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Coming Clean

Amid opioid devastation, industry and regulators scour for solutions

By Meagan Parrish, Senior Editor

A day rarely goes by without opioids making headlines in the national news. With overdoses still at staggering highs (the Centers for Disease Control and Prevention estimates that 115 Americans die every day from opioid overdose), it has become one of the most devastating health problems in U.S. history.

Recently, however, the front lines have shifted from the doctor's office to the streets as illicit fentanyl — a potent opioid that's often made in China and smuggled into the U.S. — becomes the prime source of overdose and death.

But that doesn't mean the pharmaceutical industry is done grappling with this crisis. In fact, by many measures, the legal, regulatory and market fallout has just begun.

Years ago, the U.S. Food and Drug Administration took calculated steps to address the situation. Now, the agency is in a full-on gallop towards the goals of preventing addiction, curbing abuse, and expanding treatment for opioid addicts — all while attempting to protect the needs of chronic pain patients.

Meanwhile, several key industry players have launched other programs to help — from educating healthcare professionals about prescribing opioids to adjusting formulations to deter abuse. R&D teams have also sprung into action to develop alternative painkillers or new opioid medications that carry fewer addiction risks. Dozens of new drugs to treat pain and addiction are also on the horizon and could soon be in reach.

While opioid lawsuits continue to play out in the legal system, outside the courtrooms, focus has shifted towards mitigation strategies, as regulators, manufacturers and researchers help pick up the pieces of the opioid storm.

THE BLAME GAME CONTINUES IN THE COURTS

The history of the rising prescription rates for narcotics and addiction have been well documented, and despite the changing patterns of drug abuse, pharmaceutical companies are still taking the brunt of the blame. The American legal system is fast becoming the main theater for the ongoing drama.

What began as a handful of local governments suing major opioid manufacturers such as Purdue Pharma and Johnson & Johnson a few years ago, has turned into an avalanche of litigation. Currently, drugmakers and distributors are staring down more than 250 lawsuits from states, counties and even hospitals.

Many of the plaintiffs are hoping to recoup the various costs associated with the rising needs of addiction treatment. Even though many opioid abusers are now hooked on heroin or fentanyl, the plaintiffs accuse manufacturers of misleading the public about the addiction risks associated with prescription painkillers and often point to Purdue's marketing of Oxycontin as the prime trigger of the epidemic.

More than a decade ago, executives from Purdue pleaded guilty to charges that they misled the public about Oxycontin's risks and agreed to pay $634 million in fines that were divvied up between private parties, and state and federal agencies.

But Purdue has also netted about $35 billion in sales from Oxycontin since it began marketing the drug in 1996, and many of the plaintiffs claim that the company hasn't paid its fair share for the medication's impact.

The company is certainly facing a mountain of legal costs now and finds itself in a tricky conundrum: If Purdue settles any cases, it could lead others to sue. For this reason, the company is reportedly hoping instead for a global settlement — similar to the settlement that was made with tobacco companies in 1998. A U.S. district judge in Cleveland reportedly has the same goal, and has been in talks with manufacturers and various agencies about coming to an agreement before all of the parties involved become entangled in years of costly litigation.

Critics point out that manufacturers may not be willing to pay a sum even close to the estimated $500 billion a year opioid addiction costs the country. Pharma companies could also make a strong case that they

shouldn't be forced to financially compensate for addiction now that the epidemic is more closely linked to street drugs.

Because these talks just began this winter, it remains to be seen if manufacturers will walk away with a settlement deal or be stuck in the long, legal shadow Oxycontin has cast for years to come.

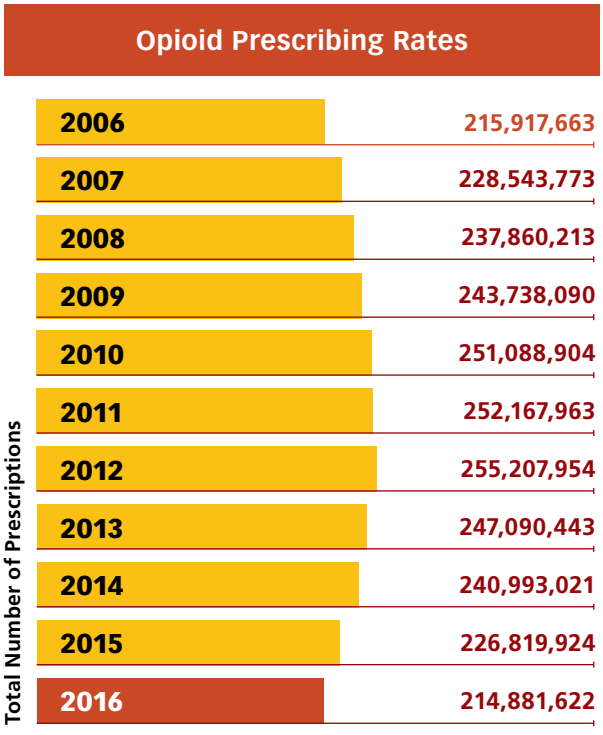
THE INDUSTRY RESPONSE

Like many industries, the pharma world has never been without some controversies. And after any disaster, there's always a period of introspection when the dust settles, the damage is assessed and the hard lessons are learned, so that mistakes won't be repeated.

