

# CHEM *FINE & SPECIALTY CHEMICALS* Manager 1/2017

## INTERNATIONAL



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### Markets & Companies

Megadeals Reshape the Chemicals Industry, The Chemical Footprint in Pharma, Iran's Pharma Market, M&A, News & Opinions

### Innovation & Applications

Bioelectronics to Transform Medicine, Flow Chemistry and Micro Reaction Technology, Greening of the Chemical Value Chain

### Strategy & Management

Fine Chemicals Business Outlook, Approaching the Final REACH Deadline, China's Outbound Foreign Investment Strategy

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## MARKETS & COMPANIES

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# The “Merger Endgame”

## A Surge of Mega Deals Will Reshape the Chemicals Industry

*After robust yet modest chemicals M&A activity in 2016, expectations for the year ahead are high. The value of completed deals in 2016 decreased slightly against 2015 to around \$100 billion. However, the pipeline of M&A deals is at a record level, with more than \$300 billion of potential transactions. This is more than twice the value of the pipeline at the end of 2015 (which itself was an all-time high) and more than the combined deal activity of 2014, 2015, and 2016.*

This strong M&A pipeline is driven by a handful of mega deals, each of which will break deal-size records if completed. In the decade leading up to last year, not one deal had exceeded the \$20 billion mark. As of early 2017, four deals individually valued at between \$40 billion and \$70 billion are under way.

### Drivers of Deal Activity

At the heart of this trend is an acceleration toward greater scale in chemicals value chains and segments. In area after area, companies have focused their portfolios to reach higher levels of consolidation and are reaping the benefits of mar-

ket reach, capability, and efficiency through M&A.

The shift is most prominent in industrial gases where the top five companies represent 86% of the revenues generated by the top 20 companies, even without considering the announced deals. Air Liquide closed its acquisition of competitor Airgas in the middle of 2016 for \$13 billion — the largest deal completed that year — and at the end of 2016, Praxair and Linde announced their intent to merge, a deal that would be valued at \$43 billion.

In agrochemicals, multiple deals are under way or have been announced, including Dow Chemical’s and DuPont’s merger, Bayer’s acquisition of Monsanto, and ChemChina’s acquisition of Syngenta. Similar M&A



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activity is happening in fertilizers, paints, and coatings. In paints, the race for the merger endgame is in progress, with Sherwin-Williams intending to acquire Valspar. Moreover, PPG continues to attempt the acquisition of AkzoNobel even though a recent offer was declined by the target company. And in fertilizers, Potash is planning the acquisition of Agrium.

While these mega deals will likely face hurdles, particularly from anti-trust authorities, it is anticipated that major deals in the pipeline will be approved and completed during 2017.

### M&A Outlook

Looking ahead, we expect consolidation to accelerate further in chemicals segments where customer industries exhibit high levels of consolidation or are trending in this direction, including segments such as consumer goods, automotive, electronics and coatings.

In addition, deal activity is spurred by chemicals companies' balance sheets and investment portfolio decisions. A slowing demand outlook

*“Diversified chemicals companies are increasingly shifting their portfolios toward more specialty pure play models.”*

combined with high investor expectations leads companies to turn to M&A as an alternative to organic investment options that don't provide the required returns. In our survey of chemicals executives conducted for the A.T. Kearney Chemicals Executive M&A Report 2017, more than half the respondents saw these factors as important drivers of deal activity.

Moreover, diversified chemicals companies are increasingly shifting

their portfolios toward more specialty pure play models, incentivized by the higher multiples investors award to specialty and solution-focused chemicals companies. A prime example of this trend is the merger of Dow Chemical and DuPont, where the company will be split into three parts with two solution and specialty businesses and one feedstock-oriented business.

China has steadily increased its share of global deal volume to become the number one country of origin for transactions, representing 24% of all deals. This reflects the pattern of emerging market firms seeking access to advanced technologies, services, application know-how and customers — a factor that A.T. Kearney's study identifies as the most important driver for future activity. Already in 2016, the number of completed deals with an emerging market acquirer and a developed market target more than doubled compared to the previous year

while the total number of deals remained stable.

We expect this trend to continue as government-driven consolidation in industries such as steel, coal, and chemicals in China creates more national champions that in turn pursue international growth strategies through M&A. A prominent example is ChemChina. The group has been building a strong position in agrochemicals by acquiring Adama and Syngenta as well as establishing the company in rubbers and plastics by acquiring Pirelli, complemented with the acquisition of machinery company Krauss Maffei. We expect similar trends to continue in India, although at more muted levels.

Although currently a small share of M&A activity, chemicals activity in the Middle East is also expected to pick up as companies expand their chemicals portfolios, partly driven by the uptake of direct oil-to-chemicals processes, which provide favorable economics for crude oil produ-

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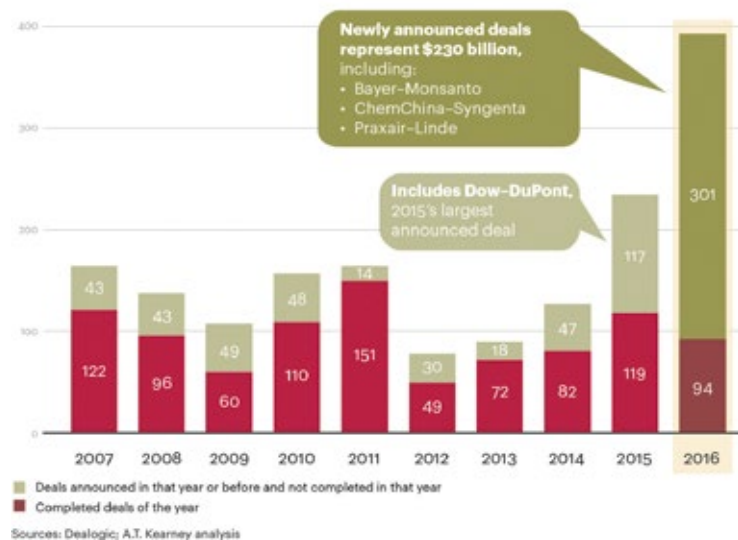
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**The backlog of pending deals is at a level never seen before with more than \$300 billion of potential transactions**

Completed and pending deals 2007-2016, deal value in \$ billion



**Top 10 completed deals in 2016**

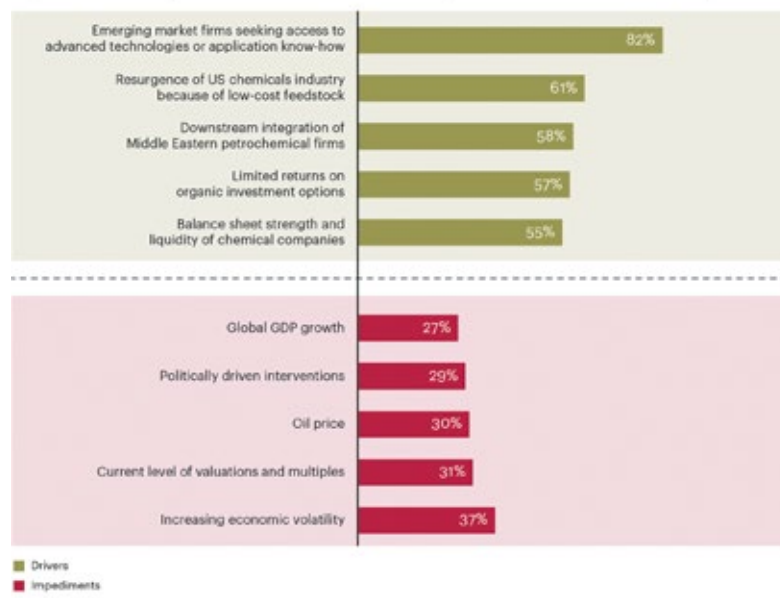
Acquirer (nationality)	Target (nationality)	Deal value (in \$ bn)	Primary announced deal rationale
Air Liquide SA (France)	Airgas Inc. (USA)	13.4	Vertical integration, Regional expansion
Dow Chemical Co. (USA)	Dow Corning Corp (50%) <sup>1</sup> (USA)	4.8	Product extension
Westlake Chemical Corp. (USA)	Axiall Corp. (USA)	3.5	Product extension
BASF SE (Germany)	Chemetall GmbH (Germany)	3.2	Product extension
CHS Inc. (USA)	CF Industries Nitrogen LLC (11.4%) (USA)	2.8	Business diversification
Dalian Rubber & Plastics Machinery Co Ltd <sup>2</sup> (China)	Jiangsu Hengli Chemical Fiber Co Ltd (99.99%) <sup>3</sup> (China)	2.8	Business diversification
Lotte Chemical Corp. (South Korea)	Samsung SDI Co Ltd (Chemical business) (South Korea)	2.0	Business diversification
WL Ross & Co LLC (USA)	Nexeo Solutions LLC (USA)	1.7	Product extension
Existing Shareholders (USA)	Ingevity Corp. (USA)	1.6	Business diversification
Dmitriy Lobyak (private investor) (Russia)	Uralkali OAO (18.66%) (Russia)	1.5	Financial investment

✓ Vertical integration
✓ Regional expansion
✓ Product extension
✓ Business diversification
✓ Consolidation and/or scale
✓ Portfolio restructuring
✓ Financial investment

<sup>1</sup> Joint venture between Dow Chemical and Corning  
<sup>2</sup> Controlled by Hengli Group  
 Note: All deals are 100 percent ownership acquisitions unless otherwise indicated.  
 Sources: Dealogic; A.T. Kearney analysis

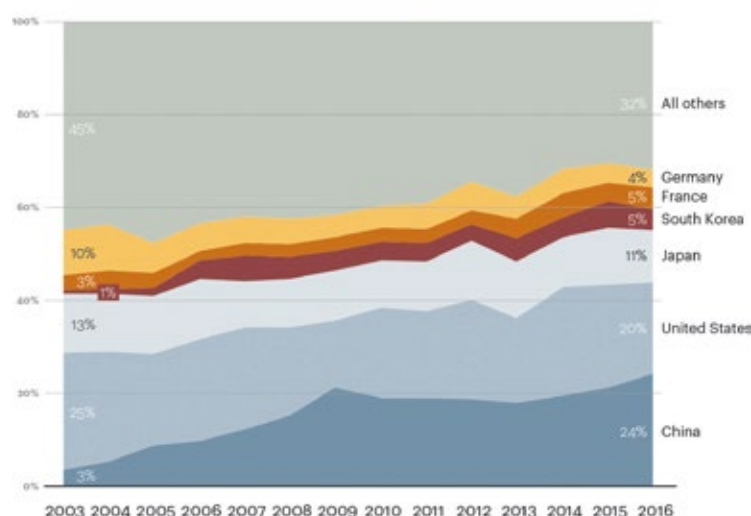
**Several drivers support continued M&A, but chemicals executives see economic volatility as a potential disruptor**

Top drivers and impediments of future M&A activity, share of executives selecting trend<sup>1</sup>



**Regional investment dynamics have fundamentally changed and made China the leader in acquisitions**

Regional composition of chemicals M&A activity by acquirer origin (% of deals)



cers. This could trigger partnerships with North American, European or Chinese companies, but it could also prompt acquisitions, with a focus on gaining access to global markets.

