PHARMA & BIOTECH
CHEManager INTERNATIONAL
1/2017

Markets & Companies
Pharma's Next Patent Cliff, The Return of Large Scale Mergers, CMOs as Strategic Partners, Expert Opinions, Company News

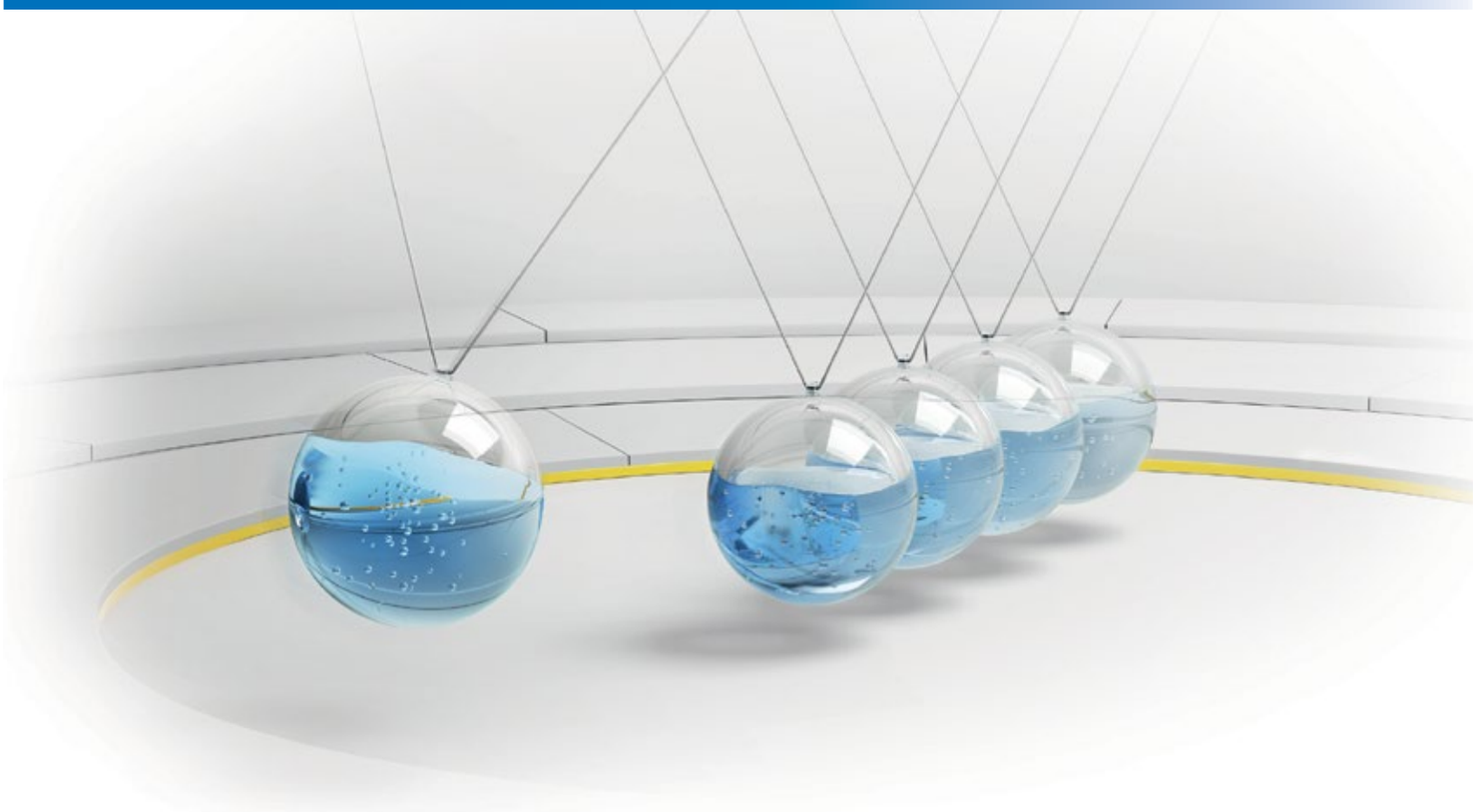
Strategy & Management
How to Cure Complexity in Pharma Companies, The Potential of Precision Medicine, Digitalization Transforms R&D

Manufacturing & Supply Chain
Procurement Challenges, Supply Chain Integrity, Patient Safety, Risk Assessment for Excipient Manufacturers

WILEY

Rentschler Biopharma

Passion for Performance



Rentschler – A world-class biopharmaceutical CDMO

- Full-service provider from gene to vial and from concept to market
- Contract development and manufacturing with quality excellence
- Experts in mammalian cell culture
- State-of-the art facilities and technologies
- Extensive track record with more than 40 years in biopharma

- We are a biotechnology pioneer
- We are listening to our clients
- We find solutions where others don't even look

Rentschler Biopharma SE
Erwin-Rentschler-Str. 21 · 88471 Laupheim · Germany
info@rentschler-biopharma.com · www.rentschler-biopharma.com

©monticelllllo - stock.adobe.com

© freshidea - stock.adobe.com

© alexskopje - stock.adobe.com

New Rules For Pharma

On the Way to a More Consumer-Oriented Industry, Pharma has to Deliver Much More than Drugs

Pharmaceutical companies are experiencing numerous challenges such as increasing cost pressures, declining autonomy or protocol-driven care. The reaction has to go beyond traditional instruments such as consolidation. In this new era, pharma has to become more proactive with wide communities of patients and meet the needs of different consumer groups. The industry also has to deliver positive results for society: health, well-being and optimal management of illness.

© Sisacorn/Shutterstock

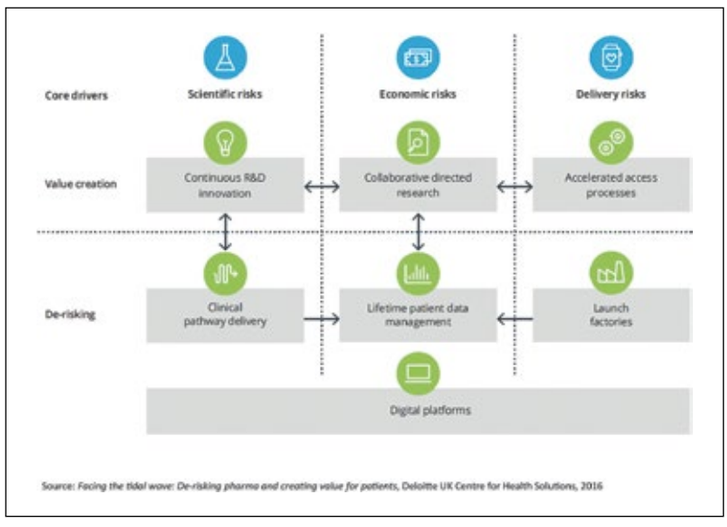
Some experts call it the New Health Economy. What they mean is the fact that pharmaceutical and life sciences companies are experiencing a wave of competing challenges. As the strategy and consultant firm PWC reports in its 2017 Pharmaceuticals and Life Sciences Trends, these challenges include consolidation among providers, especially hospitals, intended to produce efficiency gains; changing demands and expectations of patients, who seek a greater role in their own care; increasing cost pressures from payers; and the declining autonomy of the individual physician as rule-based, protocol-driven care becomes ascendant.

For the pharma and life sciences industry this means finding new and correct answers in order to further achieve profitable and sustainable growth. As the accounting firm Deloitte points out in its 2017 Global Life Sciences Outlook such growth won't come easy. "Looking across a landscape of challenges, the mismatch between increasing Research & Development (R&D) expenses and the payer and public demand for lower-cost treatments is a game-changing issue because it will likely affect both the direction and speed of the sector's future development."

In the past mergers and acquisitions (M&A) has been one of the most effective tools for pharma executives to face the challenges of the industry. M&A as well as divestiture activities play a significant role in life sciences companies' strategies to gain scale and to add new markets, new drugs, and novel technologies, states Deloitte. The financial online portal Seeking Alpha adds, because of organic growth slowing, pricing pressures and blockbuster drugs going off-patent, a number of key players will need to "buy" their way into growth and stave off growing competition.

In 2017 Johnson & Johnson's $30 billion acquisition of Actelion has set the tone. The latest prominent example is Gilead Sciences' intention to buy Kite Pharma and its CAR-T cancer-killing technology for $11.9 billion. The acquisition is the answer to the question investors have been asking Gilead management for more than two years: "What will you buy to deliver new growth to the company in the wake of declining hepatitis C sales?"

In the view of Seeking Alpha one of the key ingredients supporting M&A activity is cheap debt financing. On this background John Rountree, managing partner at the pharma consultancy Novasecta, mentioned in an interview with CNBC that there would be more consolidation in the industry. "I think consolidation is more likely driven by people wanting to have access to innovation rather then particularly cost-cutting."



Seven options for developing the pharma business model.

Deloitte specifies that one area to watch is deals that combine life sciences with technology. Companies could benefit greatly from analytics and digital investments, especially as these capabilities are not generally developed in-house. Also, if life sciences organizations don't use M&A and strategic partnering to join this community, they risk being leapfrogged by the technology companies.

But there are also some concerns regarding the M&A activities of pharma as Joanna Shepherd, professor at Emory University School of Law in Atlanta, says: "As pharmaceutical M&A has soared, so too has concern over the impacts of consolidation on the drug industry. These concerns are premised on the idea that merging competitors into one firm will reduce incentives to develop new drugs."

However, she explains, this view is largely based on an outdated understanding of the innovation ecosystem in the pharmaceutical industry. In the current system, where little drug innovation originates internally, a merger's influence on internal R&D

expenditures or development projects is often immaterial to aggregate drug innovation.

Attention on Continuous R&D Innovation

In any case M&A activities mostly are only one element of pharma companies to maintain or strengthen their position in the changing markets. According to Deloitte's 2017 pharma report, given the number of changes and challenges life sciences companies must also pay close attention to continuous R&D innovation. Driving and sustaining clinical innovation persists as a life sciences sector priority. There are not only soaring R&D costs, increasing pricing pressures, growing market share for generic pharmaceuticals and biosimilars, and heightened scrutiny by regulators that are having a dampening effect on clinical innovation; there is also the demand for new, innovative treatments.

Continuous R&D innovation also has a direct positive effect for the pharma companies itself, says Deloitte. It can help improve the operational effectiveness of research organizations. Furthermore reducing development complexity should materially improve returns.

Collaborative Product Development

For better results in R&D, collaborative product development can also be essential. This can span the spectrum of openness, and potential partners may be found in government, academia, traditional biopharma and new industry entrants. As Deloitte reports, life sciences thus can fill in-house capability gaps and overcome R&D and marketplace challenges by externally sourcing innovative ideas, knowledge, skills and technologies.

Another major industry trend is the rapidly increasing importance of analytics, PWC explains. Pharma companies have begun to realize real benefits from the evolving data ecosystem, using new methods for rapid acquisition, curation, analysis and visualization of large, diverse data sets in cloud-based storage and distributed computing power platforms.

Changes in Pharma Supply Chains

Beyond this Allen Jacques, vice president of pharma supply chain at FusionOps, also sees the pharmaceutical supply chain as a trigger for market success. Although one of the most complex supply chains in the world, it has historically been resistant to transformation.

"In many ways, 2016 was a turning point," Jacques said. "Today there's more pressure than ever before on the supply chain to be redesigned. The remit for supply chains of 2017 and beyond will be to start actually driving real revenue for businesses instead of just passively supporting revenue-generating operations."

Deloitte adds that forward-thinking life sciences companies are transforming their traditional, linear supply chain into a dynamic, interconnected system that can more readily incorporate ecosystem partners and evolve to a more optimal state over time.

"Pharmaceutical and life sciences companies are experiencing a wave of competing challenges."

Connecting with Customers and Consumers

Beyond this, today payers and consumers are the most important stakeholders for pharma companies. Increasingly engaged and empowered health-care consumers are demanding services and solutions that are coordinated, convenient and customized. According to findings from the Deloitte 2016 Survey of US Health Care Consumers, there is also a growing consumer appetite for using technology-enabled care. Social networks have become powerful customer engagement tools and offer a more personal and open dialogue than traditional marketing channels like commercials or advertisements.

Deloitte points out that large pharmaceutical companies focused on traditional markets have often lagged in responding to the industry's changing focus toward holistic patient management. Now many companies have only a small window of time to frame their strategies for operating in a new, customer-centered, digital ecosystem or risk being disintermediated by fast-moving entrants that are developing digitally enabled products and programs to cater to changing patient expectations.

One of the most interesting consumer engagement challenges facing life sciences companies is how to increase consumer trust and improve the overall reputational perception of the sector. More and more companies are increasingly seeking to help patients navigate the complexities involved in receiving a diagnosis, deciding on treatment, securing financial assistance, connecting with other patients and community experts, and supplementing clinical education.

End-To-End Evidence

In the end the question of pricing is also essential for pharma companies. "Every pharma executive knows there is intense interest these days in what a drug is really worth," PWC explains. Pharma companies need to find new ways to define value that resonate with stakeholders. Thanks in part to social media and advocacy groups, patients are becoming much more active in making their voice heard. "The resulting health-care system will focus increasingly on paying for the value rather than the volume of medical care; in other words, it will be a more consumer-facing industry," PWC argues.

In this new era, pharma companies will have to become more proactive with large communities of patients and go beyond lip service in meeting the needs of a wide swath of consumers. In the New Health Economy, pharma companies should not only focus on sales but also have to concentrate on delivering positive results: health, well-being and optimal management of illness among targeted populations.

Thorsten Schüller, CHEManager

The Expanding Role of Contract Manufacturing

CMOs Are Evolving from Service Providers to Strategic Partners

In the shifting pharmaceutical landscape, contract manufacturing organizations (CMOs) and big pharma could see significant benefits. The findings of a new A.T. Kearney study can help pharma companies unlock value beyond lowering costs and enable CMOs to become competitive international players, far beyond their role as an extended workbench.

