) have the capability to perform continuous-flow chemistry at commercial scale using microreactor technology. In addition to enhanced process and product consistency, flow chemistry enables manufacturers to perform hazardous reactions or use challenging conditions not possible in traditional batch modes. For example, highly exothermic reactions or reactions that involve highly reactive reagents can be performed using flow chemistry because only very small quantities of reagents and products are present at any given time and control of the reaction conditions is much greater.

In addition, because scale-up generally involves the use of more of the same microreactors in parallel, it can be achieved much more quickly without the need for extensive studies, and production can be flexibly scaled to meet demand. Reduced resource consumption and waste minimization are additional benefits, as is observed for continuous biopharmaceutical processes.

In fact, pilot- and small commercial-scale equipment with built-in parallel microreactors are now available for larger-scale continuous processes. Microreactors for the continuous processing of liquid/solid and multi-phase systems are also under development and offer the potential to expanding the applicability of the technology. Efforts are also directed toward the development of continuous separation and purification technologies that have not traditionally been designed for this type of operation, particularly with respect to solids handling, and much progress has been made, particularly with continuous crystallization at larger scales.

Effective online analytical capabilities are also leading to increasing implementation of online tableting systems for small-molecule drug product manufacturing. In this case, continuous processes generally have fewer steps and therefore reduce the amount of manual operations, which leads to increased productivity and safety. Here again, better process control leads to improved product consistency and quality. The smaller footprint of continuous tableting processes also leads to lower capital costs. Overall development times tend to be reduced as well. Recent enabling equipment technologies have

included systems designed for the accurate handling of poorly flowing solids, even at very low material volumes. Progress has also been made in the development of the intelligent feed-forward and feedback loops and control systems that are required for the complete integration of all steps in the tableting process.

SPECIALIZED REQUIREMENTS FOR HPAPIs

One of the fastest growing segments of the pharmaceutical market comprises formulated drugs based on highly potent active pharmaceutical ingredients (HPAPIs). This rapid growth is largely attributed to the growing number of antibody-drug conjugates (ADCs) that have recently been approved or are in development. These drugs are attractive because they are highly targeted therapies that deliver highly potent and often cytotoxic drugs (payloads) to specific sites in the body by linking them to antibodies that are taken up only by only specific types of cells with the right antigens. Because the active drug is only released at the site of action, ADCs can be delivered systemically without causing harm to healthy cells.

However, the highly potent components of ADCs must be manufactured in facilities with equipment and procedures designed to mitigate the risks they present. As the need for such specialized equipment has increased, innovative equipment manufacturers have begun to work with process engineers at HPAPI producers to develop systems with the necessary protective functionality. Increasingly, HPAPI manufacturers are relying more on isolation and containment through equipment and facility design, and less on personal protective equipment. For instance, not only are reactors available in contained systems, but downstream purification equipment, including balances, rotary driers, pressure filter driers, and slurry vessels are being installed in isolators that meet exceedingly low occupational exposure levels. In the future, if single-use systems can be developed that are compatible with organic solvents, disposable technology would likely prove highly beneficial to HPAPI manufacturing.

GROWING USED EQUIPMENT MARKET

At the same time that demand for innovative equipment for continuous processing, single-use technology, and systems for the manufacture of highly potent compounds is being driven by the need to reduce costs and increase efficiencies, demand for used pharmaceutical equipment is also rising as the result of increased levels of industry consolidation and outsourcing. As large companies acquire smaller firms or merge with larger entities, they often turn to resource recovery (the sale of redundant facilities and equipment) to achieve initial and ongoing cost savings. Simultaneously, CMOs must rapidly expand their capacities in order to meet the growing requirements of sponsor companies that are outsourcing to achieve further cost savings and gain access to specialized technologies and capabilities. Increasing demand for generic drugs, particularly in emerging markets, is also pushing these manufacturers to seek sources of readily available, low-cost process R&D, processing and packaging equipment.

In fact, high-quality used equipment is often sold at 40-50 percent, and sometimes as little as 20 percent, of the original price. In addition, used equipment is immediately available, compared to new equipment, which in some cases can take weeks or even months to obtain if back-ordered. In many cases, a delay of that length could cause a CMO to lose a project. Used equipment can also serve as cost-effective back-up equipment for critical processes.