**New Levels of Uncertainty**

While these signs all point toward more M&A, several disruptors could radically change the direction of the industry, chief among them macroeconomic factors related to trade and tariffs, taxation, economic growth, and interest rates. With new levels of

uncertainty brought on by political upsets such as Brexit and the US election, chemicals companies are facing difficult questions about what their

*“Economic volatility is the strongest impediment to M&A growth.”*

environment will look like in the next 12 to 24 months. The executives we surveyed say economic volatility is the strongest impediment to M&A growth.

The potential for chemicals M&A activity in 2017 to reach its highest level ever raises two questions: Which chemicals chains will be the next to consolidate? What further deal activity could this trigger? In the words of Airgas CEO Pascal Vinet, such moves may reinforce “the need for others to reassess their position and continue to adapt.” His words about whether we have seen the last mega deal in the industrial gases market also seem appropriate for other chemicals chains and segments: “It is difficult to imagine, but never say never.”

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## Cambrex Expands Small Molecule Chemical Development and Manufacture

The small molecule industry continues to experience strong growth with the continued worldwide growth in API volumes and increased outsourcing requirements by large innovator companies, as well as the increasing use of generics, and the additional opportunities in developing markets. This demand has led to the situation where there are periodic shortages of North American CMO capacity, especially at critical volumes. Cambrex has invested over \$200 million since 2012 in facility expansions, equipment, technology and EHS upgrades to meet these demands, and to enhance the standards in quality, customer service, flexibility and reliability.

In 2016, the company made significant investments at its three global manufacturing plants.

A 72 million Swedish krona (\$9 million) investment to expand large scale manufacturing capacity at its Karlskoga facility in Sweden, including the installation of new multi-purpose reactors ranging from 4 m<sup>3</sup> to 12 m<sup>3</sup> and upgrading of the control room within an existing plant on site.

The installation and commissioning of a new pilot plant at its manufacturing and R&D site in Paullo, Milan, Italy. The cGMP plant, which can produce batch sizes from 1 kg to 15 kg, was constructed in order to meet customer demand for small-scale API volumes, and will also provide custom manufacturing of NCEs and intermediates for early stage drug development and clinical trials. The new facility is equipped with a hydrogenator that can operate at 30 bar and two separate lines of 150 liters glass lined and stainless steel reactors. ISO 8 classified, the plant is also equipped with a static dryer, milling and micronisation capabilities.

The company also completed and validated a \$50 million state-of-the-art production and warehousing expansion at its cGMP Charles City, Iowa site. The new 7,500 square feet multi-purpose manufacturing facility will initially add a total of 70 m<sup>3</sup> of glass lined and Hastelloy reactors ranging in size from 7 m<sup>3</sup> to 16 m<sup>3</sup>, along with 6 m<sup>2</sup> Hastelloy agitated filter dryers to provide a flexible, multi-purpose configuration, and will be capable of handling potent APIs at an Occupational Exposure Limit (OEL) of down to 1 µg/m<sup>3</sup>. Additionally, a further 7,500 square feet manufacturing shell has

been constructed which will be fitted out to customer specification.

Additionally, Cambrex also acquired PharmaCore, a company specializing in developing, manufactu-

ring and scaling up small molecule APIs for clinical phase projects based at a 35,000 square feet GMP site in High Point, North Carolina, USA for \$25 million. Cambrex incorporated

the facility with its 15,000 square feet chemistry laboratory and a 13,000 square feet pilot plant, as well as the more than 60 employees, into its network of manufacturing sites. (rk)



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# The Chemical Footprint in Pharma

## Pharmaceutical Companies Are Powering Economic Growth in Europe

*The chemical industry is the most important supplier of the pharmaceutical industry, but it can't keep pace with the economic strength and R&D intensity of pharma. This underlines a report of the German economic research institute Wifor. The study measured the economic footprint of seven selected European pharmaceutical companies in the European economy and concluded that they have a huge contribution to powering growth in the business landscape.*

The pharmaceutical industry is powering growth in Europe, drives employment and has a high Research and Development (R&D) intensity. These are the main results of a study from the independent economic research institute Wifor, a former spin-out of the

Technical University of Darmstadt, Germany. The institute investigated the direct and indirect economic impact of seven selected pharmaceutical companies in Europe as well as their contribution to the entire European economy between 2010 and 2014.

The research also showed that the chemical industry is highly linked to pharma companies as their main supplier. With 12% of all inputs used, the chemicals sector is most prominent in this field. Together with the second largest supplier industry, basic pharmaceutical products and pharmaceutical preparations, the top two supplier industries represent almost €7 billion or approximately 20% of the intermediate consumption and thereby stand out compared to the others. As Wifor states the disproportionate increase of intermediate goods and services for production purposes is the source for high indirect and induced economic effects in the EU economy.

In the scope of the investigation, which was done on behalf of the European Federation of Pharmaceutical Industries and Associations (EFPIA), were AbbVie, AstraZeneca, Boehringer Ingelheim, Ipsen, Janssen, Novartis and Sanofi. In 2014, these seven selected companies together generated 41.3% of the direct gross value added (GVA) generated by the European pharmaceutical industry and thus represented a significant share of the whole sector. Wifor used GVA as an important factor of measuring economic strength.

The economic footprint of the pharmaceutical industry was measured in order to quantify the macroeconomic contribution of these







companies to economic growth, employment and innovation in Europe between 2010 and 2014. In addition to direct economic effects, the study also accounted for indirect and induced economic effects, so-called spillover effects.

### Huge Growth Impact

The analysis showed that the growth impact of the selected companies is significant. They not only contribute €34.6 billion to European GDP by generating direct GVA, but are also able to multiply this effect by a factor of 2.3. Thus, direct and spillover effects in total contribute €77.9 billion to European GDP. This means for every Euro of direct GVA by the pharmaceutical industry, 1.3 additional Euros is generated for the whole European economy.

Despite a declining direct GVA between 2010 and 2014 in Europe, the increase in total intermediate consumption shows that more GVA was generated along the supply chain, including the chemical industry. The linkages between the selected companies' intermediate consumption and the EU economy result in rising indirect and induced effects and high multipliers.

Even on a global level the pharmaceutical industry proves to be an economic powerhouse. In 2013 it generated €330 billion of GVA, which corresponds to 3.6% of the GVA coming from the global manufacturing industry. This is combined with a high annual growth rate (CAGR) of the global pharmaceutical industry, which was 5.5% between 2005 and 2013. "Pharmaceutical companies have been striving to improve their productivity since the beginning of the new millennium. They scored early success by bringing down selling, general, and administrative (SG&A) expenses between 2004 and 2011, but more recent cost-reduction efforts have yet to reshape the structure of their P&L", comments the consultant firm McKinsey & Company in a recent article headlined "Rethinking Pharma Productivity."

### Health Industry Makes German Economy Fit

Similar impacts can also be seen on a broader level in Germany's health industry. An analysis of the German Ministry of Economics (BMWi) for 2016 makes clear that the health sector as cross section industry is of high

and growing importance for the German economy. Such the health business contributes significantly to fulfill important core economic-politics goals. The GVA of the German health sector reached 12% of GDP in 2016, which means that every eighth Euro has been generated in this field. With

*"Advances in technology and analytics are opening up opportunities for powerful tech entrants."*

a total GVA of nearly €340 billion the health sector is nearly as big as the whole GDP of Austria. Furthermore it is employer for 7 million people in Germany. The industrial health business, which includes pharmaceutical and medical device companies for example and which is one of the biggest and most important players within the health sector, generated €71.1 billion. This was the fifth part of the GVA in the whole health sector.

As the Wifor report also highlights, the seven selected pharmaceutical companies were also able to sustain a high level of productivity and efficiency in Europe. In comparison to the pharmaceutical industry in the EU28 area, these companies achieved higher and above average levels in terms of labor productivity and GVA rates, which is the ratio between the GVA and the production value. Furthermore, the selected companies' labor productivity is more than €73,000 higher than the pharmaceutical industry's labor productivity.

### Driver For Employment

The same holds true for employment effects. Although the number of directly employed persons decreased by 7.6% from 2010 to 2014, the total employment multiplier increased by 0.5 percentage points from 2010 to 2014. The selected pharmaceutical companies supported nearly 865,000 jobs in the European labor market making them a strong driver of employment. Throughout the labor market almost five additional European jobs were supported for each job created by the pharmaceutical industry. This shows how strong the companies are linked to the overall EU economy.

On a global scale, the pharmaceutical industry employed over 4.8 million people in 2013. In addition, the sector's average labor productivity,

i.e. an indicator of GVA generated per employee, reached €68,489.

### Investment In Innovation

As a third core result Wifor highlights the pharmaceutical industry's heavy investments in innovation. This stresses the significance of the selected companies' R&D efforts for the Europe business landscape and that the companies make an important contribution to achieving the EU target of 3% internal R&D spending of GDP. In fact these companies have already surpassed the EU 2020 strategy's target of a R&D intensity rate of 3% by a factor of almost six.

Wifor concludes that the high internal R&D expenditures imply a concentration of highly qualified human capital and point to a source of competitiveness through innovation. Even compared to the chemical industry, the manufacturing industry and the IT sector the pharmaceutical industry in the EU28 invests more in inter-

nal R&D per generated direct GVA. "A high investment intensity in R&D activities is seen as one key asset to master the challenges of the future faced by the European Union, such as rising labor cost, lower numbers of direct employees and the relocation of lower specialized tasks and jobs to the European outskirts", says Wifor.

But the pharma industry faces a threat. Advances in technology and analytics are opening up opportunities for powerful tech entrants to engage with patients and consumers in radically new ways and to launch innovative healthcare offerings in conjunction with payors and providers, says McKinsey. "These entrants threaten to disintermediate pharma companies as the primary owners of patient data and take control of their value story. Should that happen, it would have drastic repercussions for pharma's R&D and commercial models."