Dr. Oliver Scheel, A.T. Kearney

Dr. Carola Schlumbohm, A.T. Kearney

Dr. Constanze Schmidt-Rhode, A.T. Kearney

Three trends are shaping the CMO industry:

- Demand for CMOs in regard to service offerings and technological requirements is growing. Historically, pharma companies turned to outsourcing for chemical active pharmaceutical ingredients (APIs) and simple finished dosage forms (FDFs), primarily in generics and consumer health. Now, they are outsourcing high-potency APIs, bio-APIs, biopharmaceuticals, advanced bulk, and new molecular entities (source: PharmSource).
- CMOs are evolving from service providers to strategic partners. CMOs now cover the entire value chain of pharma production, including specialized services such as R&D. New agreements and stronger partnerships are emerging, with CMOs buying manufacturing sites or taking on construction projects to support manufacturing requests.
- M&A activity in the fragmented CMO landscape is spiking. This is leading to plans for geographic expansions and upgrading of technological capabilities.

Market, Technology, and Geographic Overview

The global CMO market had $72.7 million in revenue in 2015. By 2020, it could surpass $108 million. The US is the largest market, but Asia Pacific is expected to see double-digit growth, and Europe will remain a CMO hub.

The market is divided into three segments: APIs, intermediates (bulk), and FDFs, which include solids, semi-solids, liquids, and injectable doses. The largest segment is API and intermediate CMOs, with around 80% of the market and predicted growth of 8% until 2020. 95% of revenue is generated by CMOs that focus on chemical APIs. However, by 2020, CMOs focusing on biotech APIs will increase their revenue share to 9.5%, and generic APIs will make up 65% of the market (source: Frost & Sullivan). FDFs are predicted to grow at 9% until 2020, mainly due to the need for oncology and immunology products.

More than half of the top 30 CMO manufacturing sites are in Western Europe, and 22% are in North America and Asia Pacific (fig. 1). Europe is a hub for well-developed FDFs, including solids, non-sterile semi-solids, and liquids as well as injectable and non-injectable sterile products. Europe also leads in small and large API manufacturing, but in emerging markets, these players have marginal production capacities for APIs. Our study of more than 300 CMOs sheds light on the technology distribution across regions, supporting the theory of Europe as a global hub and confirming Asia Pacific's growing capabilities. Trends indicate outsourcing will occur for high-potency APIs, bio-APIs, biopharmaceuticals, and advanced bulk as well as new molecular entities. In particular, Europe and the US could benefit, thanks to advanced equipment, labor, and technologies. This will most likely balance out any short-term revenue losses from manufacturing low-cost off-patent molecules and low-end intermediates or solid-dose manufacturing in Asia Pacific. However, as Asian companies upgrade their facilities and focus on quality, manufacturing speed, equipment use, and product yield, the region will become more attractive.

The CMO Landscape

The landscape is highly fragmented, with more than 400 companies holding less than 2% of the market and as much as 49% of revenue coming from the top 10 CMOs (source: Frost & Sullivan). Suppliers differ in the va-

riety and complexity of services they provide and the regions they supply.

- Our research reveals six categories of CMOs, based on the following criteria (fig. 2):
- Portfolio broadness. The number of types of API, bulk, and FDF capabilities. (Note: A supplier that covers more than three of five categories — solids, semi-solids and liquids, injectables, small APIs, and large APIs — is considered to have a broad portfolio.)
- Technological fitness. The high-tech technologies the CMO offers: large-molecule APIs, special products, or sterile products (bulk and FDF)
- Economic scale. Company revenue (US dollars) and revenue growth (CAGR)
- Ownership. Private-equity owned, publicly traded, or family owned

Because suppliers in the same category have similar predispositions, CMOs can use our categorization to inform decisions about factors such as M&A, partnerships, and technology while pharma players can use it to find a CMO that fits their needs.

M&A Activity

The top CMOs have been on an M&A splurge, with 2016 and 2017 seeing massive deals. Most acquisitions by big CMOs between 2012 and 2017 were in Europe, followed by North America. Despite Asia Pacific growth predictions, most CMOs have not targeted Asia or India. However, there have been acquisitions of Indian (Piramal) and Chinese (WuXi AppTec) players in Europe and joint ventures in the US, including Bioepis' partnerships with Samsung and Biogen. Most of these acquisitions aim to add either value to the portfolio or services across the value chain.

In addition, 2015 and 2016 saw acquisitions in contract research and contract development and manufacturing organizations, underscoring the fact that players are aiming to cover more of the value chain. This has disrupted the CMO landscape. Despite being a regional industry 15 to 20 years ago when pharma outsourcing began, many CMOs are now international and tech-savvy. A handful are reaching the scale of big pharma and poised to become true partners; others are deciding whether to focus on technologies or regions or to cover more of the value chain (fig. 3).

Novel Business Models and Partnerships

Despite their strategic importance, CMOs are not always seen as true partners. We believe three business models will transform CMO–pharma relationships:

- Value-chain expansion. CMOs become strategic partners, offering pre-clinical development and research services to create a one-stop shop that covers the entire value chain of a product group.
- Flexible capacity. CMOs invest in equipment and facilities to build dedicated capacity and offer flexible production capacity with full-service capabilities for a specific product group.
- Risk sharing. CMOs reduce their prices but gain benefits if the product is successful (mostly small, virtual pharma players seeking to improve their credibility).

Several companies are already using these models. For example, Patheon has a flexible capacity partnership with Flexion Therapeutics and is responsible for building a manufacturing site, installing and validating equipment, and manufacturing Flexio's FX006 drug. And Catalent has entered a value-chain expansion partnership with Mitsubishi Gas Chemical Company to promote Catalent's GPEx technology in Asia. Catalent will engineer the cell lines and carry out development, and Mitsubishi will provide phase III and commercial manufacturing and use GPEx technology to offer biosimilar cell lines to pharma partners.

Charting a Path Forward

Strategic partnerships can yield an array of benefits, from lowering costs to improving production and supply chain performance. In addition, our Purchasing Chessboard sheds light on the demand and supply position of CMOs compared with the demand position of pharma companies (fig. 4). The top left quadrant shows where CMOs have a strong negotiating position; the bottom right shows where pharma companies can capitalize on competition among CMOs.

Based on our study and our project experience, we offer the following recommendations.

CMOs

- Evaluate your risks as a hybrid CMO. An unclear focus, such as on geographic reach or the technology portfolio, puts profitability at risk. As the market consolidates, smaller and hybrid CMOs are merging with other CMOs to control costs.

"Despite their strategic importance, CMOs are not always seen as true partners."

- Focus on profitable segments, or grow in scale. Concentrate on areas where you have the strongest supply power. CMOs with a focus on areas such as solid dose will need to improve their capacities quickly because price is a differentiating criteria and competition is high.
- Know your peers and their financial resources. No longer does outsourcing automatically lead to more CMOs. Pharma is now on the radar of large private equity firms that bet big on growth, as seen with Aenova and Stada.

Pharma Companies

Know your partner and its network. The Purchasing Chessboard (fig. 4) can help you choose the right partners. Applications in the bottom right quadrant require partners with similar capabilities to compare prices, set up shorter contracts with regular price checks, and leverage the supply base in each geography. Those in the top left must monitor dependency, e.g., with regular market tests and a review of supply and quality performance.

Watch emerging markets, especially in Asia Pacific. For new products ready to be launched in Asia, secure the supply with flexible CMOs that deliver products to the markets. CMOs are seeing growth in Asia, which pharma companies can secure by setting up or redesigning their Asian footprints.

The authors would like to thank Marc Berenbeck for his valuable contributions to this article.

Dr. Oliver Scheel, partner, A.T. Kearney, Düsseldorf, Germany

Dr. Carola Schlumbohm, consultant, A.T. Kearney, Düsseldorf, Germany

Dr. Constanze Schmidt-Rhode, consultant, A.T. Kearney, Düsseldorf, Germany

Dr. Enzio Reincke, principal, A.T. Kearney, Berlin, Germany

oliver.scheel@atkearney.com
enzio.reincke@atkearney.com
carola.schlumbohm@atkearney.com
constanze.schmidt-rhode@atkearney.com

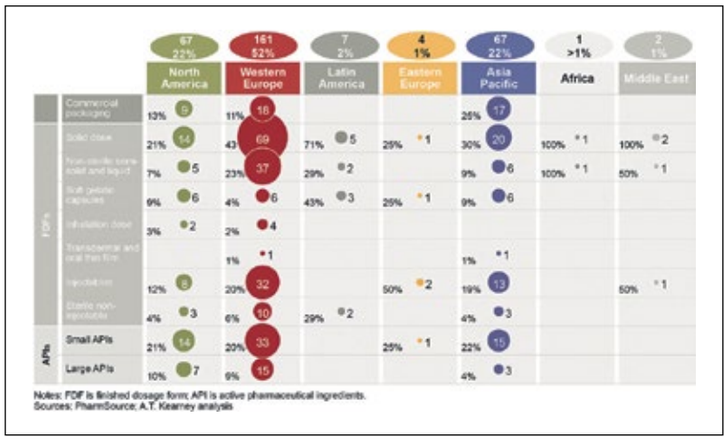


Fig. 1: Most contract manufacturers are based in Western Europe.

Fig. 2: Contract manufacturing organizations fall into six categories.

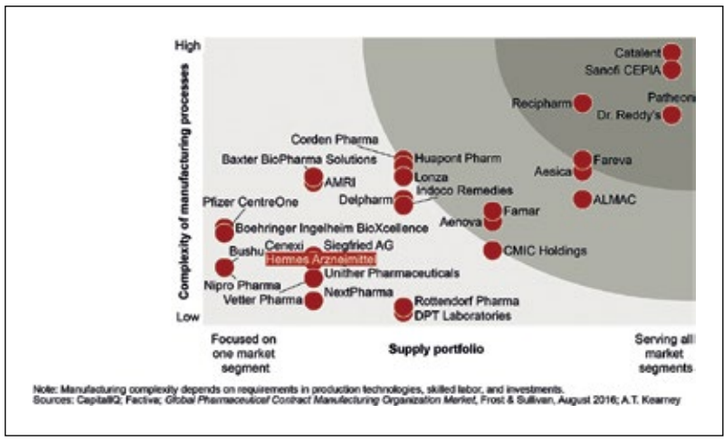


Fig. 3: Suppliers differ in the variety and complexity of services.

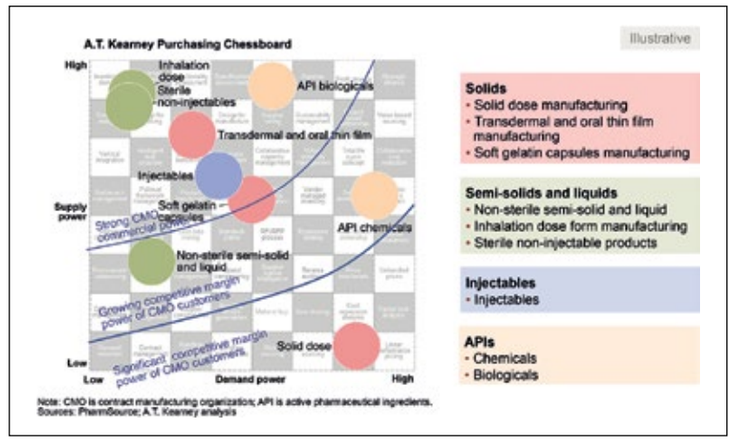


Fig. 4: Strategic partnerships can reduce costs and increase value.

M&A

US drugmaker **Catalent** has agreed to buy **Cook Pharmica**, a CDMO based in Bloomington, Indiana, for $950 million in cash, boosting its position in the fast-growing biologics area.

Israeli generics giant **Teva** has unloaded its contraception, fertility, menopause and osteoporosis products to **CVC Capital Partners** for $703 million. It also sold its emergency contraception brands to Foundation Consumer Healthcare for $675 million.

Anglo-Swedish drugmaker **AstraZeneca** has agreed to sell the remaining rights to its anesthetic drugs portfolio to Mauritius-based **Aspen Global Incorporated (AGI)** in a deal worth up to $766 million.

Lonza has acquired Swiss contract manufacturer **Micro-Macinazione** to create a global micronization services leader by building on Lonza/Capsugel's existing micronization clinical and commercial manufacturing capabilities based in Quakertown, PA, USA.

Sanofi buys **Protein Sciences**, a privately held vaccines biotechnology company based in Meriden, CT, USA. The French drugmaker agreed to make an initial payment of $650 million and up to another $100 million of milestone payments.

People

Novartis CEO Joe Jimenez will leave the Swiss-based drugmaker in early 2018. He will be succeeded by Vasant Narasimhan, who joined Novartis in 2005 and currently serves as chief medical officer and global head of drug development.

Torbjörn Wärnheim, director Pharmaceutical Innovation and Development at **Moberg Pharma** since 2013, has now been appointed as a member of the Swedish pharmaceutical company's management team.

Piramal has appointed John Fowler as chief operating officer of its contract development and manufacturing business. Fowler, who most recently served as Divisional CEO at Johnson Matthey, will be responsible for Global Operations and R&D.

Envigo has made two appointments to its executive committee: The UK contract research services provider has appointed Craig Boyd as chief commercial officer and Lizanne Muller as president of EMEA Operations.

Manufacturing

US API manufacturer **Cambrex** invests $24 million in a new HPAPI facility at Charles City, IA, USA. The plant will have a total reactor capacity of 2,200 gallons consisting of a range of glass and Hastelloy vessels to manufacture batches from 50 kg to 300 kg.

Saltigo is implementing a major investment program of approximately €60 million to be completed by the end of 2017. The program has seen flow into the renovation/expansion of plants at the CMO's Leverkusen site.