In the case of opioids and other potentially addictive medications, the tone of the conversation throughout the industry has taken a dramatic shift in recent years according to Ed Elder, the director of the Lenor Zeeh Pharmaceutical Experiment Station and a professor at the UW-Madison School of Pharmacy.

"For a long time, the industry focus was on providing the benefit [of painkillers] and not mitigating the risk," he says. "Now there's a been a lot more focus on...finding mitigation strategies to address that."

Even though many in the industry have been accused of causing the epidemic, they are now stepping up to show they have some of the best solutions, too.



Source: Centers for Disease Control and Prevention

Among the dozens of opioid manufacturers in the U.S, you'd be hard pressed to find one that has taken more of a leading role on that front than Purdue. So far, Purdue has expressed support for limiting the length of first opioid prescriptions, the use of prescription monitoring programs, switching to abuse-deterrent formulations for opioids and most recently, promised to stop its sales force from touting the benefits of opioids to doctors.

The industry's biggest lobbying arm, Pharmaceutical Research and Manufacturers of America (PhRMA), has also taken a leading

"For a long time, the industry focus was on providing the benefit [of painkillers] and not mitigating the risk. Now there's a been a lot more focus on finding mitigation strategies to address that."

role in the issue. Late last year, PhRMA announced that it is embarking on a multi-year, multimillion dollar initiative to address the opioid crisis that includes a partnership with the Addiction Policy Forum. The effort will funnel money toward state and local programs for addiction treatment and help families impacted by opioids.

PhRMA has also joined forces with the National Institutes of Health to accelerate research toward non-addictive pain medications and new treatments for addiction, and is an outspoken supporter of limiting initial prescriptions for narcotics, while protecting patient access to medically necessary painkillers.

"The industry has taken substantial steps forward on the issue," says Nick McGee, director of public affairs at PhRMA. "Because it is a broad and complex issue, it's going to take all relevant stakeholders to help solve the problem. Our goal is to be a part of that comprehensive solution."

THE REGULATORY ROLLOUT

The FDA recently began taking a myriad of new steps to tighten controls around narcotics. Last fall, the agency notified 74 manufacturers that it is expanding rules that previously only effected extended release (ER) opioids to immediate release (IR) painkillers as well.

Currently 90 percent of all prescribed painkillers are IR and are many people's first exposure to narcotics. The new requirements mandated under a Risk Evaluation and Mitigation Strategy (REMS) will require manufacturers to provide training to healthcare professionals about safe prescribing practices for IR opioids and prompt them to consider alternatives.

"For the first time, this training will also be made available to other healthcare professionals who are involved in the management of patients with pain, including nurses and pharmacists, which is in addition to prescribers," FDA Commissioner Scott Gottlieb said in a statement about the change.

All told, the existing REMS, which already impact 64 ER formulations, will now include an additional 277 IR medications.

The agency is also considering a new rule that would mandate that certain IR opioids come in blister packs of possibly two-or six-day supplies, so that prescribers are encouraged to dispense them for smaller durations of use.

So far, the FDA has been conducting stakeholder meetings about the potential change and hasn't issued any final word on what the new regulation would require. Gottlieb admitted last year in an interview with CNBC that the changes could be "uncomfortable" for drugmakers because they would increase manufacturing costs.

Earlier this year, the FDA took a more direct step with manufacturers of loperamide, an anti-diarrhea drug, when it asked them to voluntarily change how the drug is packaged and sold. Because loperamide, sold under the brand name Imodium, can induce a mild opioid-like high in large quantities, a growing number of people have been abusing the drug in recent months, and at least a few have died. Although the FDA stopped short of mandating changes, the agency asked that manufacturers switch to blister packs and that distributers who sell the drug in bulk limit quantities available in an individual package.

On top of these targeted changes, the FDA has also rolled out its own comprehensive plan to combat opioid abuse, including the creation of a policy steering committee and a plan to fast-track approvals for new addiction treatments and non-opioid analgesics — which is fast becoming another pressing issue in the midst of the epidemic.

Whenever the FDA posts proposals for more stringent measures on opioids on the Federal Register, the comments from hundreds of pain patients pour in. While the regulatory focus is still on limiting pills from the doctor's office — and the measures have already begun to make a dent in America's prescribing rates — many believe it is becoming too difficult to get relief for legitimate pain. And many patients with chronic conditions are now being weaned off of the medications that have given them the ability to function in everyday life.

As the healthcare world turns away from narcotics, it is now turning to pharmaceutical companies to offer up new ways to treat pain.