*Thorsten Schüller, CHEManager*

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# Rediscovering a Sleeping Giant

## Iran's Pharmaceutical Market Offers Multinational Companies Growth Opportunities

*Iran has one of the longest histories of medical practice in the world. In the modern era, however, the Middle East country has fallen off the world's medical and pharmaceutical radar. Crippling international sanctions have restricted trade with Iran, severely affecting the pharmaceutical sector. But since January 2016, most international sanctions have been lifted under the internationally agreed Joint Comprehensive Plan of Action (JCPOA). As a result, early movers have the opportunity of gaining a head start in entering the Iranian market, provided they are aware of the risks and ambiguities and know how to mitigate them.*



The Iranian pharmaceutical market has much to offer for new entrants. Being a trade crossroads due to its geographic location, Iran is an ideal export hub for Central Asia (population: 400 million) and, in addition offers positive market dynamics, an established pharmaceutical infrastructure, skilled workforce, and a competitive landscape. Iran's pharmaceuticals sector is made up of about 100 companies. The country's pharmaceuticals market — valued by BMI Research at \$1.9 billion in 2015 — is predicted to grow at a compound annual growth rate of 6%. Some 60 pharmaceutical plants currently produce almost 40 billion drug units each year. More than 80% of Iranians receive a secondary education, according to the UN. But pharmaceutical companies must have a thorough understanding of Iranian market conditions to maximize opportunities and avoid pitfalls.

### Enter — Prepare Well

The Iranian healthcare system exhibits unique features that present both opportunities and hurdles for new entrants. Thorough preparation, including acquiring a deep knowledge of structure, decision makers and key stakeholders, is therefore essential, as is fostering good relationships with market players.

**Regulators and funding bodies:** Authorization from two government “gatekeeper” bodies is essential to successful trading in Iran. The first is the Food and Drug Administration of Iran (FDA), an agency that authorizes the import and manufacturing of all drugs, and controls the Iran Drug List (IDL). The second is the Supreme Council of Health Insurance (SCoHI). It decides which drugs can have their costs reimbursed and at what level. The costs of most drugs in Iran are reimbursable,

so securing this status ensures a strong competitive advantage.

**Providers:** Prescribed medicines account for about 90% of sales value of drugs consumed in Iran, according to BMI research. This means the prescribing physician is usually the key decision maker in the buying process.

**Pharmacies:** There are around 8,500 pharmacies in Iran. About 55% are linked to public institutions, enjoying a large market share due to their near-monopoly position in the provision of scarce and expensive drugs. About 85% of patients present pharmacists with a predetermined prescription, but in the case of OTC drugs, which make up about 15% of total sales, pharmacists can advise patients.

**Patients:** Iran's high proportion of prescription drug sales limits patient choice, but they have growing decision-making power in the expanding OTC market.

**Existing market players:** About 100 domestic pharma companies are active in Iran and can serve as accelerators for multinationals entering the market. Most are affiliated with government-backed investment companies.

### Consider the Regulatory Framework

**Approval process:** FDA authorization is a prerequisite for the sale of drugs in Iran. The application process to introduce new drugs is not dissimilar to those in developed markets, but may be less transparent and more time consuming.

**IP rights:** Under current legislation, pharmaceutical formulae and compounds are not patentable, leading to extensive unauthorized production of generic medicines. However, with Iran currently seeking World Trade Organization membership, this is likely to change as the country will have to adopt the WTO's patent protection terms.

**Pricing:** Drug prices are determined by the FDA's Pricing Commission. It decides on the expenses incurred by producers and importers for each drug, and then fixes a price taking into account the upper range of cost.

**Reimbursement:** Health insurers pay 70% (outpatient dispensed) or 90% (inpatient dispensed) of the cost

of drugs with reimbursement status. The remaining amount is paid by users. Most drugs have this status, but some drugs commonly used in the West do not.

### Land — Start Smart

The setting up of backend functions will vary depending on the choice of



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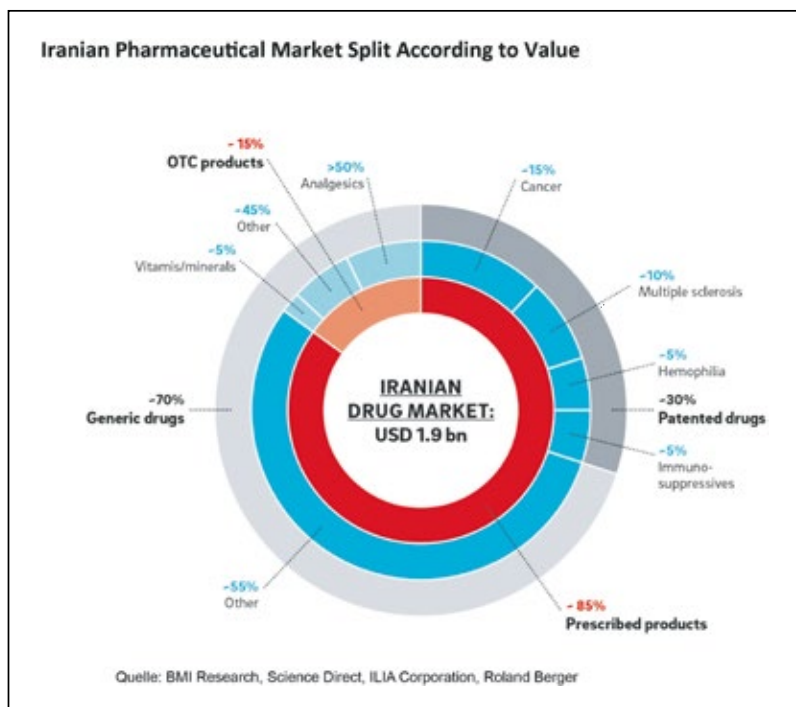


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Stefan Haid, Roland Berger





local production or import. But in both cases the route to market is identical.

**Sourcing:** Half of the raw material used in drug manufacturing in Iran is imported. But local sourcing is on the rise, and a number of base materials required to make rare medicines have reportedly been produced since 2013.

**Manufacturing:** Whether carried out at self-owned facilities or those of partners, manufacturing in Iran must abide by certain cultural rules. Selected medicines and dosage advice must be halal compliant, for example.

*“Early movers have the opportunity of gaining a head start in entering the Iranian market.”*

**Imports:** Finished pharmaceutical products are shipped in by importing companies, which are often subsidiaries of large local pharma groups. These offer significant opportunities to tap into local expertise. Import taxes and custom tariffs range between 0 and 65% depending on whether the product has a locally produced equivalent.

**Distribution:** Drugs are primarily distributed by six government-owned companies. But smaller private operators are increasingly entering the market, with about 20 currently active. Overall, the 10 largest distributors have a 75% market share. This level of consolidation makes the leveraging of existing local networks an attractive option.

**Exports:** Iran’s government is keen to promote the export of medicines to help chip away at its negative trade balance. By 2025 it hopes to have balanced exports and imports of medicines; as such, drug export income is tax exempt, and initiatives are underway to improve manufacturing practices.

### Succeed — Win Fast

Several areas of unmet or growing demand exist in the Iranian pharma market. For example, increasingly blurred lines between OTC and prescription drugs mean that a significant number of prescription medicines can be bought directly by users. The market for vitamin and dietary supplements is expected to become another important area according to Euromonitor.

In the prescription sector, there are several supply gaps owing to the fact that many prescribed drugs cannot be produced locally. An expected epidemiological shift towards chronic diseases is likely to crank up this demand further.

Generic drug makers can also benefit from Iran’s long tradition of favoring generic prescription medicines to keep down costs.

### Leverage — Benefit from Partners and Competitors

Collaboration with local players is the dominant strategy employed by international companies wanting to establish a foothold and grow in the Iranian pharma market. Such partnerships offer new entrants access to infrastruc-

ture, distribution networks and key stakeholders. Tie-ups with domestic companies have proven particularly beneficial for companies wishing to establish import-export businesses, as local expertise can be tapped to help manage regulatory compliance.

Foreign investment in the Iranian pharmaceuticals market is picking up pace and becoming increasingly ambitious. In addition to the partnership strategies being employed by the multinationals, most of which focus on distribution, other companies are establishing a bricks-and-mortar presence.

### Conclusion

There is little doubt that Iran offers multinational pharmaceutical companies clear growth opportunities. But it is not a straightforward operating environment and its unique character presents risks rarely found in most developed or developing markets. In order to mitigate these, it is recommended that new players comprehensively investigate local market mechanics,

the regulatory framework, business culture and domestic competition before entering. New entrants may also wish to consider partnering with local firms to smooth their landing and enhance growth once operational. They should also closely study the actions of competitors. Prevention, after all, is better than cure.

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# Meeting Customers' Changing Needs

## Delivering the Best Value without Compromising Product Quality and Patient Safety

*Johnson Matthey, which was founded in London in 1817, is celebrating its 200th anniversary this year. Through the constant application of new ideas and new processes, the company has built an organisation that has sustained two centuries of growth and managed to adapt well to changing markets. Fine Chemicals is one of Johnson Matthey's five divisions. It provides pharmaceutical customers around the globe with a range of services and solutions, including active ingredients, custom development services, catalysts and chiral technologies. CHEManager asked Antoine Bordet, the division's managing director, Europe, about his business outlook for fine chemicals and pharma manufacturing, the benefits digitalization could have for the industry, and the trends that will affect the fine chemicals industry in the future.*

**CHEManager:** *How do you think the business outlook has changed for fine chemicals and pharma manufacturing, over the last few years?*

**A. Bordet:** We have a broad-based business that encompasses supply of controlled substances, other generic APIs and catalyst technologies, as well as providing custom pharma services to innovators. With such a broad participation in pharma materials and services we see a variety

of outlooks depending upon which segment we consider. The overall outlook is, however, very positive.

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*“Future innovations will be heavily dependent upon digitalization.”*

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With strong market trends to outsource various elements of the pharma value chain, we are optimis-

tic that this will translate in market growth over and above the wider economy.

**What recent trends have you observed for fine chemicals and pharma manufacturing, in terms of your customer needs and challenges?**

**A. Bordet:** The need for our customers to innovate and develop effective medication is greater than ever. With the decline of the traditional large-volume blockbusters, customers are increasingly focusing on smaller indications, sub-segments of disease populations and generally striving hard to find effective treatments for unmet needs. This is bringing an array of technical challenges as therapies become more complex and challenging to synthesize. Consequently, the speed with which products need to be driven through clinical development is increasing. The other major trend is for quality, which is often taken for granted in the industry, but no longer seems to be standard given that many high-profile issues are emerging. Product and service providers need to excel in all these areas to meet customer needs effectively.



Antoine Bordet,  
Johnson Matthey  
Fine Chemicals

**What do you think has been driving these trends?**

**A. Bordet:** There is a movement towards providing better solutions to smaller patient populations, through orphan therapies, precision medicine, companion diagnostics and ultimately the personalization of treatments. This has resulted in innovations that require more refined and advanced technical solutions and the emergence of much more complex small molecules. Product volumes are decreasing as products become more potent and the once clear boundaries between primary manufacture, pre-formulation and secondary manufacture have become increasingly blurred.