German CDMO **ChemCon** has put into operation a new state-of-the-art cleanroom at its Freiburg site. Simultaneously with its opening, the first project moved into the new facility for immediate production. (mr, rk)

Staying Focused

How to Turn Challenges Caused by Consolidation into New Business Opportunities

Challenges caused by a merger or an acquisition can be manifold, no matter whether it is your own organization that is going through M&A and the integration phase or any of your outsourcing partners or customers. Distractions or disruptions are pre-programmed and sometimes inevitable, thus, it gets hard to maintain business as usual. In such a phase it is important not to lose focus on customer relationship and ongoing projects. CHEManager International asked executives and opinion leaders in the chemical and pharmaceutical market to share their experience and advice. For instance, we wanted to know:

- Will the consolidation in the pharmaceutical industry level off or will it even intensify?
- Does the consolidation in the pharma industry create a necessity for CROs/CMOs to consolidate?
- How big of an issue is a merger or an acquisition for ongoing projects?
- How can outsourcing partners maintain their focus and guarantee confidentiality in their projects?
- Read the insightful answers of the experts here.

Confidentiality is a Potential Pitfall

Dr. Magid Abou-Gharbia, FRSC, Director Moulder Center for Drug Discovery Research, Associate Dean for Research Temple University, Philadelphia, PA, USA

Mergers certainly bring the risk of lost focus and a chance for confidential information to become compromised. The temporary loss of job security that comes with any merger inevitably leads to a loss in productivity. To overcome this problem supervisors and project leaders must remember that they are professionals and are still bound by contractual obligations. They must take an even greater and more detailed day-to-day oversight role to insure that projects continue to progress. Confidentiality is another potential pitfall during a merger.

Acquiring or merging partners do not wish for any newly generated confidential information to be revealed to employees who are destined for outplacement and some currently engaged contractors may not wish for their projects or confidential information to be shared with the acquiring or merging partner. To combat both the loss in productivity and risk of sharing new confidential information with employees who will be outplaced the merger team must move quickly, making job decisions in a timely manner.

In a perfect world these details would already be worked out before the merger is announced so that they can be acted upon quickly. To avoid the sharing of unwilling contractors' confidential information, many big Pharma companies have employed what is referred to as the "Clean Teams". These teams are made up of external expert consultants who had extensive Pharma experience in their earlier career. These teams are "neutral" to the merger and are bound by strict confidentiality. Often they are used to objectively evaluate projects for two merging partners and make go/no go recommendations, but such teams can also be employed to act as a filter for evaluating and deciding what confidential information can be provided to an acquiring or merging partner.

Ensuring Better Efficiency and Consistency

Mark Rogers, Global Technical Director, SGS Life Sciences

Between 1993 and 2015, drug companies spent an estimated $1.7 trillion on M&A activity, with 74% of this activity attributed to only 20 companies. 2014 alone saw 185 deals of which 22 were valued at more than $1 billion. This trend continues today with nearly $34 billion being spent on M&A in the first quarter of 2017 (according to DCAT Value Chain Insights) and is likely to continue and perhaps even escalate. In particular, the political climate in the USA, advocating lower corporate tax rates and supporting repatriation of overseas revenue, may provide pharmaceutical companies even more incentive to pursue acquisitions to augment their growth. This trend in M&A has been primarily driven by a need to compensate for reductions in growth as a result of investment in early phase pipeline development, aptly demonstrated by the very recent, $11.9 billion acquisition of Kite Pharmaceuticals by Gilead.

Interestingly, the CRO/CMO service industry has also undergone a similar trend with increasing M&A activity. For example, the estimated global deal value in 2015 is estimated at $12 billion, according to the Clinical Trials Yearbook 2016. A major driver for this comes from increased competition as a result of active outsourcing partner consolidation by the pharmaceutical industry, to ensure better efficiency and consistency, particularly following acquisition. M&A in the CRO/CMO sector has been sought primarily to improve the global footprint, acquire higher levels of technology and provide a broader portfolio of services. There seems to be little evidence that M&A in the pharmaceutical industry has resulted in any significant loss of business for the CRO/CMO sector but rather, has been grounds for scope change and perhaps some downsizing. Despite the magnitude of the M&A activities, the fundamental and primary demands on the pharmaceutical industries outsourcing partners for quality and on-time delivery will continue to dominate, regardless of the size or activity of the pharmaceutical business.

Changes in Portfolios and Pipelines are Likely

Dr. Marcus Hannakam, Global Head Business Line Pharmaceutical Ingredients, Heraeus Precious Metals

We think consolidation will proceed as far as merged companies can still handle themselves in such dimensions. Currently, we see the wheel of M&A turning even faster, although the financial burden of M&A may be substantial. A key objective of M&A is consolidation and thus improvement of financial KPIs. Therefore, changes in portfolios and pipelines are likely, and early projects in freshly merged companies are subject to review in their new environment. Financial restraints can hamper bringing early innovation to commercial launch.

Heraeus has been a key manufacturer of selected anti-cancer hAPIs for some 30 years. Top quality and comprehensive service bundled with our team's expertise in precious metals is our key here. Today, our portfolio also comprises various organic hAPIs and specialties. The clear focus of our strategy is on challenging hAPIs for oncology. Heraeus entered into its CDMO activities for new entities some years ago. Despite a fast ramp up, Heraeus has proven to be a reliable and confident hAPI partner through all the preclinical and clinical phases of our valued customers.

So far we haven't been affected, because all of our customers and partners for hAPIs count on our long-term reliability as a value, which is independent from their in-house set-up. But reshaping companies could put off early projects if their strategy changed. However, they could outsource advanced projects to a CDMO with proven expertise and reputation. We see both approaches in the market.

Pharma R&D Productivity Needs Improvement

Elliott Berger, Vice President, Global Marketing and Strategy, Catalent Pharma Solutions

With the ever-increasing share of new molecules being developed by smaller players, the trend for larger pharma to supplement their pipelines with acquisitions in targeted therapeutic areas will continue. Pharma R&D productivity still needs significant improvement and this is part of that trend. Larger deals may reemerge as US tax reform is implemented. Pharmaceutical partners must adjust to help support the changing needs of pharma innovators. Smaller innovator companies are taking their molecules further into development, but have very specific areas of expertise and need broader support from their partners to reduce risks, get the right expertise and resources and progress their programs faster to limit cash burn and reach key milestones. Larger pharma will continue to consolidate their supplier bases with fewer partners that are able to provide more of the best, specialized services for their increasingly challenging pipelines. The ability to provide expert solutions and technologies for more of their molecules and for one molecule end-to-end should prove increasingly attractive.

Big pharma plays a major role in financing, improving and driving clinical trials through to approvals for molecules acquired from smaller innovators. While smaller innovators are now increasingly capable of taking more molecules all the way to market, with support from financial markets, and experienced CDMOs with service offerings spanning the development cycle, it is likely that at least some of those molecules would not make it through the expensive and lengthy process and reach patients without this support.

A Partner to Relieve the Strain

Denis Angioletti, Chief Commercial Officer (CCO), Cerbios

Consolidation in the pharma industry is a process which looks likely to continue for a few more years, pushed forward by the need of pharma companies to keep their revenues growing, improve cost efficiency and expand their pipeline faster. It may continue to see both megamergers as well as the acquisition of start-ups and small companies by larger firms.

From the perspective of CROs/CDMOs, this does not automatically mean the need to undergo the same process, at least from the point of view of their own business scope. In many cases, the M&A processes are even generating opportunities for CRO/CDMO companies where a merged company makes divestments of sites or products, or decides to focus its own resources on a certain area of priority leaving a lot to outsourcing. The same comes from the need of these companies to reduce their fixed costs, ending up looking for preferred suppliers to add value to their internal capabilities.

In such an environment, what is important for a CRO/CDMO company is to have its own excellences so as to become the partner of choice for the pharma industry; one of the big issues during M&A is that it comes as a dramatically complex process and what anyone would like in such a situation is to have a partner to relieve the strain. In this respect, independent mid-size CDMO companies with specialized technologies do have a great opportunity in being able to deliver their service with faster decision- making processes and customer-oriented services as compared to larger and more complex firms.

Consolidation is here to Stay

Dr. Jane Griffiths, Global Head Actelion, Janssen Pharmaceutical Companies of Johnson & Johnson

Consolidation in the pharma industry is here to stay: as market competition increases, M&As are one of the fastest ways for companies to obtain critical mass, allowing them to broaden their product range or branch into new therapy areas whilst extending their geographical reach. Acquisitions also enable cost savings to be achieved through the consolidation of functions and systems and realizing economies of scale. Additionally, acquisitions enable companies to strengthen their financial position, in some cases providing an immediate revenue boost. The rate of consolidation will be limited by the search for companies that are strategically and culturally aligned, ideally that can add immediate value to the bottom line.

The contracting environment will likely mirror activity in the pharmaceutical industry, particularly as CDMOs are set to become less of a vendor and more of a long-term strategic partner to pharma. CDMOs looking to remain competitive will need to consolidate to match the scale and reach of consolidated pharma companies, as well as provide more end-to-end capabilities, and become more agile to meet supply chain complexity.

Aggregate innovation has held strong despite dramatic increases in pharma M&A activity. Concerns about the impact of consolidation on drug innovation are misplaced because most drug innovation today originates not in traditional pharmaceutical companies but in biotechs. In these smaller firms, a culture of nimble decision-making and risk-taking facilitates discovery and innovation.

Earning a Large Chunk of the Cake

Daniel Mueller, CEO, Senn Chemicals

The most obvious effect of consolidation in the pharmaceutical industry is a pronounced shift to those activities within the organization that provide the most profitable returns, closely followed by outsourcing activities where smaller profits can be generated. Chemical as well as pharmaceutical manufacturing in house are very cost intense activities regarding investments and maintenance. If the equipment and infrastructure cannot be optimally utilized then costs of goods manufactured tend to be higher than sourcing the same goods from specialized CMOs with maximized utilization of resources. The well-organized CMOs can step in and earn a large chunk of the cake by delivering highest levels of customer service.
Short decision paths, efficient development and manufacturing processes, ability to deliver highest quality, flexible employees and organization structures, all of which smaller organizations have an advantage over larger consolidated corporations, are the key success factors for CMOs. This can be achieved either by specializing and optimizing the in-house processes or by improving the cost structure through mergers or acquisitions. Simply put: well positioned CMOs have a huge opportunity to grow and be successful due to the trend of consolidation in the pharmaceutical industry.

Setting High Standards

Deepak Sapra, Vice President and Global Head of CPS Business, Dr Reddy's Laboratories

In the pharmaceutical world, the key attributes for mutual trust are usually quality and regulatory compliance, confidentiality, reliability — particularly the commitment to stick to commitments — and flexibility. A CDMO, which has experience in collaborating with organizations of different sizes and sets high standards in these key attributes, is more likely to meet the requirements of the acquiring company and is in a better position to facilitate a smooth transition and keep the project going. How big of an issue an acquisition becomes for an ongoing project depends on the nature of the merger or acquisition. This plays a key role in decisions on future and ongoing projects. Big pharma, for example, focusses very closely on the strategy of the newly formed entity and on whether the current ongoing projects fit into it. Regular and transparent communication during the transition plays a key role and timely communication can enable the continuation of ongoing engagements.
The purpose of the transaction also holds a key. For example, a specialty generics company recently acquired a dermatology-focused CMO. This was not a positive signal for the existing customers of the CMO, because they were afraid that the acquisition would mean a greater usage of the capabilities and capacity for internal purposes of the takeover company, and external customers would have a lower priority.
Another situation worth considering is when a molecule has been outsourced to a CDMO by a small pharma company, and the CDMO gets acquired by a large pharma company. The dynamics are different in this case. Pharmasource highlights that an impact in the large molecule space is more likely, as the big pharma company might take the asset internally as soon as feasible. However, in such situations where the molecule changes hands, the willingness of the acquiring pharma company to fund any modifications or facility expansions is limited, because the pharma company is looking to get the molecule quickly through the clinical phase and realize the returns on the investment.

Both Positive and Negative Effects

Simon Edwards, Vice President Global Sales and Business Development, Cambrex

It is somewhat obvious that consolidation to fewer customers means fewer suppliers. In addition, when pharma companies merge there is usually at least a temporary slowing down of clinical development and a longer term reduction in the number of products in the pipeline. This can lead to products that the CRO/CMOs were working on being delayed or worse discontinued just based upon new selection criteria of the new company rather than whether they would have got to the market or not.
There are both positive and negative effects of acquisition on pharma/CDMO or pharma/CMO relationships. In terms of negatives, consolidation ultimately means a reduced customer base for CMOs, while existing projects can get delayed, either due to personnel changes, or as project decision-makers become reorganized. Additionally, projects already outsourced prior to any merger can be terminated during strategic reviews, once the portfolio is reassessed in the merged company.
Alternatively the outsourcing strategies of the two companies may be different i.e. one outsources routinely and the other does not. It can therefore happen that a product that was outsourced is now brought back in-house to the new combined company. If a merger gives the company access to idle manufacturing capacity there will be less need for outsourced service providers and inevitably, for a period of time, the new company becomes "less easy to do business with" and discussions for new business/projects will take time as roles are allocated.
On a positive note, incumbent CMOs can potentially gain access to a new pipeline of products that they previously were not involved with. This occurs for example when the CMO is working for a customer who might be big or small but after the merger the CDMO is exposed to a new pipeline of opportunities it had not had access to before. So it can sort of go both ways. Also, if the pharmaceutical company grows in market share as a result of the consolidation, then they might require more volume from their CMO partners.

APIs: Evaluating Supply and Demand

Trends and Factors that Shape the Market for Active Pharmaceutical Ingredients

The market for active pharmaceutical ingredients (APIs) is approximately $140 billion and is projected to reach nearly $190 billion by 2020. So what does the market show?

©monticelllllo - stock.adobe.com

The API market is roughly divided: 60% for the captive market (produced internally by pharmaceutical companies) and 40% for the merchant market (produced by third-party providers for a pharmaceutical company). On a geographic basis, Western Europe and the US lead in terms of experienced API producers. What are the factors influencing API supply and demand?