THE R&D FIX

According to PhRMA, there are about 40 new medications in the development pipeline for treating addiction and at least 40 new analgesics in the works as well.

One of the most promising fronts for offering pain relief while bypassing the euphoric side effects that can get patients hooked include drugs that target specific pain receptors instead of the central nervous system.

According to PhRMA, there are about 40 new medications in the development pipeline for treating addiction and at least 40 new analgesics in the works as well.

"The industry has accomplished this in other therapeutic areas, like treating cardiovascular disease," Elder says. "Applying those concepts is an exciting way to go."

One such non-opioid medication that's generated a lot of buzz is tanezumab, which is being developed by Pfizer Inc. and Eli Lilly and Company. Designed to treat low back pain and osteoarthritis — two of the biggest prizes in the chronic pain market — the drug works by selectively targeting, binding to and blocking nerve growth factor. The FDA has given the medication fast track designation and it is currently in phase 3 clinical trials.

On the pre-clinical side, research teams have been getting inspiration from nature to develop drugs from exotic sources. One group at the University of Utah received a $10 million grant last year to study a kind of cone snail that uses a harpoon-like tooth to stab its prey and shoot them with a paralyzing venom. The team hopes to identify the compounds in the venom that contain pain-relieving properties and turn them into medications.

Another field of research that's cropped up involves genes that impact the sodium channel NaV1.7, which controls pain signals to peripheral nerve cells while avoiding signals that travel to the brain. Several companies such as Teva Pharmaceutical Industries, Johnson & Johnson and Pfizer have explored the sodium channel angle and then abandoned the quest after disappointing results. But a slew of other companies including Amgen, Roche and Regeneron Pharmaceuticals are still in the hunt for success and have various medications in early clinical trials.

Meanwhile, scientists are also looking at using existing technologies to make a new class of opioids that don't have side effects such as respiratory depression and rising tolerance, which can lead to increased use.

Although it could be years before these new treatments make it to market, pharma companies are stepping up to fill the rising need for new pain-relieving treatments.

BOTTOM LINE?

The opioid epidemic has become a watershed event for the pharmaceutical

"It's best to find solutions now that work for your business, before someone is mandating solutions for you."

industry that will leave a lasting mark for years to come. As new regulations take shape that could impact a slew of medications, pharma companies throughout the supply chain would be wise to take proactive steps to mitigate addictions risks for users and find ways to be a part of the solution.

Recently at the AAM Access! 2018 Annual Meeting, the director of global policy at Walmart, Betsy Hall Collins, echoed these sentiments during a presentation about the impact of opioids on the pharma world. The retail giant announced this year that it will give away free packets of DisposeRX, which can be used to dispose of old medications, to customers receiving an opioid prescription.

"It's best to find solutions now that work for your business, before someone is mandating solutions for you," she said.

Pharma Gains Momentum

As the industry looks towards a strong 2018, survey respondents report satisfaction and security despite mounting pressures

By Karen Langhauser, Chief Content Director

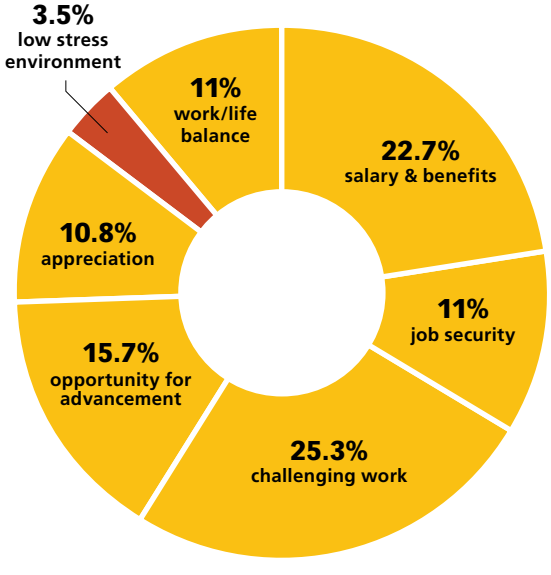
For the 14th consecutive year, Pharmaceutical Manufacturing readers have provided insightful feedback on careers and salaries through our annual survey. We query readership to gain a sense of how their pharma careers are treating them — both financially and emotionally — and speculate on how those answers reflect the bigger industry picture.

ABOVE AVERAGE SATISFACTION

Job satisfaction in the pharmaceutical industry remains good — more than 89 percent reported their satisfaction levels within the range of "very high" to "OK," which is exactly the same as last year's survey.

Results varied by respondent demographics. Of the 307 respondents who indicated their gender, 94.5 percent of women were in the very high to OK range, and 88.5 percent of men reported as such. When broken down by industry segments, those working for consulting companies reported the greatest amount of job satisfaction, with a whopping

What is most important to you for job satisfaction?