Quality is also a critical factor; 10 to 15 years ago there was a belief that outsourcing could be achieved at a much lower cost without compromising on quality, but this has not





turned out to be sustainable. Our industry works hard to deliver the best value we can for customers, but this can never be done whilst compromising product quality and ultimately patient safety.

*Recent research by PWC suggests that chemical companies plan to invest 5 percent of annual revenue on digitalization over the next 5 years. What benefits do you think digitalization could have for the industry and more specifically for Johnson Matthey?*

*A. Bordet:* Certainly, we envisage data and digitalization playing an increasing role in our industry. The way this has transformed chemical process development through techniques such as design of experiments (DoE) is a good illustration. Future innovations such as continuous processing will be heavily dependent upon digitalization, and collecting and processing information in real time to manage quality and productivity. These advances will over time begin to impact areas such as logistics, customer management and most likely every aspect of operations.

*Brexit could cloud the economic outlook in the UK. Does Johnson Matthey anticipate any specific effects of it on the company?*

*A. Bordet:* Brexit will obviously affect our business to some extent and we are monitoring the process very carefully. With that said, Johnson Matthey is a global company with fine chemical operations in the UK, US, China and India, and we are confident in being able

*“Brexit will affect our business to some extent and we are monitoring the process very carefully.”*

to manage such changes when they occur. We are celebrating our 200<sup>th</sup> anniversary this year and have seen many developments over the past two centuries, where we have managed to adapt well to changing markets.

*Do you think acquisitions/mergers are a crucial success factor for fine chemical companies? What other factors do you think are important?*

*A. Bordet:* At Johnson Matthey, we do not consider M&A as an activity in its own right, rather as a means to an end. We consider customer needs and attractive markets and then look at how best we can address these needs. For example, we can acquire

*Do you have any predictions on what trends will affect the fine chemicals industry in the future?*

*A. Bordet:* We believe that outsourcing will continue to increase over the coming years with pharma companies

requires service providers to consider the breadth and scope of their offerings. With such a highly fragmented industry we are likely to see further consolidation. New pharmaceuticals being developed are becoming more complex and more potent, which will continue to present new challenges to the types of facility and technologies that are needed to support customers. There will also be continued pressures to make healthcare more affordable and accessible both in established and emerging markets.

Overall these are very positive trends for the continued development of new and effective medication, and for the fine chemicals industry's role in supporting pharmaceutical companies by providing value-adding products and services that enable cost effective healthcare.

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capable companies that enable our customers' progress and complement our strategic vision, as we have done on several occasions in recent years such as the Pharmorphix solid state business. To summarize, we look for M&A with sound strategic rationale.

*How is your division able to address the needs and challenges that you have been discussing?*

*A. Bordet:* We continue to develop broad offerings to fully engage across the small molecule process development and commercialization value chain. These offerings are underpinned through differentiating technologies and capabilities, and are supported by our global assets base. Overall we remain geographically and technically aligned to our customers and are focused on helping them to get their complex therapies to market effectively and then providing reliable commercial supplies.

*Johnson Matthey is celebrating its 200th anniversary this year. What does that mean for the Fine Chemicals division?*

*A. Bordet:* Two hundred years is a fantastic milestone for any company. Within the division we can celebrate some amazing achievements. For example, one of our businesses produced the active ingredient that was used in the first ever pharmaceutical administered by injection, in 1854. Today our customers still benefit from our advanced technical expertise and commitments to quality and manufacturing.

focusing their efforts on new drug innovations and marketing. This bodes well for contract manufacturing. However, as the trend continues this

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## Janssen Gains Access to PeptiDream's Technology

Janssen Pharmaceuticals has entered into a collaboration with Japanese biopharma PeptiDream. The deal, which gives Janssen access to PeptiDream's peptide discovery platform system (PDPS), could be worth up to \$1.15 billion for the Tokyo-based company.

The proprietary technology will be used to identify macrocyclic/constrained peptides against multiple metabolic and cardiovascular targets chosen by Janssen, which will then be optimized into therapeutic peptides or small molecule products. The US group also has an option on peptide-drug conjugate (PDC) use and applications.

Janssen has the rights to develop and commercialize all compounds resulting from the partnership. In

return, PeptiDream will receive an upfront undisclosed sum, research funding and various milestone payments that could potentially total up to \$1.15 billion. It is also eligible to receive royalties on sales of any products that make it to market.

PeptiDream's CEO and president, Kiichi Kubota, said the company has greatly expanded its capabilities over the past few years and looks forward to working with Janssen to discover and develop the next generation of first-in-class and best-in-class therapeutics.

Over the past 7 years, PeptiDream has established discovery collaborations with several major pharma companies. (eb, rk)

## Lilly to Invest \$850 Million in US Operations

US drugmaker Eli Lilly has announced plans to invest \$850 million in its US operations during 2017. Lilly's new CEO, David A. Ricks, said the money will fund projects that are already underway as well as new projects planned to be initiated throughout the course of the year. The company is "on a path to launch 20 new products in a 10-year time frame," he added.

Specifically, the plans call for "massive investment" in diabetes products manufacturing. From 2012 to 2016, Lilly spent some \$1.1 billion to boost this franchise, including upgrades to existing facilities and the addition of new capacity and capabilities. Investments in the re-

cent past included upgrades to existing facilities as well as the addition of new capacity and capabilities and an expansion of its US manufacturing workforce by more than 1,000, the company said.

The manufacturing expansion, along with the introduction of several other new treatments over the last two and a half years, will allow Lilly to continue to be a leader in diabetes care, said Enrique Conterno, president, Lilly Diabetes and Lilly USA. He said spending is being driven by demand for the company's products, as well as its "robust pipeline" of potential medicines in development targeting cancer, pain, diabetes and other unmet medical needs. (dw, rk)

## Codexis in Protein R&D Pact with Tate & Lyle

Codexis has signed a second multi-year supply deal with multinational food ingredients company Tate & Lyle to supply a proprietary enzyme. The deal strengthens the previous agreement that was signed last December.

This latest pact sees Codexis apply its CodeEvolver protein engineering platform technology to research and develop novel enzymes in support of Tate & Lyle's new food ingredients. Under the terms of the agreement, Codexis will receive a payment from Tate & Lyle during the second quarter for enzyme technology improvements that the US firm had previously developed independently. Codexis will also be eligible to receive certain R&D service fees and milestone payments over the

next two to three years. "This agreement also highlights our strategy to enhance shareholder returns by developing novel protein technology on our own account and subsequently using that de-risked technology as a base to create enhanced customer partnerships. We successfully employed this strategy here with Tate & Lyle and are poised to do so similarly with our diagnostics enzymes and novel biotherapeutics pipeline," said John Nicols, president and CEO of Codexis.

Michael Harrison, SVP of new product development at Tate & Lyle, added that the two companies had developed a highly productive technical partnership over the past four years. (eb, rk)

## Astellas Pays €800 Million for Ogeda

Japan's Astellas Pharma has agreed to buy privately held Belgian drug developer Ogeda in a transaction worth up to €800 million. The acquisition expands the Tokyo-headquartered group's late-stage pipeline and is expected to contribute to its mid-to-long term growth.

Formerly named Euroscreen, Ogeda is a clinical-stage drug discovery company that discovers and develops small molecule drugs targeting G-protein coupled receptors (GPCRs). Its lead investigational candidate is fezolinetant, a proprietary, oral, small molecule that is currently being developed to treat menopause-related vasomotor symptoms (MR-VMS). A selective NK3 receptor antagonist, the

drug acts on specific neurons that control body temperature to directly address the basis for hot flashes in menopausal women. Positive data from a Phase 2a study was released in January 2017 showing that 80 menopausal women suffering from MR-VMS saw a significant improvement when they took fezolinetant compared to those taking the placebo.

Under the terms of the deal, Astellas will make an initial payment of €500 million for 100% of Ogeda's equity on completion. Ogeda shareholders are also eligible to receive another €300 million when certain clinical development and regulatory milestones for fezolinetant are achieved. (eb, rk)

## BP/DuPont JV Buys Nesika Energy

A joint venture between BP and DuPont has bought US biofuels company Nesika Energy for an undisclosed sum. The deal includes Nesika's ethanol facility in Scandia, Kansas, USA.

Butamax Advanced Biofuels, owned 50% each by BP and DuPont, will now start detailed engineering work to add bio-isobutanol capacity to the Kansas plant, which will continue to produce ethanol both before and after the project is completed. Investment costs and capacity details were not disclosed.

The addition of bio-isobutanol is the next step in Butamax's plans to commercialize the renewable material. It can be used to increase the renewable content of gasoline and as

a lower carbon alternative to fossil-based isobutanol in chemical applications.

"The Nesika facility will serve to demonstrate our technology at scale as well as validate process and biocatalyst improvements. Our plan is to broadly license our technology, and Nesika and the technology deployed at the site will play a key role in that activity," said Stuart Thomas, CEO of Butamax.

Once the Kansas plant has the capability to produce bio-isobutanol, it will be used as a demonstration facility for potential licensees to see the technology in operation as well as serve as a proving ground for future developments. (eb, rk)

## Quaker Chemical to Merge with Houghton

US chemicals and fluids companies Quaker Chemical and Houghton International are to merge, creating a world leader in the metalworking and primary metals industries.

Under a definitive agreement, shareholders of Houghton International will receive \$172.5 million in cash and a 24.5% stake in the new entity, which represents around 4.3 million shares of newly issued Quaker Chemical stock. In addition, Quaker Chemical will assume Houghton's net debt of about \$690 million as at year-end 2016. The companies have similar-sized revenues, with Quaker posting sales of \$747 million in 2016 while Houghton's totalled \$767 million.

The deal has been approved by both company's board of directors, with full support from the Hinduja Group, which will become Quaker Chemical's largest shareholder. Hinduja is an Indian conglomerate that holds more than 95% of Houghton's equity.

Quaker Chemical has secured financing of \$1.15 billion from Bank of America Merrill Lynch and Deutsche Bank Securities to support the transaction, which includes \$200 million of additional liquidity for future needs.

Michael Barry, chairman and CEO of Quaker Chemical, said the proposed deal combines two highly complementary businesses. (eb, rk)





## Lanxess Expands Global Pigments Capacity

Germany's Lanxess is expanding its global production of synthetic iron oxide pigments in order to keep up with increasing demand, particularly in the paints and coatings industry.

In Krefeld-Uerdingen, current capacity of 280,000 t/y for red and black pigments will rise gradually by about 23,000 t/y by 2019. In addition, Lanxess will modernize its site in Porto Feliz, Brazil, adding another 2,000 t/y of yellow pigment capacity. The projects will take total global production from 375,000 t/y to 400,000 t/y.