Patricia Van Arnum, DCAT Value Chain Insights

APIs: the Demand Side

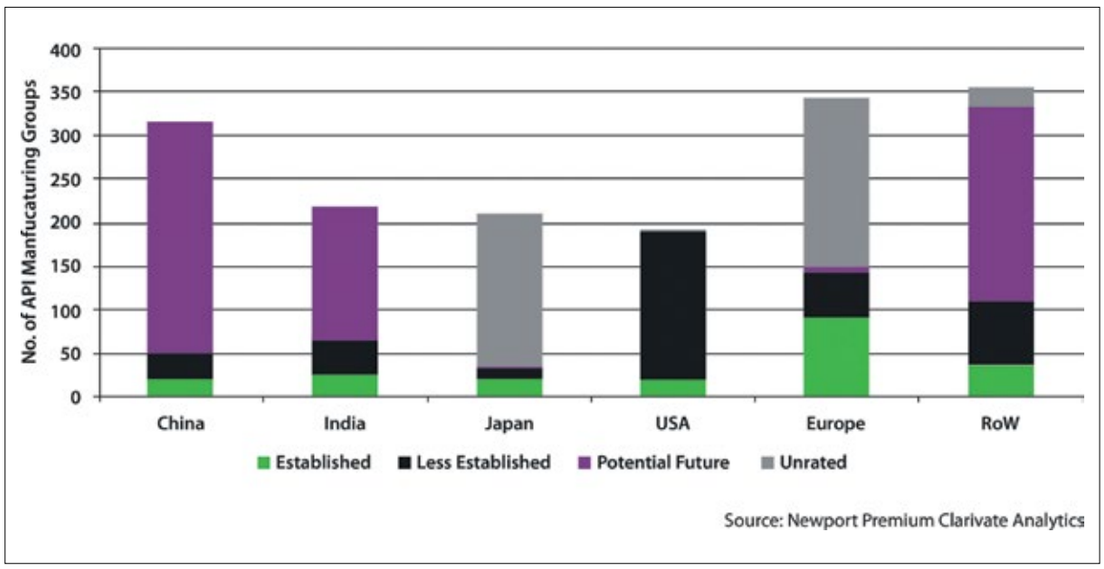
Demand for APIs is influenced by a variety of factors, including overall pharmaceutical industry growth, product demand for therapeutic areas, and financing trends, particularly for smaller pharmaceutical companies, noted Kate Kuhrt, head of Go-to-Market for the Life Sciences business at Clarivate Analytics, a provider of insights and analytics. Kuhrt spoke at DCAT Sharp Sourcing, a one-day conference for sourcing, procurement and supply management executives and suppliers, organized by the Drug, Chemical & Associated Technologies Association (DCAT).

On the demand side, Kuhrt points to several favorable indicators. Overall pharmaceutical industry growth is expected to be approximately 6%, according to information from the 2016 CMR Factbook from Clarivate Analytics. This estimate is compatible with other industry estimates. A December 2016 analysis by QuintilesIMS forecasts that total spending on medicines is expected to reach $1.5 trillion by 2021 and will increase at a 4 – 7% compound annual growth rate through 2021, which is down from the nearly 9% growth level seen in 2014 and 2015. (Note: Spending is measured at the ex-manufacturer level before adjusting for rebates, discounts, taxes and other adjustments that affect net sales received by manufacturers.) The impact of these factors is estimated to reduce growth by $127 billion, or approximately 35% of the growth forecast through 2021.

In looking at new global product launches, small molecules, or new chemical entities, still dominate APIs, but the share of biologic-based new molecular entities (NMEs) is increasing with ranges from approximately one quarter to one-third of new NMEs launched on a global basis (tab. 1).

Another important trend relates to research and development (R&D) spending by molecular type. Kuhrt pointed out that the amount of R&D spending is nearly evenly divided between small molecules (52.3% in 2015) and biologics (47.7% in 2015).

On a therapeutic basis, oncology/immuno-modulators represent the leading class both in terms of global new product launches and R&D spending. Anti-cancer/immuno-modulators accounted for 30% of first NME launches in 2015 and 28% of global R&D spending, according to the 2016 CMR Factbook. Alimentary and metabolism was the next leading therapeutic area, representing 20% of new global NME launches in 2015 and 10.4% of R&D spending.



Active Pharmaceutical Ingredient (API) Manufacturers by Top-Producing Locations.

In terms of global product launches for NMEs, the major pharmaceutical companies account for the large amount of launches although mid-tier and other companies play a significant role. In looking at first NME global product launches from 2010–2015, the major pharmaceutical companies led in 2011 (17 or 55% of new NME launches), 2013 (16 or 55%), 2014 (26 or 57%), and 2015 (25 or 57%). Mid-tier and other companies led in 2010 (14 or 66% of new NME launches) and 2012 (14 or 54%), according to information from Clarivate Analytics.

Financing trends are an important measure of the health of smaller pharmaceutical companies, particularly in private financing needed to fund pipelines and operations. In 2016, the pharmaceutical industry as a whole tallied $38 billion from public and private financing, according to BioWorld, part of Clarivate Analytics. At DCAT Sharp Sourcing, Kuhrt pointed out that only 24% of this funding was from private financing, and public financing accounted for 56% of this total.

"We saw in 2016 that more deals are being made outside the US," said Kuhrt in further breaking down trends in private financing. Citing analysis carried out by BioWorld, Kuhrt explained that there was an increase in the number of European companies attracting venture capital. "Also, we are seeing that China is witnessing a greater involvement by private-equity investors with close ties to the Chinese government in biotech innovation," she said. "It is also worth noting that there are an increasing number of deals being concluded by Canadian biopharmas, with five private companies receiving venture backing in 2016." Overall, BioWorld reported the US led in private financing in 2016 with $5.77 billion raised, followed by Europe ($1.43 billion), Asia/Australia ($700 million), and Canada ($410 million).

APIs: the Supply Side

On the supply side, the global API market is valued at approximately $140 billion, noted Kuhrt, with several industry estimates showing roughly a 60%/40% split between the captive market and the merchant market. Overall, the API market is expected to increase at an annual growth rate of 6.6% and reach $186 billion by 2020, according to information from Persistence Market Research, a New York-based market research firm, with biologics accounting for 30% of the market. In 2016, the merchant API market was approximately 41% of the global API market compared to 60% for captive use, according to Mordor Intelligence, a Hyderabad, India-based market research firm. This level is consistent with levels provided by the Chemical Pharmaceutical generic Association (CPA), which represents Italian manufacturers of APIs

Year	Number of chemical entity NMEs first launched on worldwide markets and percentage of total first launches	Number of biopharmaceutical entity NMEs first launched on worldwide markets and percentage of total first launches
2005	21 (66%)	7 (33%)
2006	18 (72%)	7 (28%)
2007	16 (76%)	5 (24%)
2008	16 (76%)	5 (24%)
2009	17 (65%)	9 (35%)
2010	15 (71%)	6 (29%)
2011	22 (71%)	9 (29%)
2012	19 (73%)	7 (27%)
2013	24 (83%)	5 (17%)
2014	34 (74%)	12 (26%)
2015	28 (64%)	16 (36%)

Tab. 1: Number of First New Molecular Entity (NME) Launches by Active Substance Type, 2005-2015. Source: 2016 CMR Factbook, Clarivate Analytics

Classification	Percentage of Global API Producers
Unrated	12%
Local	57%
Potential Future	15%
Less Established	9%
Established	6%
Big Pharma	1%

Tab. 2: Global Active Pharmaceutical Ingredient (API) Producers by Type. Source: Newport Premium, Clarivate Analytics

"Overall pharmaceutical industry growth is expected to be approximately 6%."

Kate Kuhrt, head of Go-to-Market for the Life Sciences business, Clarivate Analytics

Location	Number of Experienced API Producers	Percentage of Global Total of Experienced API Producers
US	202	36%
India	65	12%
China	49	9%
Japan	37	7%
Italy	32	6%
Germany	23	4%
Spain	16	3%
France	16	3%
Rest of World	110	20%

Tab. 3: Experienced Active Pharmaceutical Ingredient (API) Producers by Headquarter Location. Source: Newport Premium, Clarivate Analytics

and intermediates, in a 2010 analysis. That analysis reported the merchant market at 38.6% and the captive market at 61.4%. Within the merchant market, generics account for between 43.5% (Mordor Intelligence) and 48.7% (CPA).

On a molecule basis, most of the market is still in small molecules although the biologics segment is growing faster, noted Kuhrt. Also, growth in the API market is more on the outsourced or merchant market, with the exception of biologic-based APIs, where there is significant investment by the larger pharmaceutical companies. On the small-molecule side, growth drivers include high-potency active pharmaceutical ingredients (HPAPIs) and cytotoxic small molecules.

> *"We saw in 2016 that more deals are being made outside the US."*

In looking at global API production in terms of numbers of producers, local producers, focused on less regulated markets, dominate, they account for 57% of manufacturers, noted Kuhrt. In evaluating API producers, Clarivate uses a scale to indicate where an API producer resides in a spectrum based on a producer's capacity for producing for regulated markets. The classification ranges from the lowest end of the spectrum "local" (meaning producing for local markets only) all the way to "established" producers for making product for regulated markets and "Big Pharma" companies. In between, there are "potential future" companies with ambitions to enter regulated markets and "less established companies" that have successfully made inroads into heavily regulated markets. Table 2 outlines the distribution of global API producers in these categories.

Kuhrt also provided a distribution of API producers on a geographic basis using the headquarters of a given company as the basis for identifying the location of that company. In evaluating the distribution of experienced API producers using that definition, the US leads with the highest number of experienced API producers, accounting for 36% of the global total (tab. 3). In terms of market share, India and China have remained fairly even in terms of number of API producers in 2012 and 2016 while Italy experienced a decline from 2012 and 2016.

In looking at the type of API producers in each of these regions, Western Europe and the US lead with the most experienced API producers. However, it is worth pointing out the significant number of Potential Future companies in India and China (fig.).

Patricia Van Arnum, Editorial Director, DCAT Value Chain Insights; Drug, Chemical & Associated Technologies Association

pvanarnum@dcat.org
www.dcat.org

This article first appeared in the July 26, 2017 edition of DCAT Value Chain Insights, a weekly information resource on pharmaceutical manufacturing, sourcing/procurement, and supply management from the Drug, Chemical & Associated Technologies Association (DCAT), and was updated for publication in CHEManager.

Cutting the Gordian Knot of Pharma Operating Model Complexity

How Radical Simplification Can Fuel Growth and Boost Competitiveness

Pharmaceutical companies have traditionally had complex operating models, but in recent years, complexity has reached a whole new level. Instead of continuously assessing their set-up, many organizations have sought quick fix solutions to events like acquisitions, portfolio shifts or negative regulatory inspections.

At a time when healthcare leaders are looking to transform their business models to enable them to capture value from digitalization and data monetarization, radical simplification initiatives are critical. As flexibility, scalability and agility in pharmaceutical operating models will be the new drivers of performance, simplification is now a prerequisite for growth and competitiveness.

Complexity Hampering Growth Potential

After years of sluggish growth, the pharmaceutical industry is on the upswing again. Accenture Research shows that between 2014 and 2016, the FDA approved 108 new molecular entities – an increase of more than 12% compared to the period 2011 to 2013. In 2016, earnings of some of the top pure play pharmaceutical companies also increased. Furthermore, clinical pipelines also paint a promising picture with next generation treatments in development, for example, immuno-oncology, anti-interleukin mAbs and gene editing.

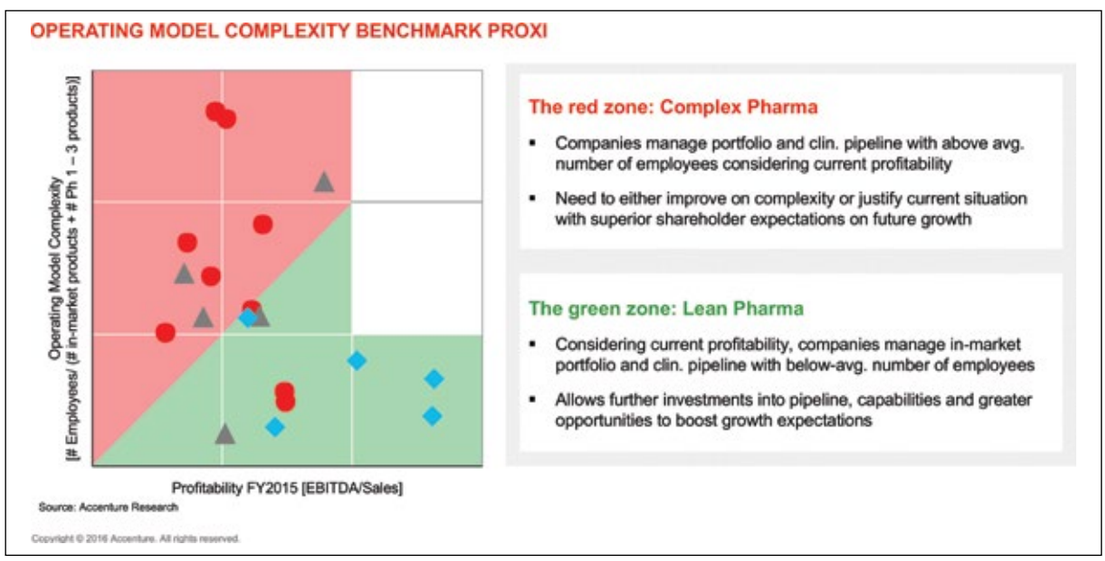
Capturing growth opportunities, however, requires pharma leaders to overcome the complexity that often drags them into a vicious cycle of inefficient processes, limited performance transparency, increasing compliance risk and deteriorating profitability. Agile pharmaceutical companies will have the advantage in today's world where healthcare segments are converging and new technology is reinventing business models. For instance, many leading pharmaceutical players are actively looking into shifting from being drug makers to taking on a broader role in the health ecosystem, where medicines are just one part of holistic treatment solutions.

Pharmaceutical companies can capture such growth opportunities by simplifying operating models. However, many have not yet embarked on that journey. Accenture research has found that some pharmaceutical companies have focused on mastering complexity when in fact they should be focusing on minimizing it. Complexity has steadily increased and now has reached a level where more than 50% of the 20 largest global pharma companies demonstrate operating model complexity levels disproportionate to their profitability.

"Radical simplification requires an entrepreneurial mindset and follows a zero-based approach."