Used equipment dealers can help larger and smaller organizations manage their excess equipment assets, from arranging whole-facility auctions, the sale/purchase of a single piece of equipment, or identifying redeployment opportunities within a company. Increasingly, third-party equipment providers are providing additional support to sellers and buyers of used pharma equipment, such as assistance with regulatory compliance. At least one used equipment dealer has taken its commitment to customer even further, offering operator training videos for the equipment it sells and hosting hands-on workshops and interactive classroom training sessions.

2015 SALARY SURVEY

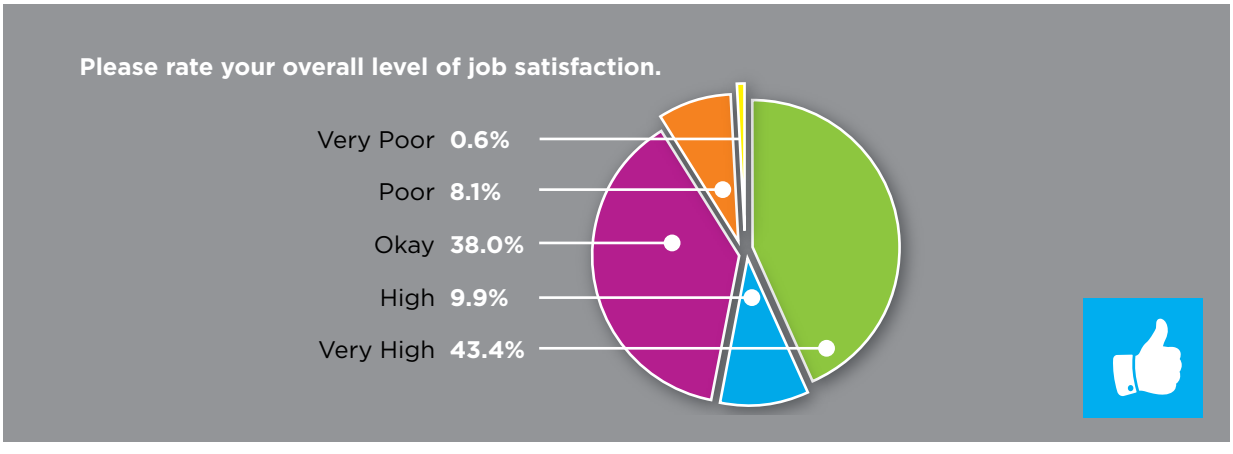
In It for the Long Haul

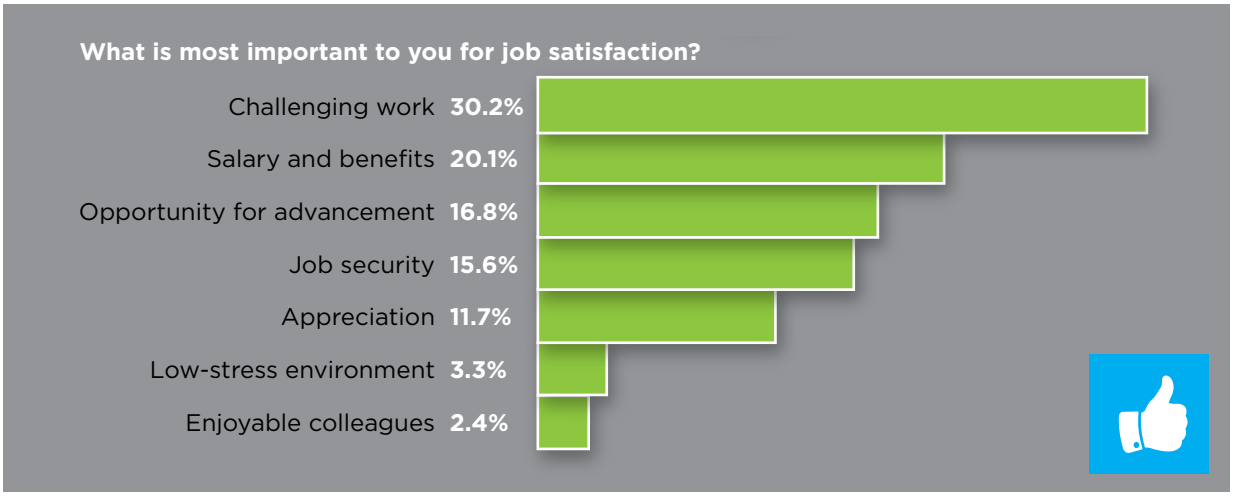
Pharma's professionals are satisfied with their careers and leery of corporate "change" related to acquisitions, restructuring and cost control

ALTHOUGH THERE are likely few professionals out there who aren't growing a tad fatigued at the constant come-ons for survey respondents, *Pharmaceutical Manufacturing*'s readers continue to support the opportunity to lend their voice to the conversation that is the Pharma industry today. Each year since the magazine began publishing in 2003, *Pharmaceutical Manufacturing* has queried its readership to get a sense of how they are feeling about their chosen profession, the general pressures they face employed by the Pharma industry, and to better understand who they are as people and professionals. Not to mention where salary levels are at—something everyone is at least a bit curious about.