79 percent ranking their satisfaction levels from high to very high. This was followed by small to mid-sized specialty pharma manufacturers, which had 61.6 percent reporting high to very high satisfaction levels.

Overall job satisfaction has been on the rise in the U.S., but even so, only just recently (in 2017) surpassed the 50 percent mark — so it would appear as though the pharma industry is way above average.[1]

perceived importance of challenging work versus salary is shrinking.

Additionally, job security and appreciation slightly declined in importance since last year, while low-stress environments and opportunity for advancement gained votes.

These results were corroborated by a write-in question, where respondents were asked what satisfies them most about their current position. Many respondents pointed out that their jobs offer new challenges and new problems to solve — and that projects are unique, interesting and diversified. Overall, respondents feel good about helping people, and find satisfaction in the belief that they are making a difference for their companies and for patients. "My company is making a major impact on improving the quality of patients' lives," said one respondent.

Respondents enjoy having the ability to make decisions independently as well as the perks of flexible hours, understanding employers and time-off.

DEFINING SATISFACTION

While "satisfaction" can be a subjective state, our survey asked readers which specific factor contributed most to their overall level of satisfaction. When asked about a variety of factors, among them challenging work, salary and benefits, opportunity for advancement, job security, stress levels and work/life balance, just over 25 percent ranked challenging work as the most important contributing factor. This was closely followed by 23 percent who ranked salary and benefits as the most important factor. While this ranking order has stayed consistent for the past six years, the gap between the

Interestingly, while only 11 percent said that work/life balance is the most important factor when it comes to overall job satisfaction, many said that freedom — in terms of working environments and work/life

Additionally, job security and appreciation slightly declined in importance since last year, while low-stress environments and opportunity for advancement gained votes.

balance — is what they like most about their jobs. Respondents enjoy having the ability to make decisions independently as well as the perks of flexible hours, understanding employers and time-off.

TALKING MONEY

Compensation appears to be healthy and reflects the sustained recovery of the pharma industry in 2017. Just over 25 percent of those surveyed have gross annual salaries between $100,000-150,000, with the next largest group (20%) making $150,000-200,000 annually. And 14.4 percent of respondents indicated their salaries are above $200,000.

According to survey results, both seniority and education factor into salaries. The majority (78 percent) of those who report gross yearly salaries exceeding $100,000 have more than 10 years of experience in the industry. Additionally, 67 percent of those who report salaries exceeding $100,000 have postgraduate degrees.

In this year's survey, almost 65 percent of respondents reported getting raises last year, with most (77 percent) seeing an increase of 3-5 percent. Just 10.5 percent of those who reported earning raises said their salaries were increased by more than 10 percent.

These numbers are slightly down from year's survey, where a greater percentage of respondents reported getting raises (70 percent), as well as a greater percentage (13 percent) seeing raises higher than 10 percent. This small drop in wage increases was projected on a global level, however. A Hay's Group 2017 forecast predicated that, adjusted for inflation, workers around the world are were expected to see real wage increases of 2.3 percent (down slightly from 2016's prediction of 2.7 percent).[2]

SECURITY IN TODAY'S MARKET

For the pharmaceutical industry, 2017 was challenged with a new administration that was both unpredictable and unconventional, a new FDA commissioner,

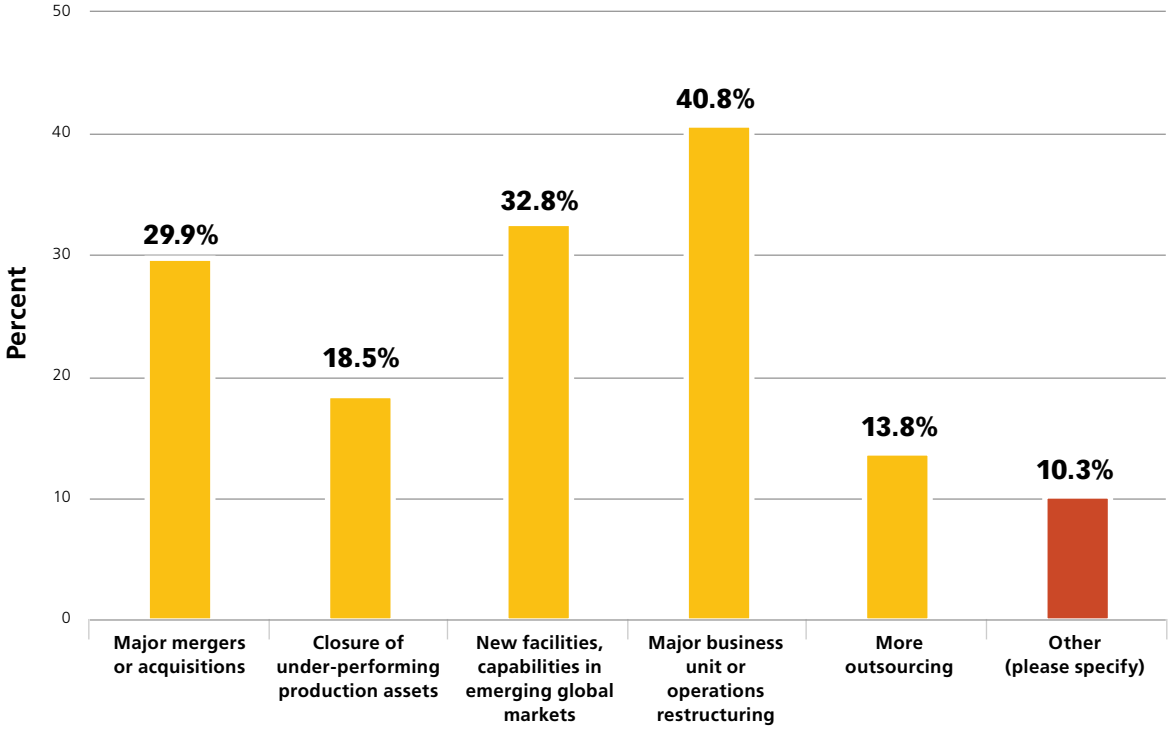
Despite all obstacles, 2017 saw the pharmaceutical sector bouncing back from what many analysts referred to as a "lackluster 2016."