Complexity Is a Competitiveness Killer

75% of 59 pharma executives that Accenture surveyed confirm that reducing complexity is a key enabler for sustainable cost reduction. However, only 19% agree that their company is consistently able to identify and remove business activities that do not add value.



Marc P. Philipp, Accenture

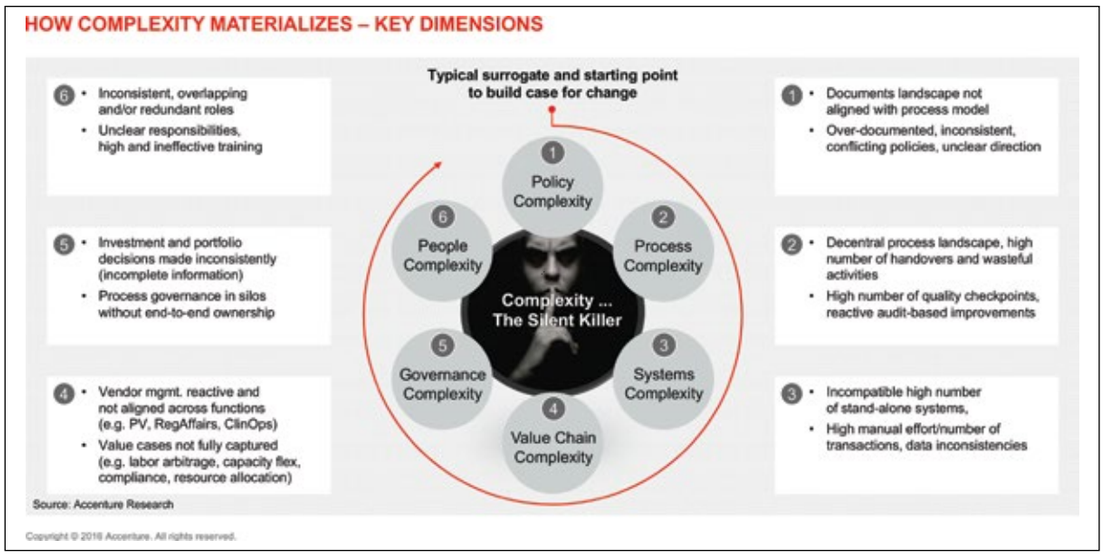
Indeed, complexity is difficult to identify and remove, as it is deeply rooted in today's operating models – and mindsets. In fact, many stakeholders – particularly middle management – have an interest in preserving complexity as their jobs depend on it.

Complexity often stems from acquisitions, new forms of collaboration, scientific innovation and increasing regulatory scrutiny. It manifests across all key pharma functions and is an increasing concern in preclinical research, clinical development, manufacturing and supply chain. Complexity often cuts across everything from policies and processes to systems, the value chain configuration, the governance model as well as the organizational and workforce dimension.

From Lean Six Sigma to Radical Simplification

Traditionally, pharmaceutical companies have often aimed to simplify by pruning their portfolio or streamline individual processes by applying proven methods which deliver incremental improvements, such as Lean Six Sigma. While this approach continues to provide value to business, it is often too one-dimensional and not effective when it comes to transforming into agile and simple pharma operating models. Whereas Lean Six Sigma reduces process variation, improves process control and reduces waste, companies should challenge the process itself.

Radical simplification requires an entrepreneurial mindset and follows a zero-based approach. Technology can substantially help reduce complexity when organizations use auto-



mation, robotics and artificial intelligence. In addition, it is essential for leaders to have a start-up spirit, looking for innovative ways to improve speed-to-patient, quality, compliance and cost base.

A pharmaceutical company's risk and return portfolio should serve as a starting point for simplification. Although many pharma businesses do not have a clear picture of their risk exposure and profit drivers across the value chain, exhaustively identifying and evaluating impact and likelihoods of potential opportunities and threats across patient safety, regulatory, legal and business risk is a valuable baselining exercise. Then, leaders can derive fit-for-purpose measures against their risk and return portfolios, which are typically much simpler and more effective compared to what has typically been there. Instead of incrementally improving an over-complex model, a redefinition of the important pieces often creates a much higher impact.

When organizations embark on a simplification journey, it is important to make resulting effects stick. Sustaining a simple and agile pharma organization is as difficult as creating one – so working on culture and behavior, governance mechanisms and continuous improvement models is a critical final step towards making biopharma operating models deliver superior outcomes for making patients' lives better.

Marc P. Philipp, senior manager, Accenture GmbH, Berlin, Germany

marc.philipp@accenture.com
www.accenture.com

At the Forefront of Technological Breakthroughs

Science that Enables Solutions for Clean Air, Improved Health and Sustainable Use of Natural Resources

2017 marks the 200th anniversary of UK specialty chemical and sustainable technologies group Johnson Matthey which – back in 1817 – began as assayers, testing the purity of precious metals. In April 2017, Johnson Matthey has announced the rebranding of its businesses. The group headquartered in Royston, UK, said the initiative was designed to increase its focus and build a more collaborative organization as well as reflect its position as a science-led group. The business is now aligned with the global priorities of cleaner air, the efficient use of natural resources and improved health. Dr. Ralf Kempf asked Robert MacLeod, the chief executive of Johnson Matthey, about the reasons for the rebranding, and the trends that will affect the company's activities in the future.

© iStock – Johnson Matthey

CHEManager: What is the rationale behind Johnson Matthey's updated brand? How will the new brand and business restructuring impact the positioning of your Pharma offering?

R. MacLeod: Johnson Matthey has been in business for 200 years. Our focus on sustainable technologies and products has become increasingly significant over time to address changing market and societal needs. Our technologies are used by manufacturers across many industries, including pharmaceuticals, petrochemicals and automotive, to improve the function, performance and safety of their products at a lower environmental cost. We have always applied our cutting-edge science to solve industry challenges, and we are now focusing our expertise on developing efficient and effective technologies to enable the provision of improved, affordable healthcare, clean air and the most efficient use of natural resources. Our recently refreshed branding reflects our commitment to tackling these global challenges and continuing to use our science to build a cleaner, healthier world for future generations. This unified purpose across our business is embodied in our new strapline: inspiring science, enhancing life.

For the pharmaceutical markets we continue to provide our core offerings of custom pharma solutions, controlled substances, catalysts, and APIs & life cycle management. Through our complex chemistry solutions and differentiating technologies, we enable our customers to optimize their chemical processes and accelerate their innovations, ultimately to create a healthier world. Our products and services include the development and supply of APIs, as well as catalysts and other intermediates used in the development of pharmaceutical products. We also offer the full spectrum of drug development and manufacturing services, from discovery through to commercial manufacture and product life cycle management, broadly addressing the need of innovators and generic pharmaceutical companies.

Robert MacLeod, chief executive, Johnson Matthey

Which market trends do you see as most important for your businesses?

R. MacLeod: The improved life expectancy of our expanding population is driving demand for more affordable healthcare, and the market for APIs is growing steadily. Pharmaceutical companies are looking for more cost-effective ways of delivering complex high quality products and are increasingly outsourcing their API manufacturing requirements. Our breadth of custom manufacturing services, combined with our expertise in complex chemistry, scale up and working in highly regulated environments, makes us well positioned to deliver a strong pipeline of new products to improve health.

We are seeing changes in the way that small to medium-sized pharmaceutical companies want to engage with their suppliers. These include streamlining their supply chains and reducing service providers. With our broad capabilities we can provide for customers' needs across a wide section of the value chain, helping to save time and ensure quality, while also building stronger partnerships and trust with our customers. In addition, having a global asset base that balances cost without compromising quality gives optimal robustness across the supply chain, and is very attractive for pharmaceutical companies.

There is also increasing interest from both innovator and generic companies in adopting risk- and benefit-sharing approaches with their suppliers. We have already developed flexible business models, where we are prepared to look at innovative ways to support our partners.

What will be the core technologies and key drivers for positioning the Pharma offering in the market? And what are your strategic plans for it?

R. MacLeod: Our technologies include unique catalysts, solid form sciences, as well as advanced capabilities with drug conjugates and linkers, chromatography, large scale cryogenics and high containment. We are particularly focused on advancing our existing capabilities in particle engineering and highly potent APIs. We apply these technologies and our complex chemistry capabilities to deliver valuable products and services. Our Pharma offerings are differentiated

through specialist technologies and expertise, while delivering on speed to market and quality, for both innovator and generic customers.

Pharmaceutical companies are also continually looking for improved efficiencies and more sustainable processes. Our leading range of chiral, chemo- and biocatalytic products helps these customers to develop highly efficient and sustainable catalytic processes. Through minimizing waste and reducing cycle times, our products can contribute to economically viable processing.

Overall, our Pharma offering not only helps companies to bring new treatments to market more quickly, increasing their R&D productivity, but also brings much needed efficiencies to manufacturers, resulting in more affordable healthcare for future generations.

Our strategy is to deliver sustainable growth using our existing market-leading technologies and through developing the next generation of technologies to meet global challenges and opportunities across our markets. We will continue to maintain a robust portfolio of new products and customers, supported by our global manufacturing capabilities. Johnson Matthey has a strong reputation as a premier, technology-led API development and manufacturing business and we aim to continue investing to extend our position within pharma markets.

How much does Johnson Matthey invest in R&D, especially within the Pharma offering?

R. MacLeod: Overall we invested a total of £440 million in capital expenditure and R&D during 2016 to 2017, across all of our business areas. Within Pharma, these investments have included broadening our pipeline of new generic APIs for improved health, and provided significant enhancements to diversify our technology portfolio as we continue to build for the future. We have made considerable investments over recent years. These activities include expansions to our state-of-the-art development center in Cambridge and major investment in our recently refurbished GMP manufacturing facilities in Annan, Scotland. We also acquired Pharmorphix, the leading solid form sciences business, to enhance our capabilities in API pre-formulation and development.

Which are the most important commercial assets that Johnson Matthey has acquired throughout its history? How can the company use these assets as a competitive advantage?

R. MacLeod: Historically Johnson Matthey was focused on niche API offerings such as platinum-based actives and controlled substances. In the latter case these are pharmaceuticals with additional regulatory requirements, which restrict the locations where these products can be made and distributed. Consequently, our assets for controlled substances are in the main markets of the US and Europe and we will continue to support these markets in the future. As we've expanded our capabilities to service the pharmaceutical innovator market we've added capabilities into innovator hubs, including Devens, MA and Cambridge in the UK. Also, importantly we established capacity in China, which allows us to support early stages of API synthesis from a more advantaged cost base. For our catalyst manufacturing again we have capacity in the Europe and the US, and in India and China where many generic APIs are manufactured using catalysis.

Overall our strategy has been to develop a global asset base that enables us to align with customer needs in terms of proximity to markets, and with sufficient breadth and scale to be able to provide economies of scale to bring credible value-adding products and services to the market.

The company is celebrating its 200th anniversary. What does that mean for the Pharma offering in particular, and how will this heritage benefit your customers in pharmaceuticals and find chemicals going forward?

R. MacLeod: We're very proud to have reached 200 years, this is a huge achievement for any company and we have contributed significantly to the pharma industry over the past two centuries. For example, we produced the first pharmaceutical that was administered by injection – morphine, and we have been instrumental in developing some of the well-known platinum-based therapies to treat cancer. As we move into our third century, we will continue to build on our pharmaceutical offering through further investing in R&D to expand our generic API portfolio, as well as enhancing our existing technologies and capabilities to help innovator pharmaceutical companies deliver the next generation of therapies.

Do you have any predictions on what trends will affect the pharma industry in the future and how you are positioned to impact these?

R. MacLeod: There is a clear trend for the focus to be on smaller patient populations, currently this is in areas such as orphan indications and eventually through the personalization of medication tailored to more specific genotypes. Additionally, drugs are becoming more complex and better targeted, but consequently more complex and more active, or highly potent. This has implications not only for how API service providers interact with customers, but also the types of assets they have and where they are located. We are conscious of these trends as we look at our technology capabilities and asset base and how and where we will be making future investments.

Another developing need of pharmaceutical customers is the ability to integrate API manufacture with the requirements of drug product development, as the boundaries between primary and secondary manufacture continue to blur. We are prepared for this to become an essential need as APIs become increasingly complex and present challenges for development, due to their poor solubility and low bioavailability. Therefore, we are taking steps to be able to integrate these critical drug product development capabilities into our API manufacturing services.

As more complex actives come to market, pharmaceutical companies will be looking for shorter synthesis cycles and more economic approaches to manufacturing their products. Our technologies will prove vital in being able to address these needs and, with our world-class assets across North America and Europe, we can embed our platform technologies into the manufacture and scale-up of processes.

www.matthey.com

Capitalizing On Precision Medicine

How Pharmaceutical Firms Can Shape the Future of Healthcare

By applying a deeper understanding of diseases with richer patient data and advanced analytics, precision medicine can help physicians tailor medicines to the needs of individual patients, leading to better outcomes at potentially lower costs. A global survey by Strategy& among leaders in the pharmaceuticals industry shows that companies are aware of the promise but have yet to harness with the full potential of precision medicine.

Stephan Danner,
PwC Strategy&

Dr. Thomas Solbach,
PwC Strategy&

Not only can precision medicine improve the way physicians detect, diagnose, and treat diseases, but it can also lead to more preventive healthcare. Using analytics to identify patient risks before they manifest themselves can result in considerably better outcomes, at potentially lower costs for healthcare systems. In this way, precision medicine has the potential to disrupt the entire healthcare industry, including the way pharmaceutical companies develop, manufacture, and market drugs. Few companies have been able to start capitalizing on the promise of precision medicine. Doing so requires a dramatically new set of capabilities, along with the ability to operate in an environment with regulatory uncertainty and new market entrants. The challenge is great, but the rewards are commensurate. It is up to pharmaceutical companies to act now.

Precision Medicine on the Corporate Agenda

Strategy& recently surveyed more than 100 leaders in the pharmaceuticals industry across a range of functions, therapeutic areas, and geographic markets worldwide to gauge the industry's response to precision medicine thus far. The results clearly show that executives are wrestling with the topic. Among respondents, 92% said they regard precision medicine as an opportunity, and 84% have it on their corporate agenda.