"The purpose of these investments is to support the growth of our customers," said Jörg Hellwig, head of the inorganic pigments business. Lanxess expects global demand to rise by an

average of 3% per year beyond 2018, driven by strong growth in countries such as India and the ongoing recovery of the building industry in North America and parts of Europe. Demand growth in China is also expected

to remain at a high level. "By 2025, we expect global annual growth in the demand for iron oxide to reach an average of 4%. We believe in particular that the demand for high-quality pigments with uniform global standards

will increase," Hellwig stated. China is the world's largest producer of synthetic iron oxides but the number of plants in the country has been halved since 2008 as the industry enforces environmental regulations. (eb, rk)

## Evonik in Thai Sugar Substitute Project

German chemical company Evonik is collaborating with Thailand's Rajburi Sugar to produce sugar substitute isomalt. The partners have opened a demonstration plant at Ratchaburi, Thailand, using an improved high-yield process that Evonik has patented.

By streamlining conventional isomalt production technology, researchers at Creavis, the German company's strategic innovation unit, have managed to reduce the number of process steps and use biotechnology to increase the yield. Ulrich Küsthardt, Evonik's chief innovation officer, said: "The new approach is the result of our ability to innovate and collaborate. Creavis initiated a successful project that required the unit to work closely with experts from Evonik's operational segments and our Thai partner. The new demonstration plant is a further stepping stone toward establishing a new line of business based on advanced food ingredients."

Total investment costs in the facility, which is said to be the first in Asia to make isomalt, are in the "low single-digit million euro" range, according to Evonik. Output from the plant will be marketed in Southeast Asia under the brand name Risumalt, mostly for use in food and dietary supplements. Christian Kullmann, deputy chairman of Evonik's executive board, who is designated to become CEO following the annual general meeting in May, said Southeast Asia is an important growth market for the company, and the sugar substitute has considerable potential. (eb, rk)

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# A Difficult Path Ahead

## After the Final REACH Deadline Has Passed Some Specialty Chemicals Could Vanish from the Market

*It is nearly 10 years since Europe's chemical legislation REACH was established. The regulation — described as the most complex in the EU's history — came into effect on Jun. 1, 2007 with implementation split into three phases. Now the third and final phase deadline of May 31, 2018 is looming.*

This last phase governs low-volume registrations, requiring companies to register if they manufacture or import chemicals in quantities of less than 100 t/y. As a result, many specialty chemicals will need registering for the first time and experts estimate that the total number of registrations in this phase could be three to 10 times greater than the number of substances registered in the previous two stages combined.

To put this into figures, the European Chemicals Agency (ECHA) — the administration authority for REACH — predicts that between 25,000 and 50,000 substances will be registered, which would mean that 40,000 to 70,000 dossiers will require reviewing. According to US compliance ma-

agement company Euphor, 25,000 dossiers were submitted in the first phase and just 9,400 dossiers in phase two.

More substance registrations inevitably mean that more testing will be required. However, anecdotal evidence from laboratories and contract research organizations (CROs) reveals that availability is already limited at a time when demand is set to rise because of the high number of small-volume registrants and their increasing reliance on external services.

### Dangers Facing the Industry

Phase three registrants are facing several challenges. Because of the small

volumes involved, the chemicals that are affected are likely to have less existing data available and, given that many specialty chemicals are included for the first time in this phase, many companies that manufacture or import have little or no experience in preparing for REACH registration. Indeed, the proportion of small- and medium-sized enterprises (SMEs) affected by the 2018 deadline is much higher than in previous REACH phases.

“The main challenge for SMEs is the costs related to registration, especially if they need to become lead registrants,” says Carlos Miguel Fazendeiro, director regulatory affairs & regional head Portugal at German consultancy REACH ChemAdvice. He highlights too the lack of knowledge at small companies as another concern and says service providers have seen a rise in requests from SMEs needing registration support as most of them do not know where to start.

The areas where SMEs need help, explains Fazendeiro, include defining the type of registration and tes-

ting that is required, performing risk assessments and preparing chemical safety reports as well as assistance in using IT tools such as REACH-IT, Chesar and IUCLID.

The particular danger facing the specialty chemicals industry is the possibility that, once the deadline has passed, a number of substances will vanish from the market. “It is very likely that a large number of chemicals will disappear from the market as many companies, especially SMEs, will not finally register some substances due to the costs of registration, particularly in cases where the margin is not high and difficulties in obtaining financing do not allow them to continue,” Fazendeiro notes. He adds this will also affect formulators as they may be unable to source the ingredients they need after Jun. 1, 2018. “In such cases, the only option will be for these companies to import from outside the EU and register themselves,” says Fazendeiro.

One German consultant says many mixtures and compounds used in the



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global antimony market had not been registered as of early 2017 because of the lack of critical mass to form a Substance Information Exchange Forum (SIEF). As a result, he is predicting there will very likely be shortages in specialist applications, such as electronics.

### Registration Delays on Purpose?

In a white paper published in November 2016, UK-based CRO Envigo says some companies may be purposefully choosing to delay their registration programs as long as possible. This could, it notes, be due to a variety of factors including a lack of knowledge or resources to get started or assume the role of lead registrant.

Alternatively, a delay could be for business reasons, such as uncertainty around the commercial viability of a particular chemical. The organization says companies that are not currently marketing their chemical in the EU

and have no plans to do so before the 2018 deadline may be unwilling to incur the expense of committing to co-registration before having full knowledge of the concluded toxicity.

In addition, given the low margins for some chemicals, Envigo says it would not be surprising to see some companies opting to continue selling their product up until the 2018 deadline and then simply waiting to see what happens at a later date. Smaller

*"It is very likely that a large number of chemicals will disappear from the market."*

Carlos Miguel Fazendeiro,  
REACH ChemAdvice

companies may also be lying in wait, expecting a flux of larger companies to initiate the process, at which point they could join forces to split costs, it notes.

The CRO warns, however, that although having co-registrants can ease the burden, other challenges can arise including the need for complex legal agreements and cost-sharing mechanisms as well as audit-proof financial accounts that need to be created and paid for, often before receiving any fiscal contribution from other pre-registrants. "Unlike the other phases, phase 3 is clearly lacking when it comes to companies taking a proactive role in registration," Envigo says.

The potential loss of business and how to maintain some chemicals on the market for longer was also the focus of a two-day meeting in March 2017 between the European Association of Craft, Small and Medium-sized Enterprises (UEAPME) and ECHA. Speaking at the event, UEAPME president Ulrike Rabmer-Koller said: "Already now, many companies may start to think about giving up their business because of too high regulatory burdens. This is why small companies especially need as much

support as possible in this crucial phase." Rabmer-Koller urged that more must be done for SMEs in relation to chemical legislation. "Once REACH registration has ended, the game is not over. For example, REACH authorization is an even more resource intensive process. We simply need more hands-on possibilities for financial support," she said at the meeting.

Fazendeiro says those companies that seize the opportunity to register and become one of the few suppliers of a specific chemical may well see an uptick in demand after the 2018 deadline.

While the outlook after the 2018 deadline is unclear as to whether certain chemicals will be available or not, what is clear is that time to register is running out. Smart and speedy planning will help, but the risks of missing the deadline are high, whether by accident or design.

Elaine Burrigge, CHEManager

## CEFIC Identifies Ways to Improve REACH

The EU's chemicals legislation REACH — in force for ten years and now undergoing its second review — is functioning relatively well, but there is room for improvement, Erwin Annys, director of chemicals policy at the European Chemistry Council (CEFIC), said in a speech to the recent Global Business Summit held in Amsterdam and organized by the British trade publication Chemical Watch.

CEFIC has identified four areas the European Commission should look at carefully in order to help „reduce the burden“ for industry, Annys said. Foremost, he mentioned helping SMEs with the 2018 registration deadline. While saying the industry is „grateful“ for what the REACH administration authority ECHA is do-

ing, he stressed there are the 28 national helpdesks where companies can get additional help in their own language.

Weighing in on the evaluation process, the CEFIC policy chief said European chemical producers believe the Commission and ECHA need to "reflect further on cost sharing," especially as some companies are not willing to pay for the required tests. Furthermore, the authorization process needs to be improved in particular for the broader group of process chemicals, so that the same results can be obtained more easily. On the whole, the industry association would like to see the process streamlined and low-volume authorization applications simplified. (dw, rk)

## Transatlantic Deal Simplifies Pharma Inspections

Regulators in the EU and the US have signed a transatlantic agreement to recognize inspections of manufacturing sites for human medicines carried out in their respective countries. The agreement follows "robust" evidence that systems in the EU and US have comparable regulatory and procedural frameworks for inspecting manufacturers.

Under the deal, regulators on both sides of the Atlantic will now rely on each other's inspections in their own territories to ensure that sites' operations are compliant with good manufacturing practices (GMP). In future, the need for an EU authority to inspect a site in the US, or vice versa, will be limited to exceptional circumstances. (eb, rk)

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# China's Investors Advance

By Investing Overseas China Seeks to Gain Access to Technology, Expertise and Innovation

*Chinese outbound foreign investment continues to beat records year by year. The Asian powerhouse is investing in overseas markets to acquire advanced technology, know-how and brands to take back to China.*

According to PricewaterhouseCoopers (PWC), 2016 was another record year. China's outbound mergers & acquisitions (M&A) surged by 142% in volume and by 246% in value to reach a record of \$221 billion, more in one year than the previous four years combined and three and a half times the previous high in 2015.

In total, PWC says there were 51 outbound transactions that were worth more than \$1 billion, which is more than double the previous record. This includes the pending \$43 billion purchase of Syngenta by state-owned enterprise ChemChina, which is the largest transaction ever to be announced by a Chinese buyer.

## ChemChina's Growth Path

The acquisition, which represents an increasing desire by Chinese corporations to secure strategic assets, is vital for the country's food availability issues and development, and would strengthen ChemChina's agricultural portfolio, says Bocconi Students Investment Club (BSIC), part of Italy's Bocconi University. Although China has more than 20% of the world's population, it has less than 10% of the earth's arable land.

The deal would also enable Syngenta to continue its growth strategy and expand in emerging markets, particularly China, and keep the Swiss group as one of the world's largest agrochemical companies even after the Dow/DuPont merger, notes BSIC.

At the time of writing, not only the USA and China but also the EU had given the green light to the deal as the portfolio has few crucial overlaps in the European market. The companies had offered concessions in January 2017 to secure clearance from antitrust authorities. Divestments

from Syngenta's businesses in Europe are expected, along with small divestments from some units in the US. Syngenta CEO Erik Fyrwald was hopeful in mid-February that the deal would close in the first half of 2017.