and high levels of scrutiny surrounding drug prices and opioid use.

Despite all obstacles, 2017 saw the pharmaceutical sector bouncing back from what many analysts referred to as a "lackluster 2016."[3] The past year saw major advances in innovation, specifically in immunotherapy, stem cells and personalized medicines, as well as a higher number of drug approvals.

When asked how current market and competitive forces affected their companies, 41 percent of respondents noted major business unit or operations restructuring. This answer has remained in the top spot since we started asking the question in 2014. This year, 33 percent said market pressure resulted in the launch of new facilities and capabilities in emerging global markets.

How have market and competitive forces affected your company recently?



Major mergers, acquisitions and outsourcing both saw a decline in this year's survey, with only 30 percent of respondents noting the effects of M&A and 14 percent acknowledging outsourcing increases.

This is in line with market reports, as 2017 saw an unusual stagnation in pharma M&A[4] as well as a decrease in pharma spending on outsourcing activities.[5] Many experts speculate that pharma spent much 2017 on pause, waiting to see how tax reforms and cash repatriation will shake out before making any major decisions.

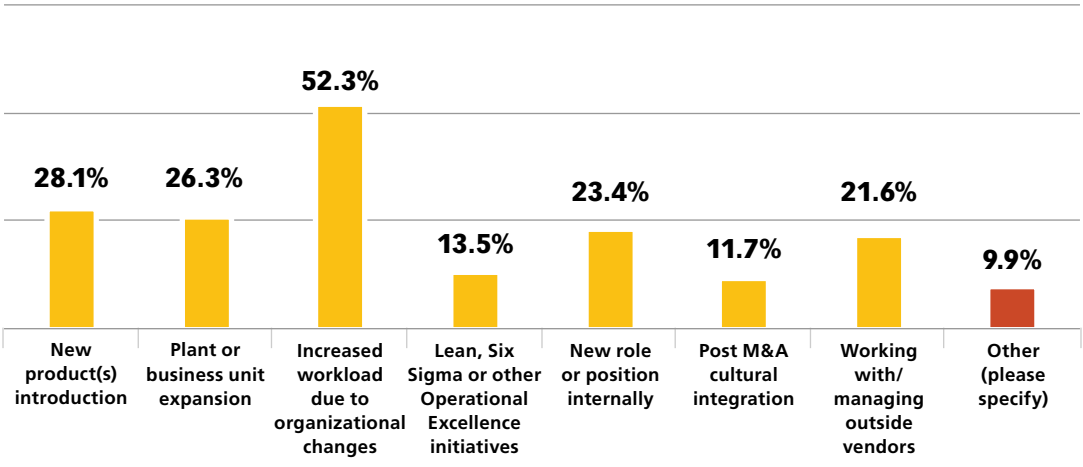
Despite a year of uncertainty, it appears as though policy from the new administration will work out in pharma's favor and survey results reflect continued positive attitudes about job security. When asked if they were more or less concerned about job security than last year, just 30 percent of those surveyed noted increased concern. While similar to last year's numbers, these percentages are way down from previous years (52.5 percent in 2016 and 48 percent in 2015).

Those who were wary of job security pointed almost equally to two top threats: "External financial pressure on my company due to expiring patents or circumstances surrounding failed product development or regulatory approval" (40 percent) and internal cost-cutting measures (38 percent). This is a sweeping shift in data from last year, where over 50 percent were concerned with internal cost-cutting and only 26 percent pointed to external financial pressure as the top threat. In fact, starting in 2012, surveys have revealed a shift from concerns about external financial pressure towards internal cost cutting — this year has halted that trend.