Job Satisfaction Rising

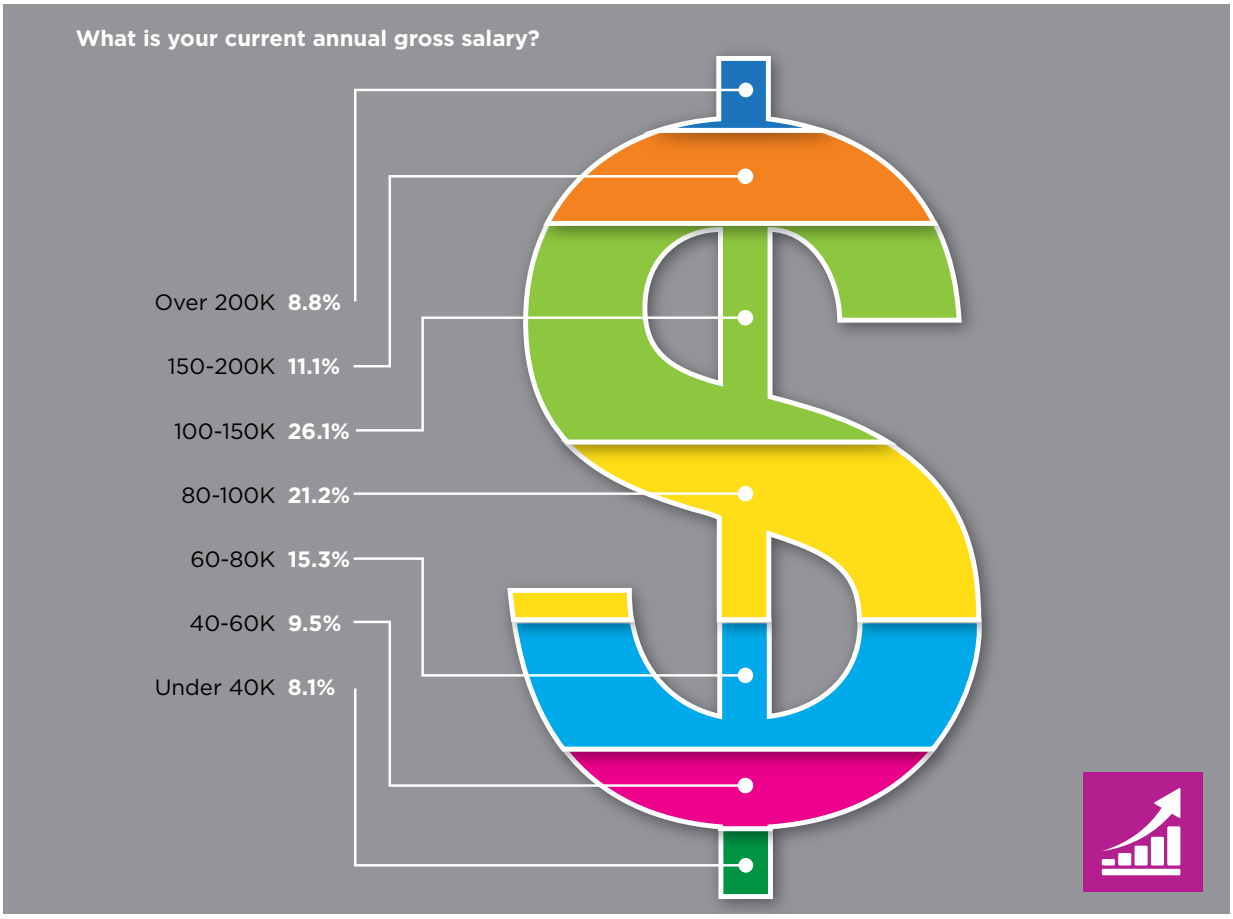
IT'S NOT a stretch to think that more money tends to make employees happy and responses to "Please rate your overall level of job satisfaction," did not surprise with 53 percent of 333 total responses rating their satisfaction as High (43 percent) or Very High (10 percent). However, most reading this would likely agree that in this industry, satisfaction is not solely predicated on one's salary; is there a man or woman out there in Pharma who doesn't garner great satisfaction from being part of an industry that's primary mission is to save lives and make people healthier?