ChemChina has a track record of overseas acquisitions. In 2006, these included Adisseo Group, a French

*"China could overtake the US and become the world's leading investor by 2023."*

animal nutrition feed firm that specializes in producing methionine, vitamins and biological enzymes and Australian polyethylene producer Qenos Holding. These were followed in 2007 with Rhodia Global Silicone, then in 2011 with Norwegian silicon business Elkem and Israeli fertilizer producer Makhteshim Agan. Last year, ChemChina acquired the world's fifth largest tire manufacturer, Italy's Pirelli, for around \$7.9 billion.

## Lianhetech steps into Europe

A much smaller transaction, but no doubt still significant for the parties concerned, was the acquisition of UK-based chemical manufacturer Fine Industries by Lianhe Chemical Technology (Lianhetech) for around £103 million, giving the Chinese life sciences company its first base in Europe. The deal was agreed in February 2017.

Located in northeast England, Fine Industries develops and manufactures complex intermediates and actives for the agrochemical and pharmaceutical industries, as well as specialty chemicals. It was previously part of Germany's Evonik (and its predecessor Degussa), and was formed in 2008 as a result of a management buy-out. The company was then acquired in 2013 by UK-based private equity firm NorthEdge Capital.

Lianhetech's acquisition includes Fine Organics, which performs custom and toll manufacture of chemicals for the crop protection, pharmaceutical and specialty chemical markets; Fine Contract Research, which focuses on synthetic chemistry; and Fine Environmental Services, which markets hazardous liquid waste treatment services by thermal oxidation. The UK group has annual sales of more than \$60 million, of which about 30% are said to go to North America and 20% to South America.

## Focus on Europe

According to the report Chinese Investment Trends in Europe 2016-2017 published by the China Europe Club at Spanish institute Escola Superior d'Administració i Direcció d'Empreses (ESADE), Europe is the primary destination for Chinese foreign investment after Asia. "The attraction of Europe for Chinese companies is clear: political and macroeconomic stability; a predictable, transparent investment environment; 500 million potential consumers with high purchasing power; highly qualified workers and executives; and industrial companies that can help to increase technological capacity and innovation," says Ivana Casaburi,







ESADE professor and director of the ESADE China Europe Club.

According to ESADE's analysis, China could overtake the US and become the world's leading investor by 2023. In terms of investment flows, it was the world's third largest investor in 2015, outranked only by the US and Japan.

Casaburi says the large-scale investment and innovation programs entered into and implemented by the EU and China in the last two years complement each other in ways that should strengthen the links between

the two regions and stimulate Chinese investment in Europe over the coming years.

Specifically, this includes Horizon 2020, also known as the 8<sup>th</sup> Framework Program, which could help encourage Chinese investment in Europe. The budget for this initiative is €80 billion to be invested in the period 2014-2020. According to Casaburi, China has already played a prominent role as financier and executor of projects under the 7<sup>th</sup> Framework Program (2007-2013) and was invited to actively take part in the R&D

projects included in Horizon 2020. China and the EU have a co-financing mechanism in place for the purpose of conducting joint research projects.

*“Europe is the primary destination for Chinese foreign investment after Asia.”*

Casaburi notes that the really interesting factor about Horizon 2020 is that it dovetails nicely with

China's interests. The initiative is designed to contribute to shifting European corporate agendas to new sectors and activities that will add value, with the aim for industry to made advances in sectors such as green technologies, biotechnology and nanotechnology, precisely the areas that Chinese investors are interested in. These, she says, will be the types of assets that Chinese companies will be seeking in Europe in the coming years.

*Elaine Burridge, CHEManager*

## China's Wanhua Plans MDI Complex in Louisiana

China's Wanhua Chemical has announced it will build a \$1.12 billion isocyanates complex in the US state of Louisiana, benefiting from a \$4.3 million infrastructure grant from the state's economic development arm and access to cheap shale gas-derived feedstock. The Chinese group is also expected to leverage the state's Industrial Tax Exemption, which exempts manufacturers from paying local property taxes for up to 10 years.

Wanhua, regarded as world's largest producer of MDI, plans to invest \$954 million in the facility, with unnamed project partners contributing \$166 million. A decision on where to build is expected to come later this year. Capacities have not been dis-

closed. The company said one of its reasons for selecting Louisiana was the deep-water transportation provided by the Mississippi River.

The US state's economic development secretary, Don Pierson, said he expects additional Chinese investment, including more projects by Wanhua and Yuhuang. “I think that we have every reason to believe that we'll see more investment from China. I think it's in compliance with what the (Trump) administration is trying to encourage: made in America,” Pierson told the New Orleans newspaper Times-Picayune. “Projects like this help our trade balance, producing commodities they own and likely ship back to their markets,” he said. (dw, rk)

## Saudi Aramco/SABIC Sign MoUs with Chinese Firms

Saudi Aramco and SABIC have signed Memorandums of Understanding (MoUs) to develop refining and chemical plants in China. The deals were done during a visit by Saudi Arabia's King Salman to Beijing on Mar. 16, when he oversaw the signing of agreements potentially worth as much as \$65 billion. The visit was part of a month-long tour of Asia to promote investment opportunities in the kingdom.

In total, Saudi and Chinese companies signed 21 deals that ranged from exploring investments in oil and petrochemical plants to e-commerce and cooperating in renewable energy markets.

The MoU between state oil giant Saudi Aramco and China North Industries Group (Norinco) is designed to

enable further strategic cooperation and downstream investment opportunities in China, including the development of a refinery and chemical plants. Aramco also signed an MoU with Nanjing, Jiangsu-headquartered Aerosun for manufacturing reinforced thermoplastic pipe and components as well as R&D activities.

Saudi Aramco said the potential investments fit with its strategy to expand its refining and chemicals portfolio in a bid to diversify assets and secure long-term agreements for its oil.

SABIC and Sinopec will study opportunities for multiple joint projects to boost China's One Belt, One Road (OBOR) initiative and Saudi's Vision 2030 plan. (eb, rk)





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# A New Type of Personalization

## Will Bioelectronics Be the Next Biologics to Transform Medicine?

*Bioelectronic technologies for modulating the signaling capabilities of the nervous system could pose challenges for producers of medicinal materials and chemicals — but also for regulators.*

The commercialization of bioelectronics has been hailed as the next stage in the growing domination of biologics in medicines. The market launch of the first major bioelectronic products may be as long as 10 years away but already leading pharmaceutical companies have started work on their development using as a platform R&D breakthroughs by top universities and research institutes.

### Technology of Bioelectronics

Around 30 years after biopharmaceuticals started making inroads into a global drugs market monopolized by small molecules, bioelectronics could be poised to provide strong competition to both chemicals and existing

biological medicines. Bioelectronic medicines are fundamentally different because they are combinations of devices and drugs and in some cases may not be considered to be pharmaceuticals at all.

They are applied through micro-sized devices to neural pathways to diagnose, monitor and treat diseases. They can stimulate, block or otherwise modulate nerve activity by being implanted on a nerve or located on the skin. By being able to change specific nerve behavior, they can alter functions in organs and modify or cure diseases without the complicated side effects of pharmaceuticals.

Bioelectronic devices have already been tested successfully to treat inflammatory diseases such as rheumatoid arthritis and Crohn's disease. They have the potential to treat a wide range of other conditions, including diseases such as cancers and chronic conditions like diabetes and asthma. Some will be able to combine diagnosis and treatment by detecting irregular nerve signals and then correcting them.

Bioelectronics will open up new opportunities for producers of medicinal materials and chemicals. The big-

gest demand could be for conductive polymers, especially organic ones, with a high degree of biocompatibility. Also there will be a big need for chemicals and biologicals which can provide functional surface interfaces with nerve cells.

### Meeting the Requirements of Individual Patients

In addition to advancing the reach of biologics, bioelectronics will introduce a new type of personalized medicine with its products being customized to meet the requirements of individual patients. Like other personalized therapies — such as gene therapy and cell tissue engineering — bioelectronics production may be decentralized with manufacturing taking place at sites close to hospitals specializing in the technology.

On the other hand, the amount of personalization could be constrained by pressure to bring down costs through the high-volume manufacture of devices and their components. One solution could be the standardization of polymers and other basic materials while customization would

be achieved through modifications to the surface cell-interacting substances. Another is the predominant use of organic polymers and surface additives with both being tuned to the characteristics of the nerve cells.

Bioelectronics have moved close to the forefront of medicine as a result of the lengthy accumulation of knowledge of bioelectricity in animals and humans since the Italian physicist and biologist Luigi Galvani discovered in 1780 that the legs of a dead frog could be made to twitch by applying a small voltage. It gradually became clear that all the human body's organs are influenced by its nervous system via patterns of electrical impulses which run along the nerve fibers. Abnormalities in the impulse patterns — or the complete absence of them — cause disease and incapacities.

With the emergence of microelectronics, key advances in the development of bioelectronics for diagnosing and treating disease were made in the 1990s. A big impetus behind the current surge in interest in bioelectronics has been research work linking inflammatory diseases like rheumatoid arthritis with signaling patterns from the brain.





## Nerve-Modulating Opportunities

The leading figure in the research has been Dr. Kevin Tracey of the Feinstein Institute in New York who discovered around 15 years ago the inflammatory reflex, a neural circuit between the brain and the vagus nerve regulating the immune system.

The cell signaling protein tumor necrosis factor (TNF) involved in systemic inflammation is, for example, controlled through impulses from the brain along the vagus nerve to the body's central organs. Tracey also found that electrical signals from the brain can also trigger vagus nerve endings to produce acetylcholine, a signaling chemical, which can instruct white blood cells to stop making TNF.

These discoveries have presented opportunities for using nerve-modulating devices to replace drugs, some with severe side effects, for treating autoimmune diseases like rheumatoid arthritis.

UK-based GlaxoSmithKline (GSK) was the first of the Big Pharma companies to start exploring in 2012 the potential for managing nerve-signaling processes through bioelectronic medicines. It invested \$50 million in US venture capital companies specializing in bioelectronics and was soon financing over 30 academic research projects across the world. Last year it set up a \$715 million joint venture, called appropriately Galvani Bioelectronics, with Verily Life Sciences, part

of Google, to develop bioelectronic treatments for diseases like arthritis, asthma and diabetes.

Other leading pharmaceutical companies which have moved into research in bioelectronic diagnostics and treatments include Johnson & Johnson, Novartis, Sanofi and Abbott Laboratories. At the same time relatively large R&D funds have been channeled into bioelectronic research projects in universities and institutes in North America and Europe.

## Developing More Effective Materials

In the US the Obama administration launched four years ago BRAIN initiative for Brain Research through Advancing Innovative Neurotechnologies. A lot of the current research in North America and Europe is focused on achieving greater understanding of the mechanisms and pathways behind signaling in neural circuits. Another priority is the development of more effective materials and chemicals for controlling nerve impulses.