Regarding specific therapeutic areas where precision medicine will likely be viable over the next 5 years, the top two responses were oncology, cited by 91% of respondents, and orphan diseases, cited by 53%. There are valid reasons for the industry's interest: Precision medicine holds the potential to change the way medicine is practiced. Precision medicine upends the medical one-size-fits-all approach in favor of in-depth patient profiling and individual treatments based on both personal data and a statistical analysis and comparison of larger cohorts. According to survey respondents, the most relevant data types for precision medicine are genomics (87%), clinical trials (72%) and electronic health records (66%). By comparison, newer and less well understood types of data such as someone's personal internet "fingerprint", lifestyle or data about food and nutrition were found to be less relevant.

Expected Benefits along the Pharma Value Chain

For pharmaceutical companies, precision medicine represents a new approach to innovating and developing drugs, in line with the demand from governments, regulators, and payors for "real-world evidence" of a drug's effectiveness and its value to those stakeholders. With populations in many markets aging, chronic diseases becoming more prevalent, and patient expectations increasing, governments and payors are looking for more evidence of value and positive patient outcomes. Potential benefits from precision medicine range across all aspects of the pharmaceutical value chain: research, development, market authorization, and post-product launch.

More than 75% of our survey respondents were confident that precision medicine will help reduce the roughly 10-year R&D cycle by about eight months on average, with one in three respondents saying reductions of a year or more are possible. In terms of R&D expenditure, 72% of those able to judge such spending (which was 77% of the total respondent base) predicted a reduction, averaging 17% of costs. Considering that global R&D spending for the industry is currently about $150 billion that translates into a potential annual savings of $26 billion.

External and Internal Barriers to Overcome

Nevertheless, respondents were well aware that they face still many hurdles until they can fully benefit from the potentials of precision medicine. 92% see the unstable or nonsecure legal and regulatory framework as the most important external barrier. But also the lack of data (58%) as well as the limited ability to integrate data sources (31%) were considered obstructive.

The main internal hurdle was the lack of capabilities, cited by 79% of respondents. In particular, most pharmaceutical companies don't yet have the capabilities in place to generate the relevant data about patients, analyze and interpret that data, and apply the insights from clinical outcomes to change future drug development. Cultural aspects within the own company (72%) and the access to data and stakeholders (59%) played an important role as well.

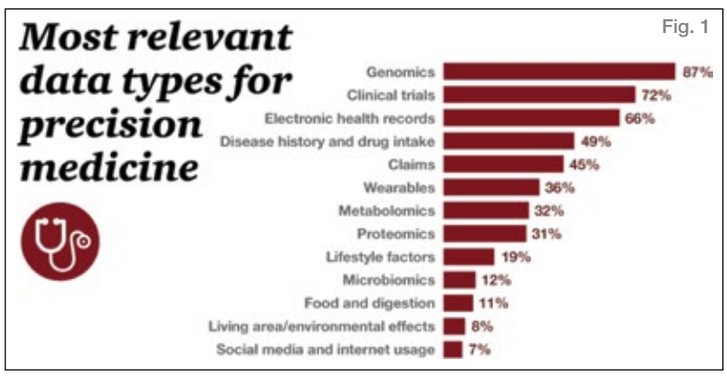


Fig. 1

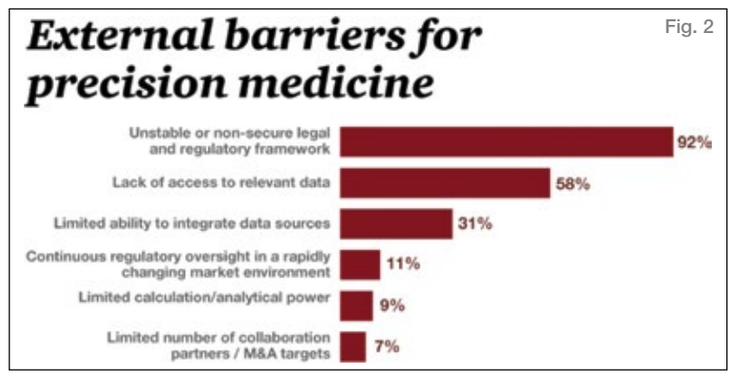


Fig. 2

Source: PwC Strategy& Precision Medicine Survey 2017

Asked for the most viable means by which they could develop data capabilities, the majority of respondents (87%) opted for "targeted collaborations beyond pharmaceutical firms" as the way forward, followed by the hiring of external experts, cited by 65%. Building these capabilities internally, although a viable choice for some companies, is slower and not necessarily cost-effective.

Building the Right Strategic Partnerships

As a result, striking the right collaborative partnerships will be tricky. There is a flood of new market entrants working on data issues, frequently from nonmedical fields such as personal technology and consumer devices. Some of these companies specialize in specific aspects of data — such as generation, collection and integration, analytics, or interpretation and usage — yet others are integrated across the full data value chain. Companies that partner with external players need to trust that the data and analyses their partners provide are both accurate and complete. Companies will also need to sort through a range of issues such as data protection, access and usage rights, and changes in the way clinical trials are set up. In order to forge the right partnerships, companies must ask themselves "What gaps in capabilities do we need to fill?" Second, companies must decide which partners are most appropriate to fill those gaps. Because they have limited experience in this new data field, companies will need to understand the landscape before they decide on specific external partners or experts to work with. All risks will remain with the pharmaceutical player as regulators will not allow the risk to be transferred elsewhere. Once a suitable partner has been found, the next issue is establishing the right engagement model. Companies will need to trust both their new business partners and the new technologies at the same time. It will require a significant cultural overhaul, particularly given that development cycles in technology are often measured in mere weeks or months. Companies will have to transform their organizational culture and embrace a more agile startup mentality.

In sum, precision medicine represents not only a business opportunity but also a clinical opportunity. At a time of greater healthcare challenges, it is a clear means of using emerging technologies to deliver better care to patients. That, in essence, is the responsibility of pharmaceutical leaders. As one respondent in our survey put it, "Precision medicine will happen, and it's better to be one of the shapers than a follower. Pioneering and taking risks to get on the train may afford greater opportunities than resistance or avoidance." In other words, pharmaceutical companies can seize this opportunity — or ignore it and watch their competitors pass them by.

Stephan Danner, managing director, PwC Strategy&, Berlin, Germany

Dr. Thomas Solbach, principal, PwC Strategy&, Frankfurt, Germany

stephan.danner@strategyand.de.pwc.com
thomas.solbach@strategyand.de.pwc.com
www.strategyand.pwc.com

Innovative Companies Have to Deal with Risks

In Times of Change the Flexibility of an Organization Will Be Part of Its Future Success

Pharma Waldhof is active in the development and commercialization of active substances, key intermediates and reagents for multiple applications in the pharmaceuticals, diagnostics, cosmetics and nutraceuticals industry. The German company has devoted itself for 70 years to the interesting field of nucleic acid biochemistry which started with the cultivation of yeast in the paper industry in Mannheim. During its history the company belonged to Boehringer Mannheim, and with the acquisition by Roche became part of the Swiss pharmaceutical company, before it got acquired by Aceto Corporation in 2004. Dr. Michael Reubold asked Dr. Lukas von Hippel, managing director at Pharma Waldhof, about the company's specific competencies and his evaluation of current and future market trends.

CHEManager: Dr. von Hippel, in the pharmaceutical market, the market share of biologicals and biosimilars is growing at above-average rates, and also in other sectors there is increasing relevance of biological and bio-based products and technologies. Pharma Waldhof looks back at 70 years in biochemistry business. How do you see this trend? Will biology be the key science of the 21st Century?

L. von Hippel: From my understanding, natural sciences are as well part of an evolutionary process: It started with mathematics, followed by physics. Out of physics, alchemy developed to become later chemistry. Chemistry split into various disciplines, now overlapping with various disciplines from biology. With this intra-disciplinary overlap we are now able to predict results of experiments better and to develop a deeper understanding how biological systems act and react. This is why the future will belong to combined scientific forces from various disciplines.

Will biology be the key science of the 21st century? Clearly not, or we would miss other disciplines like material sciences. A friend of mine, who is a psychologist, claims that this century will be the century of psychology. However, psychological reactions can be understood being the result of biochemical processes. So disciplines may merge here as well.

It may be a good advice not to forget that one discipline depends on others, and we can learn from each other.

Will we see new break-through technologies resulting from the combination of biological and other technologies?

L. von Hippel: For sure. We see this currently already in our manufacturing processes: Production asks for engineering, analytics ask for physics, cells do need media that supports growth, and media often derives from chemistry. It would be a fault to limit thinking to the set borders of a discipline. The borders fusion, so we have to learn how to bridge and understand different disciplines.

What growth potential for your business do you see resulting from this trend?

L. von Hippel: At Pharma Waldhof we are able to support quite a lot of disciplines, market segments, and customers with products that are essential parts of every human being. This is why our products have such broad spectrum of applications. DNA, RNA, nucleotides, nucleosides, co-enzymes and co-factors are widely used materials in all kinds of applications. We believe for the time being, we may know only a part of the potential applications.

Dr. Lukas von Hippel, managing director, Pharma Waldhof

Being specialists in our business field, we can support our customers with our products or the development of new qualities for certain applications or the development of a single product for a new or given application.

We observe continuing consolidation in many industries including the pharmaceutical sector and its supplier market. Where do you see the market heading, especially since biotech and biochemistry companies have become top targets for Big Pharma?

L. von Hippel: The development of companies often follows waves: Big companies are growing, later spinning off smaller parts. Pharma Waldhof is a living example: In our history, we belonged to large organizations like Boehringer Mannheim and Roche. Now we belong to Aceto Corporation where we have a unique position in its portfolio of companies and are fairly independently managed.

©psdesign1 - stock.adobe.com

From our perspective, we do strongly believe that innovation will be the driver for our future development. In our mind, innovation goes far beyond R&D. R&D is able to invent and to generate knowledge. But keep in mind, innovation is the successful commercialization of knowledge. Uber and Airbnb are examples where companies are quite successful with different and new business models, commercializing knowledge while partnering.

So, the question may be, what type of cooperation will at the end be most efficient for a company: through acquisitions of companies with certain know-how or by partnering in virtual networks. Most likely both ways will remain for longer.

What challenges or chances arising from this continuing consolidation do you expect for smaller companies like most CDMOs?

L. von Hippel: In Chinese, the character for chance and risk is the same. Not only today, times are changing quickly. So, flexibility of an organization will be part of its future success, and long existing successful companies have always shown to be flexible. Beside flexibility, knowledge will be mandatory, but knowledge is a perishable good. We all have to invest in keeping our knowledge up to date. This will be the challenge for the future — but this is nothing new.

The other topic may be management trends: from time to time, large organizations are forced to consolidate the number of partners in the supply chain. This may limit the chance for a small organization. However, if the products and services of a small CDMO are excellent, there are exemptions from every rule. We are proud to have quite a lot of well-known and highly reputed names in the industry being our loyal customers.

> *"We do strongly believe that innovation will be the driver for our future development."*

How will the market shake-up influence the innovation climate? Will it distract companies from innovation projects or will the mix-up of R&D departments spark new ideas?

L. von Hippel: Personally, I do not believe that a market shake-up will have much influence on the innovation climate, but time to market will be affected. When companies get acquired, there is a natural slow-down in innovation processes: the time integration takes will be the time missing to work on other topics.

The real challenge will be the question how to deal with risk. Innovation projects are by nature risky, so innovative companies have to deal with risks. In times where people are looking for stability and predictability, the innovation climate will be affected and the willingness to take risk is limited. The louder an organization calls for innovation, the bigger the inner resistance may be. If we accept that part of an innovation nature is limited predictability, we may have to accept as well we can hardly manage an innovation in detail. So, the question may be, when will we accept not everything in life is manageable and, thus, what the consequences are for our organization and our management style.

Innovation is crucial, but defining a proper innovation strategy and putting it into action is not a piece of cake. What does your innovation strategy look like and what differentiates it from other companies?

L. von Hippel: You may understand that I am not willing to open books here. However, there are some aspects I can disclose: Firstly, we are market driven. So we are only willing to develop a project if there is a demand and a customer commitment. Secondly, we do not have technical limitations. If we miss some technologies or skills internally, we will go for external partnerships. This is why we could in a project for example clone, express, and later use the standard set of technologies we typically use. This is per se not new, but we have developed a certain skillset of expertise in combining forces that at least I have not seen in my career elsewhere.

In 2017, Pharma Waldhof was awarded "Best Biochemical Products Provider Germany & Europe". What does that label tell about your business strategy?

L. von Hippel: We have been surprised by this recognition, because we did not apply. Obviously one of our customers or friends gave us the nomination. In the next round, the community has been asked to vote, and in the result, we got the award for Germany. Three months later, after comparison of the winners in various states, we were informed that we have been the best in Europe.

We have been pleased receiving such recognition. It is an excellent recognition for all our employees who are working every day with passion to make our success happen. This recognition clearly shows that our customers do appreciate what we try to provide every day: Quality, both in products and services, an open ear for questions, the ability to develop, and our self-understanding to be a service provider, supporting our customers to be successful.

www.pharmawaldhof.de

Digital's Transformative Power across R&D

Keeping Pace with Stakeholder Expectations in the Pharmaceutical Industry

The pharmaceutical industry is making a fundamental shift from a product — to a patient-outcome focused approach. Consequently, R&D organizations must also reflect this strategic shift — from the processes used to the capabilities in which they invest.

The healthcare industry continues to experience massive changes driven by both external and internal factors, which combined present the opportunity for a deeper reflection and a radical business model transformation. External demographic and economic pressures include an aging global population, the rise of chronic diseases, changing customer expectations, increased patient involvement and amplified regulatory scrutiny. Companies are challenged by the need to understand, prioritize and leverage the growing opportunities made available by technology proliferation and capabilities. Therefore, it is essential for R&D organizations to embrace digitalization in a more holistic way or risk being outdone by their competition.