REAL TALK: CHALLENGES

While several studies have found that

What were the biggest challenges you had to face in the past year?



moderate amounts of stress are actually beneficial in the workplace6 (when the body and brain are moderately stimulated by stress, decision-making, learning and the formation of memories are all enhanced), too much stress has the opposite effect. Has pharma found the right balance? According to the survey, 57 percent of readers feel overly stressed some of the time at work, while 21 percent feel overly stressed most of the time.

The source of the stress? More than half (52 percent) of respondents said the biggest obstacle they faced in the past year was an increasingly workload due to organizational challenges. Additionally, 59 percent of respondents failed to take all of their allotted vacation time last year, which is not unusual for American workers. (National surveys report that about 55 percent of workers across all industries leave vacation time unused.)

While the survey results overall were positive, when put on the spot to describe what made them least satisfied about their current position, readers responded with honestly. Stress again took center stage, with respondents describing their jobs as "crazy busy" and mentioning the "high level of stress related to over-commitment." Stress was seemingly worsened by management and red tape, with respondents pointing out "how simple processes can be turned into complex processes due to bureaucracy" and lamenting the "internal bureaucratic hurdles to efficiently developing processes."

A lack of clarity and transparency was also a frequent complaint. Similar to years past, management and senior leadership bore the brunt of the criticism with readers bemoaning the "siloed style of management at the corporate level" and "unclear strategic plans from senior management." Many noted the lack a of clear path to advancement opportunities. In fact, 46 percent of respondents said they do not receive meaningful feedback on job performance on a yearly basis.

SURVEY DEMOGRAPHICS

This year's study yielded 350 total responses. Examining demographic profiles revealed by Pharmaceutical Manufacturing's respondents, participants were predominately North American-based (70 percent), with the remainder of respondents dispersed in Europe (9 percent), Asia (6.5 percent), India (6.5 percent), the Middle East, Africa and Latin America.

This year, 76 percent of survey respondents were male and 24 percent female — the largest percentage of women respondents we've had in survey history.

The majority of respondents (74 percent) were 40 or older, with most possessing degrees in either chemistry, chemical

engineering or pharmaceutics. According to survey results, 20 percent fill R&D rolls, 19 percent are in quality assessment and QC, and 17 percent in manufacturing and operations. Corporate management, plant engineering and design, process control and regulatory functions were also represented.

Industry longevity dominated, with 79 percent of responding readers having seven or more years of industry experience — and an impressive 46 percent of total respondents boasting more than 20 years of pharma industry experience. Not surprisingly, over 62 percent are in supervisory roles, with 14 percent in charge of supervising more than 15 people.

Responding readers represented the panoply that is the pharma industry, with 20 percent from Big Pharma, 19.5 percent from small and mid-sized specialty manufacturers, 15 percent from generic pharma, 10.5 percent from contract pharma and 10 percent from biopharma. The remainder, including consultancies, vendor/solution providers and all others, accounted for about 25 percent of the total pie.

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Rx-Reg Vision

A painless look inside the most impactful regulatory trends and actions from the past year

By Karen Langhauser, Chief Content Director

Keeping up to speed with the ever-changing global regulatory environment is enough to make anyone's head spin — yet it's vital when it comes to ensuring ongoing compliance, as well as making the right decisions for pharmaceutical organizations.

The benefits of proper regulatory intelligence are vast, especially at a time where speed-to-market is increasingly important. Successfully implemented regulatory intelligence can shorten time from filing to approval, increase the likelihood of marketing approval and help identify new opportunities in drug development. It can also help pharmaceutical organizations plan ahead, aiding in better prediction of regulatory review times and helping to proactively avoid potential compliance pitfalls.

What follows is what we hope will be a helpful contribution to your regulatory intelligence efforts: a brief discussion of some of the most impactful regulatory initiatives from the past year and how they play into current trends in pharmaceutical manufacturing.

PAVING THE WAY FOR PERSONALIZED MEDS

The personalized medicines market — treatments tailored to the individual patient — is growing rapidly, with revenue predictions as high as $5,208.68 billion by 2022.[1] Regulatory agencies play a large role in shaping the infrastructure that enables developments in personalized medicine.

PDUFA VI

On Aug. 18, 2017, the President signed into

law the Food and Drug Administration Reauthorization Act (FDARA). This new law includes the reauthorization of the Prescription Drug User Fee Act (PDUFA), intended to provide the FDA with the necessary resources to maintain a predictable and efficient review process for human drug and biologic products.

Aside from the more visible changes to the fee structure and fees, PDUFA VI also aims to do more to integrate patient perspectives into the development and regulatory review of new medicines. Launched as a new initiative in 2012, as part of PDUFA V, patient-focused drug development (PFDD) incorporates the patient's voice into the development and review process. The FDA has committed to hold 24 disease area-specific PFDD meetings with individual patients and patient groups over the course of PDUFA VI.