Positive Salary Trends

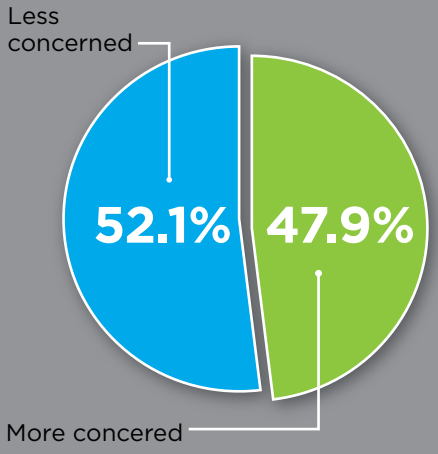
MORE THAN three quarters of respondents said they received a raise last year, supporting conjecture that retaining valued employees is a corporate priority. Raises were also significant; 80 percent reported receiving a 3-5 percent bump in salary last year.



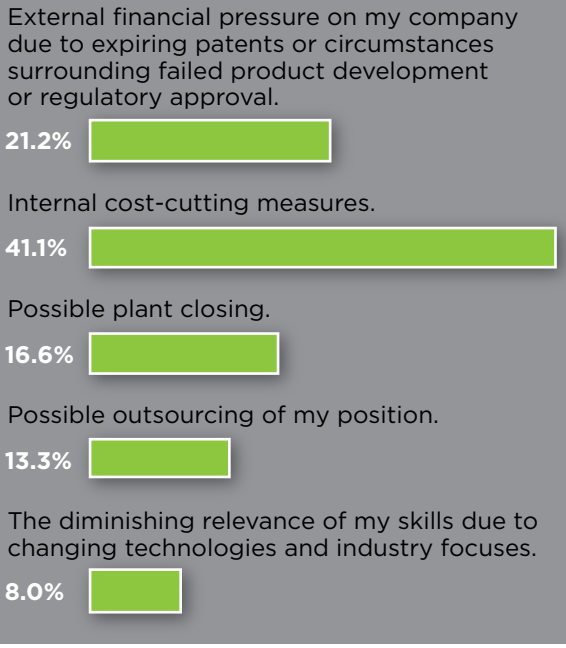
Job Security Stabilizing

WITH JOB satisfaction running pretty high, one might think that Job Security would be less of a concern, and judging by this year's responses to "Are you more, or less concerned about your job security than last year?" it seems to be true with more responding they are less concerned (52 percent v. 48 percent), pretty much a swap from last year when 55 percent indicated they were more concerned with job security. For those who say they are more concerned, about 42 percent of them cited "internal cost-cutting measures" as the primary cause of their job anxiety. Close behind and certainly not exactly news to most is the fact that 22 percent cited "External financial pressure on my company due to expiring patents.

Are you more, or less concerned about your job security than last year?