Fig. 1: With stakeholders' extensive digital adoption, we believe a more holistic embrace of digital is essential for R&D transformation

Fig. 2: Digital capabilities enable companies to master major industry imperatives

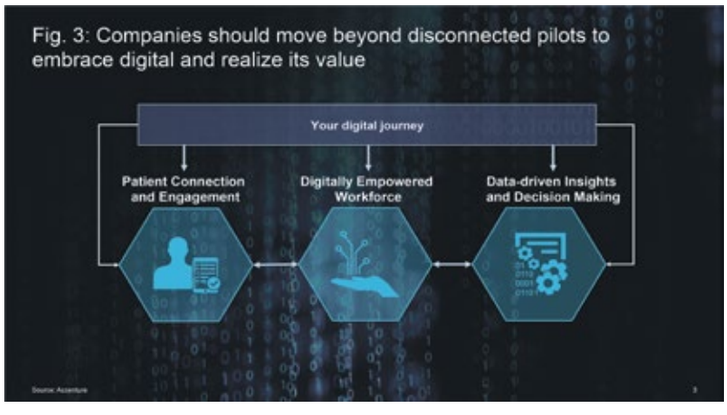


Fig. 3: Companies should move beyond disconnected pilots to embrace digital and realize its value

The industry has to shift from volume-based models to a value-based approach, which means that companies must focus on delivering outcome-based health and therapy management services. R&D organizations have an opportunity to support this by leveraging the power of digital technologies. Truly digital business models are information intensive, technology-enabled and disruptive, while focusing on creating and delivering an exceptional customer experience and amplifying internal performance.

R&D's primary stakeholders — patients, providers, payers, regulators and employees — are accustomed to living in a digital world where instant access to information and improved interactions are standard. They expect the same experiences during their interactions with pharmaceutical and biotechnology companies.

However, many R&D organizations lag their stakeholders' expectations in adopting digital. None of the typical reasons for delay — hesitancy to adopt new technologies, risk adverse cultures and the uncertainty of regulations and perception of health authorities — should prevent R&D organizations from embracing digital.

What Value Can Digital Help to Drive in R&D?

Digital capabilities can be applied across three major industry imperatives that are enablers to R&D's future success:

First, applications of digital solutions and services help to generate and document a holistic, shareable picture of patient health that finally enables a better understanding of the patient's disease. Using real-world evidence to study existing therapies and the corresponding impacts on patient lives, understanding, incorporating, and testing digital solutions and services during the drug development process, and assisting clinicians with collecting the appropriate data, finally result in the desired efficaciousness and effectiveness of products. Companies can deliver an improved patient experience, while integrating perspectives from caregivers and advocates to provide more seamless and holistic care.

Dr. Petra Jantzer, Accenture

Secondly, a digitally empowered workforce generates the opportunity to operate differently, with improved productivity both within and across functions of an R&D organization. However, effective implementation of a digitally-empowered business model requires a shift from the traditional analog mindset to an innovative and strategic approach to operations and decision making across the R&D value chain (e.g., early development, clinical, data management, regulatory, PV, medical). These equally include digital solutions and services within the workforce like virtual reality or gamification techniques across clinical groups. But it also requires a greater understanding of organizational needs and expectations of each employee and an embedded digital savviness in the organization to facilitate collaboration, innovation, agility and flexibility within the R&D functions.

Finally, digital capabilities enable companies to aggregate and synthesize historical data, internal data (e.g., clinical trial data, operational data, genomics data) and external data (e.g., electronic medical records, claims data) that empower R&D organizations to generate insights and drive scientific and operational excellence. This not only allows to make decisions in the R&D processes earlier, but it also means a shift to an informed and predictive approach — one that combines benchmarking and

statistical models to determine acceptable relevant performance deviations based upon pre-defined outcomes, as well as actions that create value for the organization.

With the appropriate capabilities and understanding of current data, companies can deploy analytics to improve both the scientific understanding of their products, and the effectiveness of their operations across R&D functions. Realizing the true value of internal and external data, in combination with analytics tools is one of the largest benefits of embracing digital for R&D. However, to work towards success, R&D organizations must interact with patients and stakeholders differently and change internal operations to generate, collect and consume the data and unlock the insights that a digital approach can uncover.

Digital Is already Transforming R&D

Early digital adopters are leveraging pilots in clinical trials and/or submitting new products for regulatory approval with a digital companion. However, there is opportunity to move beyond disconnected pilots and isolated initiatives to embrace digital, and realize the value it offers. Digital can sharpen the focus on patients and improve outcomes, provided there is a clear understanding of the impact digital has had in transforming other sectors.

In order to increase the impact of digital capabilities aligned to the industry imperatives, organizations should look to identify a holistic set of cross-functional services and solutions which can be applied to all activities within the value chain, from scientific collaboration internally and externally, to the transition from in vitro to in vivo, to phase I through phase III clinical trials and initial product submissions, to ongoing safety monitoring, product maintenance, and key opinion leader (KOL) and health authority interactions through various channels and partnership methods.

In order to assess the organization's readiness toward adoption of digital capabilities, we must look to the functional and technology leadership teams to offer insights on current and future state of the company's digital footprint, the organizational alignment, and strategy to implement digital capabilities.

This process of enquiring across the imperatives can help R&D organizations communicate the opportunities and threats that digital might pose to the business. Additionally, it helps companies to get a better view of where each opportunity and threat is coming from and the strategy and actions needed to build competitive advantage in a quickly evolving digital business environment.

Digital can play an important role in helping R&D organizations overcome today's challenges, realize the value of each industry imperative and make significant progress toward the industry's overarching, fundamental mission: to better understand specific disease states, and to create products and services that improve patient experiences and long-term outcomes.

Dr. Petra Jantzer, managing director, Accenture GmbH, Zurich, Switzerland

petra.jantzer@accenture.com
www.accenture.com

Supply Chain Integrity and Patient Safety

Labeling Solutions can Prevent Fraudulent or Incorrect Use of Medicines

Investigation into future trends in the medical and pharmaceutical sector shows that digitalization is changing supply chains in the healthcare industry. Such diverse issues like counterfeit drugs, aging population or self-medication have one thing in common: packaging and labeling solutions can prevent fraudulent or incorrect use of medicines and increase supply chain security and integrity. Partners of the pharmaceutical industry such as Munich-based Schreiner MediPharm provide customized solutions that are highly functional and offer value-added benefits. Dr. Michael Reubold discussed opportunities for innovation with Ann L. Merchant, President of Schreiner MediPharm.

CHEManager: Ms. Merchant, Schreiner MediPharm is a long-standing partner of the pharmaceutical industry. What is your track record as a solutions provider?

A. Merchant: Our customer base includes the majority of the top 20 pharma companies. With our special pharma expertise, we position ourselves as the innovation leader in providing high-quality solutions in the functional labeling space. By utilizing our innovative strength, we proactively assist our customers to find the ideal solution for their specific applications and provide support from the initial idea to commercial production. Our role is to be the enabler, while the pharmaceutical company has to decide what type of features or information they want to include in their individual solution. Ultimately, we always strive for a holistic and highly customized approach.

When you ask about our track record, we invented the hanger label and the label with detachable parts, as well as the Needle-Trap system for needle stick prevention, just to name a few. The most important aspect on the technology side is to truly understand the major trends in the pharmaceutical industry and for us to determine how we can support our customers in meeting current and future requirements.

What do you see as the major trends in the pharmaceutical industry?

A. Merchant: The mega trends are the aging population, the increase of wealth in emerging markets, and the informed patient. So, we have more elderly people who have chronic diseases. The increase of wealth in emerging markets enhances the demand for better products. And the industry is looking into how they can better connect to the increasingly well informed patient. All three of those trends actually have a direct impact on us. We are focusing on end-to-end supply chain integrity, patient centricity, connectivity and patient safety.

Regarding the supply chain, which features are you offering?

A. Merchant: If we think about supply chain security, it is a fact that there are counterfeit drugs in the market place and we want to make sure that those are tracked and found, and not used. Or, if we think about some of the new regulations, like the EU Falsified Medicines Directive — FMD —, it is very clear that you need to make sure that your outer package is sealed. So to support the implementation, we have some concrete solutions.

We help a pharmaceutical company to ensure that the patient receives a genuine product. For instance, we offer first-opening indication and tamper evidence, multi-level counterfeiting protection, as well as tracing solutions. And we try to understand what is the customer's objective, how valuable is their product, and to what extent does it need to be protected?

And this ties very well again to the FMD. The directive is going in the right direction but there are different pillars that you have to look at. The FMD requires serialization and first-opening indication, but it does not consider authentication. However, only the combination with additional counterfeit-proof authenticity features can offer a comprehensive approach against fraud, misuse and tampering. Customized security concepts, including analog as well as digital features using an integrated Near Field Communication — NFC — chip ensure that all stakeholders, if an informed expert or the end user, can be involved in the authentication process.

Do you think the pharmaceutical industry is well prepared for putting this directive into action?

A. Merchant: I would say it's a mixed bag. Some are well prepared and recognize that the improved visibility into their supply chain can offer advantages to the company as a whole. Others are in earlier stages of adoption and implementation. I think that the challenge will be with some smaller pharmaceutical companies, because it is a really large effort and it costs a lot of time and money to implement.

Supply chain agility is another area you are focusing on.

A. Merchant: Yes, the 'agile supply chain' refers to a growing market segmentation and the demand to react to different needs in different market places. Our solutions in this field include late stage customization of functional labels and additional supply chain services. Emerging markets typically have very small lot sizes from a manufacturing perspective. They have their own regulatory authorities, which means they have specific labeling requirements. So we have come up with a method where we can apply all of the features that they would like to have, while the turnaround time is only a number of days versus weeks. This is achieved by pre-manufacturing the labels conventionally with all functional features, storing them in our warehouse and customizing them at short notice via digital print. Theoretically, you could

print one label and you're done, but you still have the value-added benefits of functional labels. Thus, we are able to support the supply chain in a very agile manner.

Turning to the patient, where is your focus in terms of patient centricity?

A. Merchant: In order to ensure reliable self-medication in a growing homecare market, we developed customized label solutions for pens and autoinjectors, supporting convenient and safe handling of injection devices. Functional features include for instance grip, anti-slip varnishes and tactile elements, a temperature indicator or UV protection. Smart labels with integrated RFID/NFC inlay for interactive applications support the patient by providing access to additional product information, user videos, reminder functions or digital authentication.

Our solutions for patient compliance monitoring feature integrated printed electronics for digital monitoring of medication intake and adherence tracking which can be adapted for diverse packaging concepts. Via NFC or Bluetooth technology information can be transmitted to a smartphone for interaction between patient and physician. Digital patient compliance monitoring is also interesting for clinical trial settings with their strictly regulated environment, where non-compliance is causing longer study time cycles, higher costs and postponed drug approval processes prior to commercialization.

> *"The most important aspect on the technology side is to truly understand the major trends in the pharmaceutical industry."*

Another important area is patient safety.

A. Merchant: Yes, and it is actually the ultimate goal with regard to all medications and of utmost importance in drug dispensing. We offer solutions for the avoidance of medication errors and for needlestick prevention. For instance, there is a sophisticated label with self-lifting detachable parts for multi-dose vials to clearly identify disposable syringes after the refilling process. And our Needle-Trap system is a unique, label-integrated safety device for prefilled syringes to secure the needle after the injection with a plastic catcher — with the aim of improving patient and healthcare giver safety.

What is your vision when it comes to progress in medicine?

A. Merchant: Looking into the future, I think that advances in technology will allow medicines to be produced to specifically target cancer and diseases of the aging like Parkinson's or Dementia, and also that they will be more personalized, so that you get the medicine that works for you.

When it comes to digitalization and connectivity, as a participant in the healthcare system, I personally would like to see a better use of the data that is being generated to link findings from one doctor to another, to always understand interactions between medicines and to know which ones will work best for me.

www.schreiner-medipharm.com

Risk Assessment for Excipient Manufacturers

Current Situation and Global Evolution

There is a regulatory expectation that pharmaceutical companies will verify that the excipients produced by their suppliers are to an appropriate level of GMP. This has been achieved by auditing some suppliers, but today, the burden that generates on suppliers and their pharmaceutical company customers is both impractical and unsustainable.

Fortunately, the regulators support the verification of suitable GMP via independent, credible 3rd party certification schemes.

Tony Scott, EXCiPACT

Excipient Regulation and Guidance

The pharmaceutical industry is increasingly using risk management principles to improve product quality and better protect patients. At the same time, regulators have called for more secure supply lines and defined quality measures for excipients. However, regulating pharmaceutical excipient quality is not easy as only a small percentage of excipients are made solely for pharmaceutical use. Whilst clearly defined GMP requirements already exist for APIs, defined GMP requirements for excipients were not formalized until recently.

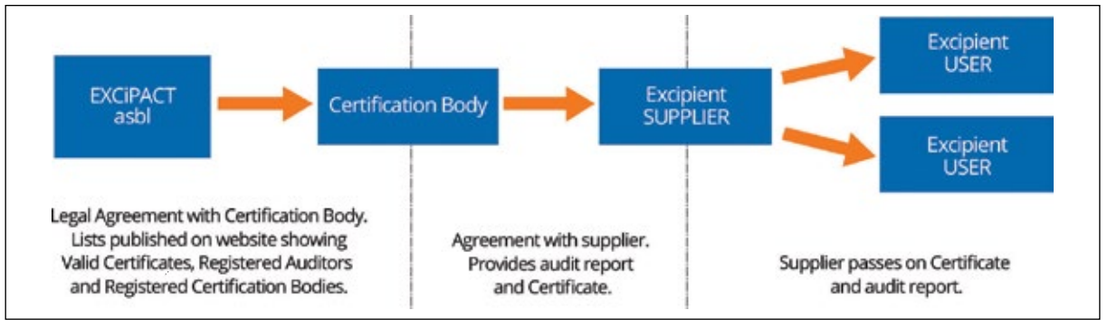
In 2011, the EU's Falsified Medicines Directive established that manufacturing authorization holders (MAH) must use a formalized risk assessment to ascertain the appropriate GMPs for ensuring excipient suitability. In 2015, the European Commission issued guidelines on the risk assessment for determination of the appropriate level of GMP for excipients. In 2016, EU drug product manufacturers (and those importing them into the EU) were required to implement risk assessments for the appropriate GMP for each excipient used. While regulations regarding GMP for APIs clearly define compliance needs, the responsibility for defining necessary GMPs for excipients in a specific drug product rests with the MAH holder.