PDUFA VI has the potential to strengthen the FDA's ability to advance the science of patient input with actions, such as placing dedicated experts into review divisions to engage with patients, patient advocates and sponsors during drug development.

21st Century Cures Act

The 21st Century Cures Act (though technically signed into law in December 2016 - a little early for our 2017 recap) is intended to provide the FDA with tools aimed at modernizing regulatory programs. In July 2017, the FDA announced a detailed work plan for the steps the agency is taking to implement different aspects of Cures, which included elements that further the goals of the personalized medicines initiative, including:

- The Center for Biologics Evaluation and Research (CBER) implementing the Regenerative Medicine Advanced Therapy (RMAT) designation, enabling the FDA to facilitate an efficient development program for, and expedite review of, new regenerative advanced therapies.

- CDER, working with CBER, outlining a plan for the development of patient-focused drug development guidances.

"PDUFA VI and the Cures Act work hand in hand to bring the patient into the drug development process and ensure that drug development is actually working to the benefit of patient outcomes," notes Lawrence Liberti, VP executive director for the Center for Innovation in Regulatory Science (CIRS). CIRS, a non-profit subsidiary of Clarivate Analytics, brings together regulators, pharma manufacturers and health technologies assessment (HTA) agencies for the purpose of advancing regulatory and HTA policies and processes used to facilitate access to medicines.

GLOBAL ALIGNMENT

The past year saw significant progress in

ICH's mission is to achieve greater worldwide harmonization in the production of medicines by developing guidelines via a process of scientific consensus.

the ongoing quest for global alignment of regulatory expectations. Harmonizing regulations across the world would greatly reduce the complexity of the drug development process, ultimately bringing new drugs to market faster.

ICH Guidances

A key organization when it comes to global alignment is the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). ICH's mission is to achieve greater worldwide harmonization in the production of medicines by developing guidelines via a process of scientific consensus between global regulatory agencies and industry experts.

"ICH's aligned guidances allow pharma companies and agencies to have greater clarity surrounding regulatory expectations," says Liberti. "In the last year, we've seen an increase in the number of participants that are formally recognizing ICH as an important way forward. Having alignment across growing markets will bring further clarity and predictability to the regulatory and development processes."

Notable new members approved over the past year include regulatory agencies from Brazil (ANVISA), Korea (MFDS) and China (CFDA), while regulatory agencies from Cuba (CECMED) and South Africa (MCC) were added as observers.

As part of the ICH process, draft guidelines are transmitted to the regulatory authorities of the ICH regions for internal and external consultation. In 2017, the U.S. FDA released several draft guidances of ICH harmonized guidelines in various stages of the ICH process, including revised ICH S5 Guidelines, an addendum to E9(R1) "Statistical Principles for Clinical Trials" and a Q&A on Q11 "Development and Manufacture of Drug Substances."

"ICH really sets a good level playing field, and I think adherence to ICH will be a key factor in promoting global alignment," says Liberti.

PIC/S

The Pharmaceutical Inspection Co-operation Scheme (PIC/S) aims to harmonize inspection procedures worldwide by developing common GMP standards and providing training opportunities to inspectors. In 2017, the organization published a revised GMP guide, as well as unveiled a new strategic plan with a strong emphasis on training and better communication with heads of regulatory agencies.

In his contribution to the 2017 CPhI Annual Report[2] Bikash Chatterjee, president and chief science officer, Pharmatech Associates, points to regulatory disparity as the greatest hurdle to broad adoption of standards (such as ICH guidances), but says "that hurdle is rapidly disappearing as a result of the success of the PIC/S."

And participation is growing. In September 2017, the PIC/S Committee invited Iran's IFDA, Turkey's TMMDA and Mexico's COFEPRIS to join, effective January 2018 - bringing the total to 52 participating authorities.

Earlier in the year, PIC/S became an ICH Observer, which allows the co-op to attend ICH assembly meetings and to participate in other ICH activities. Collaboration between the two groups serves to strengthen the role both organizations play in the quest for a global pharma marketplace with shared regulatory compliance.

ADVANCING QUALITY

Global regulatory agencies continue to stress the need for ongoing improvements in product quality and are taking action by developing regulatory approaches that support continuous improvement in quality processes.

Submission of quality metrics data

In an effort to encourage the industry to implement state-of-the-art quality management systems, the U.S. FDA is in the process of initiating a quality metrics reporting program. Through this program, the Agency intends to use quality data submitted by the industry to help develop compliance and inspection policies and improve the Agency's ability to predict drug shortages.

While the revised draft guidance for "Submission of Quality Metrics Data" was published by the FDA in late November 2016, plans are in the works for a voluntary rollout of the program starting in January 2018, with the intention of making the program mandatory in the future. The past year, however, has brought much resistance surrounding this new quality metrics program — even after the agency's revisions, the industry still has viable concerns about the program.