Many of the micro devices and their components used currently in bioelectronics are based on equipment applied in other sectors, like environmental care, energy, agriculture, food and even consumer products. Their materials and surface substances are being found to be unsuitable for applications inside the human body.

Indium-tin oxide (ITO), for example, a conductor used in solar cells, sensors and electronic displays, has been considered by researchers to be inappropriate for bioelectronic devices because of its brittleness, need for high-temperature processing and limited transparency. As a result it is being replaced by materials like graphene, which is regarded as more adaptable to neural interfacing requirements.

The need for materials with effective neural interfacing properties is a big influence on the development

*"Some bioelectronic devices will be able to combine diagnosis and treatment."*

of bioelectronic conductive polymers as alternatives to conventional, established materials like silicon and organic polymers such as polydimethylsiloxane (PDMS), poly 3,4-ethylenedioxythiophene (PEDOT) and combinations like PEDOT and polystyrene sulphonic acid (PEDOT:PSS).

Some scientists favor silicon because of its great conductivity and durability. But there is a growing group of researchers who reckon that the future of bioelectronics lies with organic polymers because their inherent biocompatibility can be extended to create a wide range of neural interfacing structures and functions.

"This combination of structural and functional flexibility makes (organic polymers) especially well suited to applications in the medical field since it allows precise modelling of various attributes of cells and human tissues," says Professor Agneta Richter-Dahlfors of the neuroscience department of Sweden's Karolinska Institute.

Just how quickly the first bioelectronic products come to market will depend a lot on the regulators, whose first task is to decide whether they should be legally classified as primarily devices or drugs. In the European Union, for example, the classification will dictate what quality, safety and efficacy standards have to be demonstrated by developers, with the requirements being stricter for drugs than devices.

Under EU law, a product is considered to be a drug if it is administered "with a view to modifying physiological functions by exerting a pharmacological, immunological or metabolic action, or to making a medical diagnosis." Many bioelectronic products would be regarded as having those characteristics. Once bioelectronic treatments are categorized as drugs they could face lengthy clinical trials because they will have to be assessed on the basis of end-points, which are rarely applied in the current clinical trials system.

*Sean Milmo, CHEManager*

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# The Greening of the Chemical Value Chain

## Market Potential and Competitiveness of Fermentation-based Chemicals in North-West Europe



point and biorefineries at the core. The industrial application of biotechnology will not only broaden the range of raw materials used as the principal input for chemical production but also generate products and materials with new properties and applications. The required infrastructure to bridge the existing gaps between the agricultural and the chemical industry and business communities, while significant, is manageable.

### Where Agri Meets Chemicals

*Global competition in the chemical market has been intensifying the past decade. Although low crude oil prices have given the European chemical industry some breathing space recently, the abundance of shale gas in the US, oil and gas in the Middle East and coal in China mean Europe is under increasing pressure to find new ways to create a sustainable competitive advantage. The key to future success lies in innovation and new strategic partnerships.*

An outstanding opportunity exists in the creation of new value chains with biobased feedstocks as the starting

#### Agri Meets Chemicals

This article summarizes a full-length report that continues to attract attention since its initial publication at the end of 2014. It also gives an outlook on a follow-up project and platform recently launched at the AmC conference — [www.AgriMeetsChemicals.com](http://www.AgriMeetsChemicals.com).

An in-depth analysis, published by Deloitte and sponsored by Rabobank among others, on the cost competitiveness of sugar from sugar beet in North West Europe, shows that biobased feedstocks can help Europe participate in this emerging segment and regain its competitive edge.

An excellent opportunity for improving the competitive position of North-West Europe lies in increasing the applications of industrial biotechnology and biobased feedstock for the fermentation-based chemical industry. This opportunity spans the entire value chain, from seed to new functional molecules with new properties. Current examples at opposite ends of this value chain include the potential of the “Energybeet”, developed by the seed producer KWS, and the additional properties of Avantium’s technology for producing polyethylene-furanoate (PEF) for Coca Cola’s PlantBottle replacing the conventional PET bottle.

In the broader economic context, a remarkable development is the ratio between the prices for crude oil and white sugar. Before the turn of the millennium, the ratio between Brent Crude and London’s No 5 contract for white sugar, both in \$/GJ, hovered around 7. However, soaring oil prices and low sugar prices in 2000 led to the ratio plummeting to about 3. The ratio continued to decline gradually until early 2015 when oil pri-

ces, due to unique measures of the producing counties, dropped to historic levels.

Climate change, its impact and uncertainties have produced another relevant development. Major global brand-owners of consumer products, such as Ikea, Lavazza, Lego and Unilever, are pushing harder for sustainability in their product portfolio, end-to-end value chains and consumer brand marketing.

### The Potential of Fermentation-based Chemical Products and Materials

The fermentation-based industry, already worth over \$127 billion in 2013, processes 200–250 million t of carbohydrate equivalents (CHEQ) annually from either sugars, starches or cellulosic origins, including finished products such as production grade white sugar and intermediates such as thick juice and cane juice. By far the largest share goes to bioethanol — 94% in terms of volume and 87% in terms of value. However, functional molecules, including plastics, provide a much higher economic value and market growth in the biobased chemical segment compared to alcohols and biogas. The projected annual growth until 2020, excluding alcohols, is 6.5%, which is well-above projected GDP growth.

Next to its relatively ease of production, the key driver for the importance of bioethanol are the significant supplements to fossil fuels for the transportation sector. Various regulatory measures in the US, Brazil and Europe stimulated the growth.

Other key fermentation products with sufficient market potential (i.e. excluding bioethanol) equate to roughly 11.6 million t of CHEQ and have a gross margin potential of \$17.1 billion. These include amino acids, organic acids such as lactic and succinic acid, as well as polymers such as xanthan.

### Sugar Can Compete against Fossil Alternatives

The attractiveness of the fermentation based-chemical industry depends



Dr. Willem Vaessen,  
Deloitte Consulting

on the price levels of the functional molecules as chemical products, the fossil-based alternatives with which they compete, the yield of fermentation processes and the market prices for biobased feedstocks.

Sugar, a major biobased feedstock, comes either directly from cane or beet or indirectly from corn or tapioca starch, and it can be competitive against fossil alternatives for selected high-value-added products. Globally, four main regions emerge as attractive locations for fermentation businesses, each with a different feedstock:

- Brazil: sugar cane
- US: corn
- South-East Asia: tapioca/cassava and sugar cane
- North-West Europe: wheat and sugar beets

The cost levels of sugar in North-West Europe are amongst the lowest in the world due to increasing crop and sugar yields in the fields and from production efficiencies. Although exchange rates and weather conditions are also relevant, the analysis of the underlying drivers show the relative cost position is likely to improve further in the coming years. The global supply-cost curve for the 2012/2013 season illustrates the impact of efficiency improvements (see figure).

Sugar beet from North-West Europe appears to be particularly cost competitive due to low inbound and outbound transportation costs, high sugar yields per hectare of land, large-scale facilities and the ability to supply ample volumes of thick sugar juice on a year-round basis.





## Market overview for key fermentation products in 2013 and annual growth projection until 2020

Category	Market Size in product output (quantity produced)	Average theoretical yield	Market size in carbohydrate input required	Market size in value	Average added value generated from carbohydrate	Market growth until 2020	Arable land use*
	MIn ton	Ton product / ton glucose	MIn ton CHEQ	Bn USD	USD / CHEQ	% CAGR	MIn ha
Alcohols	99.8	0.51	195.1	110	164	4.4%	25.08
Amino Acids	7.1	0.92	7.8	11.0	1,010	5.6%	1.00
Organic Acids	2.9	1.05	2.8	3.5	850	8.8%	0.36
Biogas	0.1	0.27	0.5	0.2	0	5.0%	0.06
Polymers	0.2	0.93	0.2	0.6	2,600	13.5%	0.03
Vitamins	0.2	0.96	0.2	0.7	3,100	2.6%	0.03
Antibiotics	0.2	1.00	0.2	0.8	3,600	4.0%	0.03
Industrial Enzymes	0.1	1.00	0.1	0.3	2,600	8.0%	0.01
<b>Total</b>	<b>110.5</b>		<b>206.8</b>	<b>127.0</b>		<b>4.6%</b>	

### Dispelling the Myth Surrounding European White Sugar

A recent EC report on industrial white sugar shines an interesting light on the wrong perception that European prices exceed world market prices. The facts are:

- EU prices were higher than the world market prices before 2009, leading companies to invest elsewhere
- EU prices were below London No 5 white sugars between 2009 and 2012
- EU prices for non-food sugars converged to world market levels in 2013

Furthermore, the EU will be lifting production quotas for food-grade sugar in 2017. Deregulation means the production volume of sugar beets sales will grow substantially. It also entails production shifts to the most efficient growing areas in Europe.

### Overcoming Investment Hurdles

Legislators and other stakeholders need to jump some hurdles to create a level playing field. The most relevant of these is the set of measures that stimulates the use of biomass for biofuels. These measures discourage investment in European facilities that produce high value-added biobased materials because they limit access to biomass for other uses and increase net costs. The unintentional consequence is the advantage given to fossil-based alternatives.

The report shows that it is worthwhile taking on these challenges. The biotechnological (r)evolution has the potential to stimulate innovation, economic growth and create jobs. The convergence of the chemical and agricultural eco-system and the biotechnological know-how in North-West Europe make for a prime location.

### A Golden Opportunity

The fermentation platform is where "agri meets chemicals": It bridges the gap between the two and thereby unlocks an attractive opportunity for both important sectors. Key is innovation in biotechnology and biorefineries, which requires new partnerships between the agricultural and chemical sectors.

The worlds of agriculture and chemicals have never been closer. Economics, technology and sustainability are driving the two together. As a result collaboration is becoming more and more important: it increases competitiveness and enables sustainable growth; it enables organizations to innovate, remove boundaries, transform and develop new products.

The chemical industry in Europe is within reach of a golden opportunity for sustainable growth. Ongoing innovation and further investments in the production of biobased materials and chemical building blocks form the core of a strategy to regain its competitive edge. The chemical industry has a key role to play in this transition towards the biobased economy. The greening of global brand

owners and consumers buying their products is one of the megatrends driving this. Stimulated by new solutions and functional properties, the shift towards the biobased economy will accelerate.

*Dr. Willem Vaessen, director Chemical Value Chain, Deloitte Consulting, Amsterdam, The Netherlands*

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# A Paradigm Shift

## Can Micro-Reaction Technology and Flow Chemistry Replace Batch Processes?

The notion of transforming process engineering production from the batch principle to continuous flow processes based on micro- and milli-reactors may not always be so easy for production staff to accept — even though in many cases it would offer great advantages. Adopted by the pharmaceutical industry in recent years, the technology platform offers potential in many respects, but although the technology as such is not at issue it experiences acceptance problems. A CHEManager round table on micro- and milli-reactors as a technology platform attended by industry experts discussed chances and obstacles of microsystem technology.