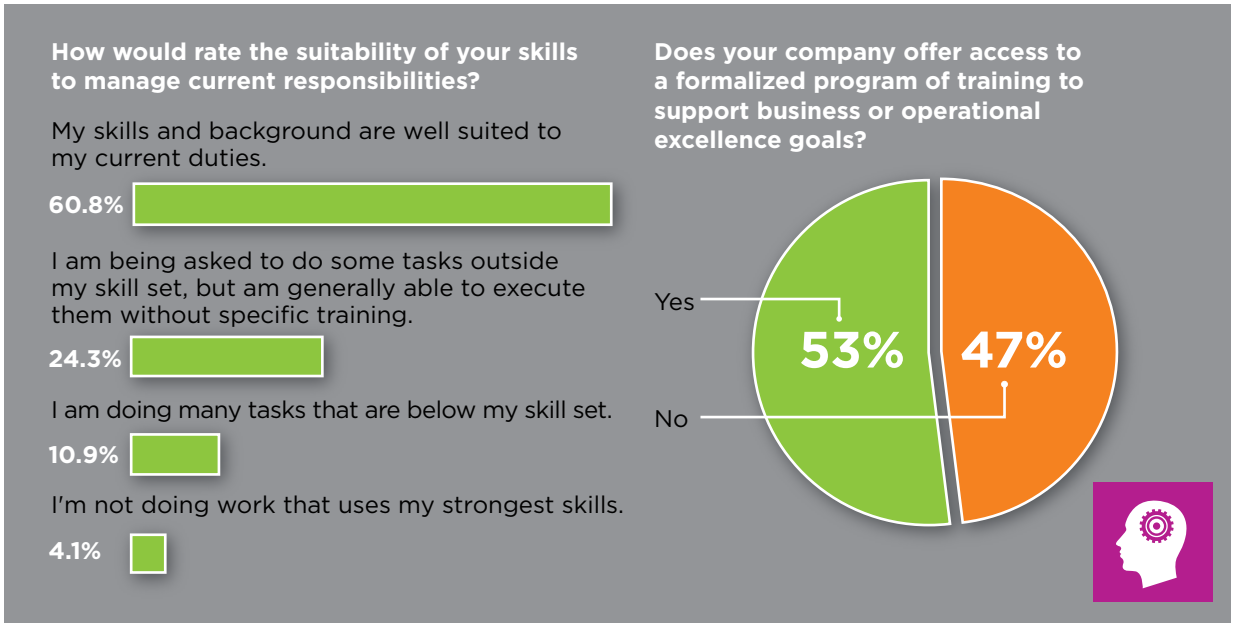


If you are more concerned, what do you think is the greatest threat to your job security?



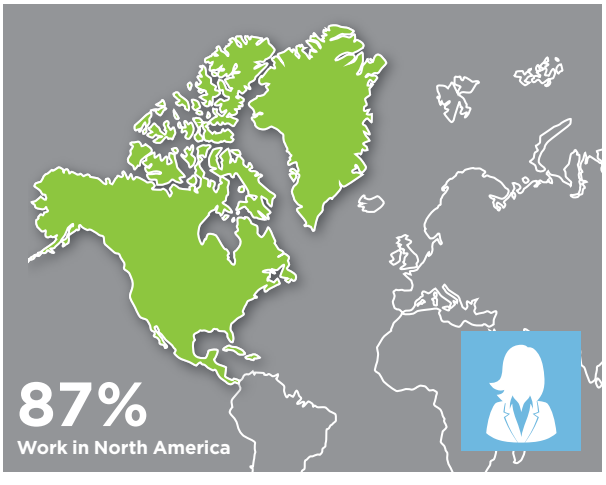
Meeting Professional Challenges

IF THERE is a primary challenge to any professional in Pharma it's staying relevant and valuable to the industry and the organization that signs your paycheck. New systems, new solutions, new processes enabled by emerging technologies, new regulations, new … whatever … will never not be a part of one's Pharma career, especially those managing processes and production capacity. Certainly, keeping up with the pace of change and ongoing technical advances is stressful. Fortunately, judging by the responses, *Pharmaceutical Manufacturing's* readers seem confident they're up to the task. "How would you rate the suitability of your skills to manage current responsibilities?" Sixty percent of 320 respondents indicated "My skills and background are well-suited to my current duties." Some are asked to do things outside their skill set (24 percent) but feel they are generally able to execute them without specific training.

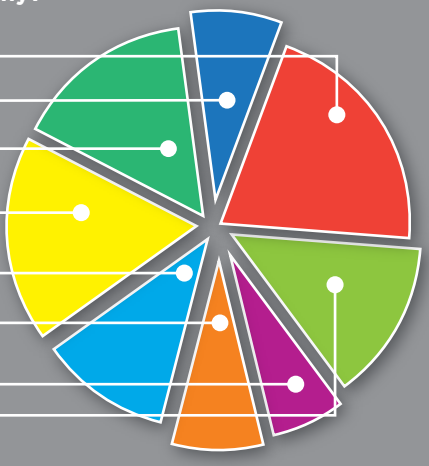


Respondent's Profile

BY IN large, most respondents were male (79 percent of 302 responses), a majority ranging in age from 30 to 54 and older with the majority having a bachelor's or master's degree in either chemistry, chemical engineering or pharmaceutics and the remainder with engineering degrees or specialties like biology or biochemistry. Most fill operational roles (52 percent of 307 responses) across manufacturing, quality assessment, plant engineering and R&D categories. 42 percent of responders say they've been working in the industry for more than 20 years with next largest chunk (30 percent) delivering their blood, sweat and tears to Pharma from 11 to 20 years. In other words, PhM's respondents continue to be in it for the long haul.