Other countries are also developing formal requirements for excipient GMPs. The US Food Drug & Cosmetics Act specifies that drugs must be manufactured, processed, packed, and held in accordance with current good manufacturing practice (cGMP), or they are deemed to be adulterated. Under US law, a new pharmaceutical excipient, unlike an API, has no regulatory status unless it can be qualified through the approval mechanisms available for components used in finished drugs. The FDA assesses and permits use of excipients as part of a New Drug Application. In 2012, the FDA Safety and Innovation Act (FDASIA) Title VII became law, expanding the FDA's authority to safeguard public health by, inter alia, enhancing the safety of the increasingly global drug supply chains. This requires drug manufacturers to include as part of a drug listing, the name, address, and unique facility identifiers of associated excipient manufacturers.

In Brazil, GMP requirements for excipients in locally sold drug products became law in 2016. In China, there are the new 'bundling regulations', consideration of local GMP regulations and, in 2015, an upgrade to the local pharmacopoeia. Other global initiatives affecting excipient quality include ICH Q3D for elemental impurities, ICH Q1B for stability requirements, QBD requirements, a Pharmacopoeial Discussion Group (PDG) monograph on harmonization, WHO initiatives on GMP and Good Trade and Distribution Practices.

Excipient Risk Assessment

Excipients come from many sources outside the pharmaceutical industry, including oil, plants, animals and mining. Over 1,400 excipients are used in drug products and the focus on risk assessments and transparency of supply chain integrity has become more prominent in regulations in recent years. However, unlike APIs, excipients are not made specifically for use in medicines. Rather they have a diversity of industrial uses from cosmetics to food which presents its own regulatory challenges. It would be impractical to directly regulate all excipient suppliers, and may even encourage some suppliers to leave the pharmaceutical sector. Therefore, the regulations require pharmaceutical drug manufacturers to conduct the risk assessment and ensure the excipient suppliers are of a suitable quality particularly as only the pharmaceutical manufacturer knows the intended use of the excipient.



Patient safety is really the concern of the MAH and is not necessarily the direct focus of the excipient supplier. However, many excipient manufacturers do their own risk assessment and adopt suitable GMP to support business with their pharmaceutical customers. To help establish a consistent approach for the benefit of excipient suppliers and users, IPEC Europe and IPEC-Americas jointly published "The IPEC Risk Assessment Guide for Pharmaceutical Excipients, Part 1 — Risk Assessment for Excipient Manufacturers — First Version 2017." This 'How To' document provides detailed guidance on a standardized approach to risk assessment as summarized in the process chart (see figure).

While all pharmaceutical manufacturers should now have the risk assessment in place to determine the appropriate GMP required for every excipient they use, questions remain on how supplier qualification should be implemented. Many prefer an audit of every supplier to provide evidence of GMP compliance. As the burden this would pose makes this untenable, supplier GMP certification schemes have become available. This approach is supported by regulators subject to certain conditions.

Excipient Certification

EC Guidelines permit the use of GMP certification held by the excipient manufacturer or supplier. While regulators have indicated that such approaches are acceptable, certain requirements must be met. These include that: the assessment must be against a standard that is suitable for excipient suppliers; the auditor must be demonstrably competent; and the certification body must have the quality management systems suitable for such a service, notably conformity to ISO 17021.

For example, the voluntary EXCiPACT GMP pharmaceutical excipient certification scheme meets these requirements and is being used as part of the risk assessment and supplier qualification process in a 3-year certification cycle that includes annual surveillance audits. Such certification assesses the quality management system of the excipient supplier together with the applied GMP, although may not meet the more demanding GMP requirements of, for example, parenteral drugs. It can also be used to certify the appropriate Good Distribution Practices (GDP) of the supply chain.

Such a certification scheme is one solution to meeting the new tougher regulatory requirements being faced by the pharmaceutical industry and its excipient suppliers. Certification is helping support supplier quality management while securing the supply chain and minimizing risk to patients.

References are available from the author.

Tony Scott, head of operations, EXCiPACT asbl, Brussels, Belgium

operations@excipact.org
www.excipact.org

Index

CPhI Worldwide 2017

CPhI Worldwide, to take place October 24–26, 2017, at Messe Frankfurt, Germany, is the leading networking event and exhibition dedicated to pharmaceutical developments, trends, products and services. Exhibitors include providers of contract research and synthesis services, suppliers of APIs, excipients, ingredients, intermediates and finished dosage forms, as well as producers of pharma manufacturing and packaging equipment. **www.cphi.com**

Chem Show 2017

Chem Show is one of the main showcases for the latest process equipment, products and services, bringing together manufacturers and innovative new suppliers with executives, process engineers, production teams and plant personnel throughout the CPI (Chemical Process Industries). More than 5,000 processing industry professionals and 300+ exhibiting companies will gather from October 31 throughout November 2, 2017, in New York City, USA, to experience innovative products, equipment and services for faster, smarter, cleaner and more efficient processing facilities. **www.chemshow.com**

European REACh Congress 2017

This year's European REACH Congress, held on November 21—22, 2017, in Duesseldorf, Germany, will move away from registration-based topics and looks to the future challenges such as voluntary versus regulatory management of hazardous chemicals at manufacturing/formulating sites. The event encourages shared learning amongst industry, service providers authorities and policy makers. **www.reachcongress.com**

Imprint

Publisher:
Wiley-VCH Verlag GmbH & Co. KGaA
A Company of John Wiley & Sons, Inc
Boschstr. 12, 69469 Weinheim, Germany
Tel.: +49 6201 606 0

Publishing Director
Dr. Heiko Baumgartner

Product Manager + Managing Editor
Dr. Michael Reubold
Tel.: +49 6201 606 745
michael.reubold@wiley.com

Editor in Chief
Dr. Ralf Kempf
Tel.: +49 6201 606 755
ralf.kempf@wiley.com

Freelancer
Thorsten Schüller, Dede Williams, Elaine Burridge, Miranda Kennedy

Media Consultants
Thorsten Kritzer
Tel.: +49 6201 606 730
thorsten.kritzer@wiley.com

Corinna Matz
Tel.: +49 6201 606 735
corinna.matz@wiley.com

Jan Käppler
Tel.: +49 6201 606 522
jan.kaeppler@wiley.com

Roland Thomé
Tel.: +49 6201 606 757
roland.thome@wiley.com

Wiley Reader Service:
65341 Eltville
Tel.: +49 6123 9238 246
E-Mail: WileyGIT@vuservice.de

Team Assistants
Bettina Wagenhals
Tel.: +49 6201 606 764
bettina.wagenhals@wiley.com

Lisa Rausch
Tel.: +49 6201 606 316
lisa.rausch@wiley.com

Beate Zimmermann
Tel.: +49 6201 606 316
beate.zimmermann@wiley.com

Production Managers
Jörg Stenger (Administration)
Melanie Horn (Advertising)
Oliver Haja (Layout)
Elke Palzer (Cover/Litho)

Original Articles:
Specially identified contributions are the responsibility of the author. Manuscripts should be addressed to the editorial office. Instructions for authors may be requested from the publishing company. We assume no liability for unsolicited, submitted manuscripts. Reproduction, including excerpts, is permitted only with the permission of the editorial office and with citation of the source. The publishing company is granted the exclusive, space and content restricted right to arbitrarily use the unmodified work/editorial contribution for all purposes for itself and for businesses that have an interest in the publishing company as defined by company law as well as to transfer the right of use to third parties. This right of use applies to both print and electronic media including the internet and data banks/data media of all types.
All names, designation, or signs in this issue, whether referred to and/or shown, could be trade names of the respective owner.

Druck: DSW GmbH,
Flomersheimer Straße 2–4,
67071 Ludwigshafen
Printed in Germany

Title – Copyright
© BillionPhotos.com - stock.adobe.com

CPhI worldwide

Co-located with: icse InnoPack P-mec FDF

24 - 26 October 2017
Messe Frankfurt, Germany

REGISTER NOW
gotocphi.com/cphi17

CPhI Worldwide:

Bringing every aspect of the pharmaceutical supply chain together in one location

"Big pharma, small pharma, specialty pharma and packaging... everyone is here!"

Cedric Roesler
CEO, Diffway

"You have to be here to be a big player in the industry!"

Cosmas Mukaratirwa
Managing Director, Cospharm

WHAT VISITORS SAID ABOUT THE 2016 SHOW*

81% rate CPhI Worldwide as the **leading global gathering** of the pharmaceutical industry

80% agree that CPhI Worldwide **is the most important show** in the pharmaceutical industry's calendar

81% believe that CPhI Worldwide is a **great show** to find new business opportunities

** post show survey 2016*

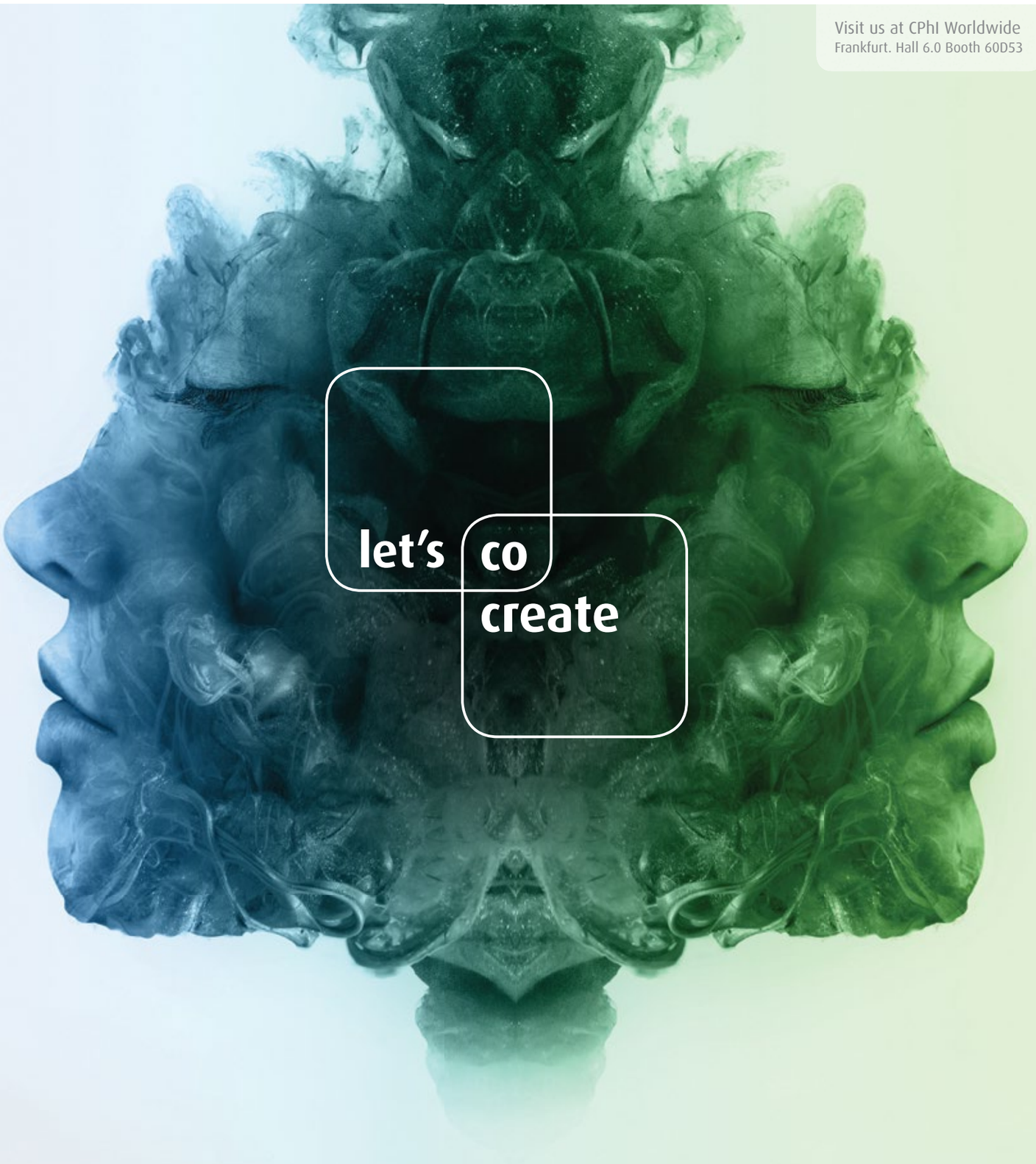
WHY ATTEND CPhI?

- **Cost Effective: 42,000** pharma professionals from **150+** countries in one location
- **Entire pharma supply chain: 2,500+** exhibitors covering **ingredients, APIs, excipients, finished dosage, contract services, packaging, machinery** and more
- **Industry developments:** stay up-to-date on market news and trends during the **Pre-Connect Congress, CPhI Pharma Innovation Awards and Pharma Insight Briefings**
- **Free access: 1 ticket, 5 shows,** 150 free seminars, innovation tours, innovation gallery and matchmaking

SAVE €140 - REGISTER BEFORE 15 OCTOBER 2017
gotocphi.com/cphi17

2017 EXHIBITORS INCLUDE: HETERO, Midas Pharma, Pharmathen, polpharma, SANDOZ

Organised by: UBM



Working together to create ground-breaking chemistry

When you need to innovate for sustainable development of next-generation technologies, let's work together to co-create solutions that give you a competitive edge. At Umicore, we offer a collaborative approach to research, development and commercial manufacturing for your complex organometallic chemistry and catalysis needs.

Together with our customers we create and deliver ground-breaking science to pioneer sustainable technologies across many industries, including automotive, electronics, chemistry and pharmaceuticals.

Let's co-create to make a difference | pmc.umicore.com

materials for a better life

umicore
Precious Metals Chemistry