In March 2017 several trade/technical organizations, led by the Association for Accessible Medicines, submitted commentary on the revised guidance, requesting further

Modern-day drug innovation requires adopting modern-day manufacturing approaches.

dialogue between the agency and industry before the FDA proceeds with its proposed metrics collection efforts. The letter stated that "such a program would require substantial resources, present significant operational challenges and complexities, and draw resources and management attention away from other programs that drive continual quality improvement."

Additionally, points out Siegfried Schmitt, principal consultant, PAREXEL, the metrics collection program is still a proposal that remains isolated to the U.S. FDA. "So far no other regulatory agency has stated that they would be interested in establishing a similar concept in their jurisdiction. With an isolated concept, there is little likelihood of widespread enthusiasm within the industry to participate in the trial," says Schmitt.

Emerging technologies

In September 2017, the FDA issued final guidance on "Advancement of Emerging Technology Applications for Pharmaceutical Innovation and Modernization," providing recommendations to companies interested in the Agency's Emerging Technology program.

While the guidance seeks to advance the use of emerging manufacturing technologies, such as continuous manufacturing or 3D printing, improved product quality is the true endgame. According to the guidance, not only should emerging technology be novel to the pharma industry, but it should "have the potential to modernize the pharmaceutical manufacturing body of knowledge related to product quality."

Modern-day drug innovation requires adopting modern-day manufacturing approaches, and this guidance is an attempt by the FDA to break down some of the traditional barriers to enable a safer, more efficient drug manufacturing environment.

WORLD EVENTS

2017 brought significant political change - the effects of which still remain somewhat of a wild card when it comes to regulatory impact.

Brexit

On March 29, 2017, the United Kingdom notified the European Council of its intention to withdraw from the European Union by March 2019. For pharma manufacturers, this

move raises concerns about the European Medicines Agency, especially for companies that want to continue marketing drugs in the European Economic Area after the UK withdraws from the EU. Brexit presents challenges in several areas, notably regulatory procedures, quality testing, supply chain management and intellectual property.

In November 2017, associations representing the European and British life science industry published a letter urging Brexit negotiators on both sides to agree to a transition period that will enable continued EU-UK partnership on the regulation and supply of medicines.

Also in November, the EMA announced that it will relocate to Amsterdam, the Netherlands. EMA has developed and made public a business continuity plan to ensure operational continuity while the Agency prepares for its relocation and the UK's withdrawal from the EU. The EMA published additional practical guidance to help pharmaceutical companies make all necessary changes to their marketing authorizations by the end of March 2019.

Trump presidency

Early in his presidency, Trump lashed out against the FDA, calling its approval process "slow and burdensome," while vowing to deregulate the drug industry. The crux of Trump's message was that reducing regulatory standards would lead to more treatments reaching the market and lower drug prices - a message that was met with concerns over drug safety.

Trump's first major FDA-related action came in the form of nominating Dr. Scott Gottlieb as the Agency's 23rd Commissioner. Sworn in in May 2017, Gottlieb echoed Trump's desire to overhaul the FDA, striving to reduce the red tape that he has often said hampers pharmaceutical innovation. Pharma critics initially voiced concern over Gottlieb, who had served on the boards of several major pharma companies and had strong ties to Wall Street. While it's almost too early to form an opinion, so far, Gottlieb has seemingly found a way to work within the FDA's system while still aggressively pushing new agency actions and policies — in particular those aimed at lowering drug prices. Under Gottlieb, that Agency has prioritized access to cheaper, generic medicines, including posting a list of brand-name drugs that lack generic competition, and fast-tracking approvals of associated generics.

In November, Trump nominated Alex Azar II, a former top Eli Lilly executive, to be the next Secretary of the Department of Health and Human Services (HHS), promising that Azar will be "a star for better health care and lower drug prices." If confirmed, Azar will succeed Tom Price, who resigned after news broke that he spent close to $1 million on air travel in his first seven months. As HHS secretary, Azar would oversee numerous

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agencies including the FDA and the Centers for Medicare and Medicaid Services.

The nomination is controversial, however, considering Azar spent five years serving as president of the U.S. arm of Eli Lilly at a time when the drugmaker was highly criticized for dramatic price increases. Azar had his first confirmation hearing before the Senate Health, Education, Labor and Pensions committee on November 29th. In the hearing, Azar attributed high drug prices in part to patent abuses that stall market access to more affordable generic drugs. "This is the most important job I will ever have in my lifetime, and my commitment is to the American people, not to an industry," Azar assured.

A LOT HAPPENS IN A YEAR

While the aforementioned regulatory actions stand out among the hundreds of guidances published in 2017 by regulatory agencies around the world, by no means is this a comprehensive list.

The past year brought with it important regulatory inroads in personalized medicines, global harmonization and quality. While political change in 2017 has left open questions for the year ahead, regulatory progress on the whole was encouraging.

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