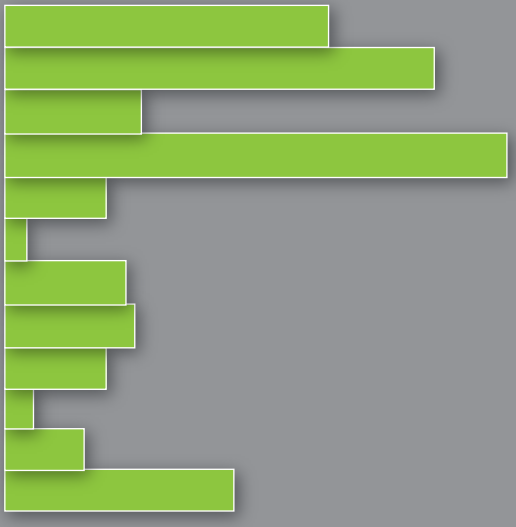


Which of the following best describes your company?

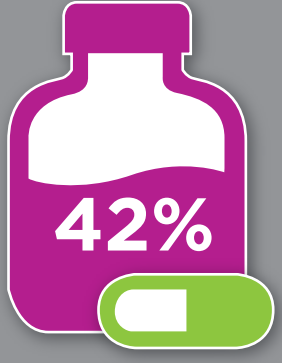


Traditional "Big Pharma" company	20.9%
Biopharmaceutical manufacturer	7.8%
Generics manufacturer	15.3%
Small or mid-size specialty pharmaceutical manufacturer	17.6%
Contract manufacturer	11.1%
Vendor or solution provider	7.8%
Consultancy	6.5%
Other (please specify)	13.0%

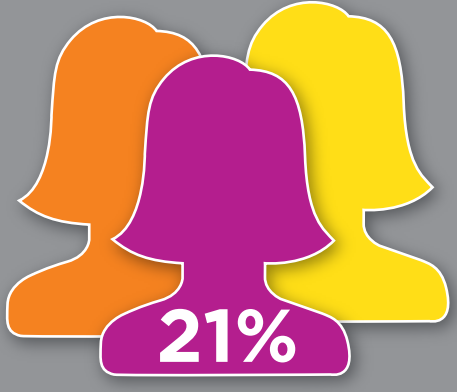
Which category best describes your job function?



Manufacturing and operations	14.7%
Quality assessment and quality control	19.5%
Plant engineering and design	6.2%
Research and development	22.8%
Process control or validation	4.6%
IT	1.0%
Facilities or maintenance	5.5%
Corporate management	5.9%
Regulatory	4.6%
Academia	1.3%
Consulting	3.6%
Other (please specify)	10.4%



have worked in Pharma more than 20 years

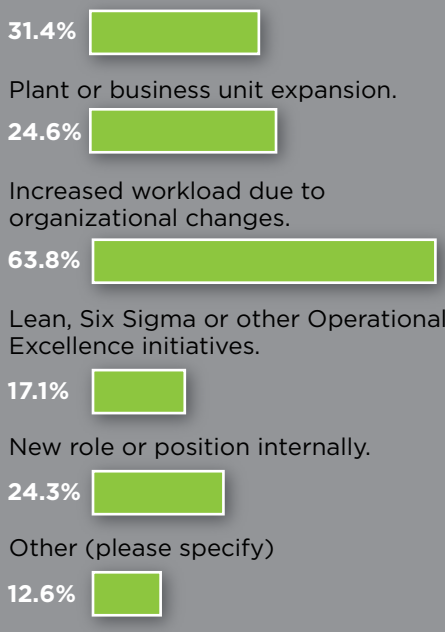


are women

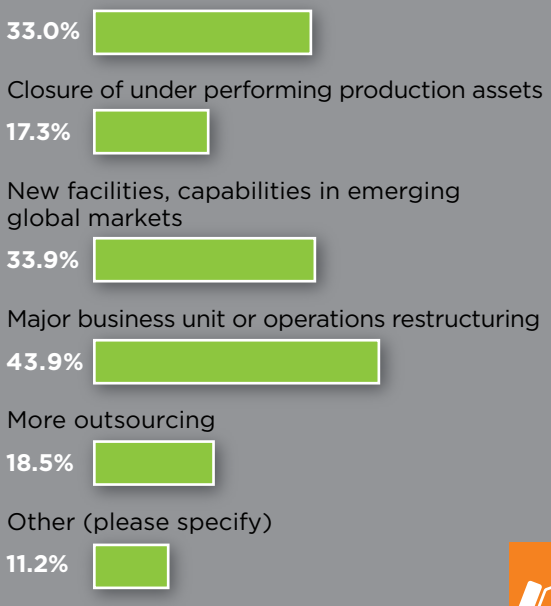
Meeting Pharma's Challenges

IT'S PRETTY clear that *Pharmaceutical Manufacturing*'s readers are feeling confident and secure, and perhaps more ready than most to stand tall and meet the industry's challenges head on. In response to "How have market and competitive forces affected your company recently?" 44 percent selected "major business unit or operations restructuring" a kind of organizational change that can vex even the most "together" companies and drive the mortals within to drink or even worse.

What were the biggest challenges you had to face in the past year? Check all that apply.



How have market and competitive forces affected your company recently? Check all that apply.



Conclusion

WHAT ARE the take-aways from this year's study? It's apparent that *Pharmaceutical Manufacturing's* readers are industry veterans, confident they'll be able to face current and future issues with hard-won operational experience and the ability to keep themselves relevant when it comes to their skills and abilities. They're in it for the long haul and it shows.

A total of 334 responded to the 2015 study, delivering more than 300 responses to every one of the 27 questions posed. Readers were not required to answer every question.

SPONSORED CONTENT:

Benefits of Used Pharma Equipment

The pharmaceutical custom manufacturing market is growing at a healthy pace as large pharmaceutical manufacturers increase outsourcing in response to major changes in the industry. Demand for drugs is increasing in emerging markets, where the emphasis is on low-cost products, while in the west markets have matured and companies have shifted focus from blockbusters to niche drugs aimed at much smaller, targeted patient groups. Cost reduction is consequently a major decision factor, and outsourcing of everything from drug discovery to commercial manufacturing is a key strategy for many.

To meet this increasing demand, many contract manufacturing organizations (CMOs) are finding they need to expand capacity through the addition of manufacturing equipment. The competition is fierce, of course, and with their customers facing cost pressures, CMOs are also concerned about reducing their expenditures. Time constraints can also be significant, with any delay in start-up costing project opportunities.

Used pharmaceutical equipment is an ideal solution in this climate, particularly when it is purchased through a reliable, established dealer that has established relationship with large pharmaceutical firms looking to achieve investment recovery through the sale of surplus equipment.

There are a number of ways that CMOs can purchase used pharmaceutical equipment other than through a reputable dealer. Online-only companies and private sales are two examples. With most of these options, however, the process is not transparent. The true source of the equipment may not be known, or may be a manufacturer with an unknown history. There can often be hidden costs as well, such as fees for moving the equipment. As importantly, compliance with the various regulations applicable to used pharmaceutical equipment sales can be challenging with such arrangements.

Established dealers of used pharmaceutical equipment, such as Federal Equipment, have ongoing relationships with large pharmaceutical manufacturers, and the equipment they offer comes with documentation of the equipment's history, including maintenance, cleaning validations, etc. Appropriate storage conditions are also provided, including warehouses that are designed to meet good manufacturing practice (GMP) guidelines. As a result, CMOs are guaranteed high-quality equipment that meets all of the requirements for pharmaceutical manufacturing.

Used equipment also has the advantage of being immediately available, with no waiting time for production. In particular, typical production, purification, formulation, and packaging systems stored in a GMP warehouse can be shipped immediately. It can be more difficult to find used specialized equipment. As the pharma industry moves more towards personalized medicine, however, manufacturers often find the need for specialized production equipment that is used only for short periods of time. For these projects, achieving investment recovery is even more crucial, so specialized systems are becoming increasingly available to CMOs.

Federal Equipment has been a trusted source of pharmaceutical processing equipment for more than 50 years. Our pharmaceutical team has extensive market knowledge, established relationships with many major pharmaceutical manufacturers, and an in-depth understanding of regulatory requirements affecting the sale of used pharmaceutical equipment. With our extensive inventory, climate-controlled, pharma-dedicated storage warehouses, and accurately appraised liquidations, we consistently exceed our clients' needs.

Matt Hicks,
Chief Operating Officer,
Federal Equipment Company.