CHEManager asked experts in microsystem technology to join a round table discussion. From left to right: Marc Winter, Corning Advanced-Flow Reactors; Dr. Stephane Varray, Lonza; Dr. Andreas Brodhagen, BASF; Dr. Volker Oestreich, CHE-Manager; Roland Guidat, Corning Advanced-Flow Reactors; Dr. Roland Richter, 3M Technical Ceramics; Dr. Bernhard Hettich, CHT; Anne Kaaden, Ehrfeld Mikrotechnik BTS; Dr. Stefan Brand, Clariant; Christoph Höver, BAM Apparatebau; Dr. Carmine Raffa and Dr. Joachim Heck, both Ehrfeld Mikrotechnik BTS.

You can call it flow chemistry or micro-reaction technology (MRT) — both terms describe a technology with enormous advantages for many pro-

cesses. The characteristic performance features of micrometer-scale laboratory apparatus must correspond to those of millimeter-scale equipment.

batch reactor use very difficult or even impossible, the characteristics of continuous flow reactors offer clear benefits. Nevertheless, MRT has yet to gain popularity; the CHE-Manager roundtable was convened to examine the background and reasons.

the right production strategy. Positive experience of the technology has been countered by a lack of acceptance, and in some cases, individual companies have not been aware of its advantages. “The technology as such is not at issue here; we can handle MRT, but we have acceptance problems. We have built two pilot systems and have experience from the laboratory scale up to production scale.”

A similar statement was made by Dr. Stefan Brand, head of Process Innovation at Clariant in Frankfurt, who



**We can handle MRT technology, but we have acceptance problems.**

Dr. Andreas Brodhagen, BASF

cess engineering applications. MRT replaces discontinuous batch processes with a continuous method in which reactions take place in extremely miniaturized structures. The main components are the mixer, with extremely good mixing efficiency, and a heat exchanger with a very high transfer of heat. These are supplemented with an infrastructure, e.g. filters, sensors, valves, pumps, and analysis devices.

Transfer from a laboratory scale — i.e. from micrometer to millimeter scale — can be carried out more simply than with established technolo-

The advantages of continuous operation in micro- and milli-reactors include:

- Ultra-fast mixing
- Highly efficient heat transfer
- Short defined dwell times
- Simple process control due to low system inertia
- High operational reliability due to minimum hold-up
- Short development times

Especially with respect to rapid, explosive, toxic or highly exothermic reactions, whose safety risks make

### Technology Has Arrived in Practice

Dr. Andreas Brodhagen, senior manager of Process Development at



**Flow Production does exist and work. Europe needs to step in.**

Roland Guidat, Corning Advanced-Flow Reactors

BASF in Ludwigshafen, emphasized that micro- and milli-reactors offer potential if they are integrated into a suitable production concept and

praised the specific improvements in MRT over the past 15 years. In specialist chemistry, the transition from batch to continuous is of interest, e.g.





to exploit new production processes which are not possible with normal batch methods. “We are working

sion for one or the other is still often made according to traditional ways of thinking.”



### *Production costs are positively influenced by MRT.*

Dr. Bernhard Hettich, CHT

with external partners for the development of MRT processes to speed up production rates, but we also have our own product which is based on MRT. Flow chemistry, batch-to-conti and MRT — where the “M” stands for micro and milli — are important topics in the field of special chemistry,” noted Brand, who also pointed out the necessity of presenting the unique features of MRT in the fields of research and production.

Dr. Bernhard Hettich, managing director and COO at Tübingen’s CHT — a global group of companies for specialty chemicals — was even more optimistic. Hettich calls

### *Different Dynamics in China and Europe*

Even though the flow-reactor and MRT manufacturers represented at the round table could point to many successes and individual applications of the conti technology platform, they complained almost unanimously about the clear regional differences currently seen in the dynamics of its implementation. “The technology platform is clearly taking off in China. Will the European chemical and pharmaceutical industry be able to jump on this bandwagon, or will China gain technological leadership?” asked



### *The way to establish MRT is via global reference projects.*

Dr. Joachim Heck, Ehrfeld Mikrotechnik BTS

himself a fan and promoter of MRT, which CHT uses in both in the laboratory and production. His experience of the technology is mostly positive, especially regarding cost: “Throughput, quality, less waste, higher yield, shorter reaction times — ultimately, these are all production costs which can be positively influenced by MRT. We now know that costs are lower — especially if you compare costs on the basis of planning on a green-meadow site. This also includes the fact that the plant has to be put into a building — for which MRT also has advanta-

Dr. Joachim Heck, Managing Director of Ehrfeld Mikrotechnik BTS in Wendelsheim. Last year the company supplied a Miprowa production reactor for the Chinese medical ingredient manufacturer Shaoxing Eastlake Biochemical for a production capacity of up to 10,000 t/y; the system was successfully commissioned in September 2016. The continuous operation millireactor is used for a strongly exothermic alkoxylation reaction and replaces more than 20 batch reactors. In the decision for MRT, achievable product qualities, significantly improved yields,



### *Successful flow reactors are available — a change of mindset is now called for.*

Dr. Roland Richter, 3M Technical Ceramics

ges in terms of facility size.” Hettich conceded, “Batch and conti are equivalent processes with clear advantages and disadvantages, but the deci-

safety aspects and rapid return on investment played a significant role.

Roland Guidat, chief reactor engineer at Corning Advanced-Flow Reactors

in Avon, not far from Paris, put it in a nutshell: “Europe is deliberating, China is creating the new industry.” Nevertheless, Guidat referred to new installations, especially in European pharmaceutical production, in which MRT has generated enormous advantages in comparison with conventional batch methods. In the production of a medicinal substance (API, Active Pharmaceutical Ingredient) the yield could be doubled, purity increased from 95% to 99%, and operating temperature increased from  $-70^{\circ}\text{C}$  to  $-35^{\circ}\text{C}$ . Ten kilograms of API were produced in seven weeks in a cGMP installation which was audited by the

challenge for the specialist chemicals and the pharmaceutical industry. Dr. Stéphane Varray, associate director of Pharma & Biotech at Lonza in Visp, Switzerland, made a provocative statement about special requirements — especially in the pharmaceutical industry: “The pharmaceutical industry needs disruptive solutions for producing new API.” The established production of API is under considerable pressure due to regulations, costs, quality, safety and time-to-market. On the road to a new generation of chemical production, process intensification is of great importance for Lonza. Here, MRT offers new op-



### *R&D in the pharmaceutical industry has realized that MRT is a new tool.*

Marc Winter, Corning Advanced-Flow Reactors

FDA. With this example, Guidat demonstrated the general advantages of MRT: rapid, thorough mixing results with less by-products, higher selectivity and therefore increased yield and higher product quality. In addition, the excellent heat exchange makes reactions more controllable.

Dr. Roland Richter, head of Sales and Marketing for 3M Technical Ceramics in Kempten, also considered the different implementation dynamics in China and Europe. “The technology is there and Asia is taking off, but Europe is still waiting.” 3M uses silicon carbide as the material for MRT.

opportunities which need to be utilized more intensively.

This was confirmed by Christoph Höver, managing director of BAM Apparatebau in Kürten: “MRT has great potential, but this potential cannot be exploited without the courage to take a decision.” Höver asserted that MRT is a niche and specialty product, but one which has great advantages, including low energy consumption and rapid implementation from laboratory to production scale. As potential users often lack empirical values for MRT — such values are common in conventional companies — the risks



### *MRT offers a unique possibility of exploiting new process windows.*

Dr. Stefan Brand, Clariant

For a long time now, silicon carbide has been used in the pump industry for bearings and seals, and this substance has proved effective. It is also FDA approved. Richter is convinced: “I do not see any problems from the point of view of risks — the material is widely used in pumps in the pharmaceutical and food industry.”

are often overestimated. Höver sees the implementation and public documentation of a demonstration project as one way to overcome these reservations.

To speed the change from batch to conti in appropriate processes, Brand called for the suppliers of flow technology to make the technical advantages such as yield and purity more apparent, and provide assistance for the evaluation of CAPEX and OPEX. Both sides know that this is not a simple matter: “Presenting proof of financial gains from the technology means that you have to lay your cards on the table, and often this is not possible due to

### *Batch to Conti – Disruptive Solutions*

The moving of product portfolios from mass production to customer-oriented specialties presents a chal-

confidentiality obligations”, said Richter. Brand confirmed that this remains a challenge, most notably for special processes, and proposed that the initial focus should be on published manufacturing costs for standard processes. In

### With Acceptance into the Future

The participants unanimously agreed that MRT enables rapid development of selected chemical processes, and



*Flow chemistry will enable the molecule of the future.*

Dr. Stephane Varray, Lonza

addition, new and innovative products could be interesting, but these also increase the importance of confidentiality agreements.

### Success Factor is Basic Knowledge

Marc Winter, senior application engineer at Corning Advanced-Flow Reactors in Avon, pointed out that many chemists and process technologists lack knowledge about MRT

as Brodhagen said: “The technology as such is not at issue here; we can handle MRT, but we have acceptance problems.” The technology platform offers potential in many respects:

- It is used as a laboratory tool, for both efficient development of new molecules and associated synthesis methods
- It offers production facilities new methods for optimization, which all significantly reduce costs — from energy savings and higher yields to more attractive product quality



*MRT has great potential – but without the courage to take a decision for the conti process, this cannot be used.*

Christoph Höver, BAM Apparatebau

and flow chemistry. A basic reason can be found in education, as the typical production tool of a trainee chemist is a batch reactor in the form of a test tube. In general, the participants in the discussion agreed that the field production engineering must be strengthened, in the training of engineers and the introduction of MRT and flow chemistry in university courses. Alternative mindsets should also be more strongly promoted through in-house continuing education programs.

- It is an excellent basis for molecularization and an enabling factor for the Internet of Things (IoT) or Industry 4.0.

In recent years, the micro- and millireactor technology platform has been intensively adopted by the pharmaceutical industry — and perhaps this indicates the start of a great future for MRT and flow chemistry in Europe.

Dr. Volker Oestreich, CHEManager  
www.ehrfeld.com

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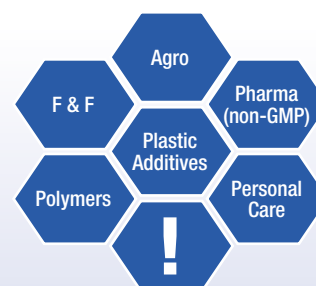
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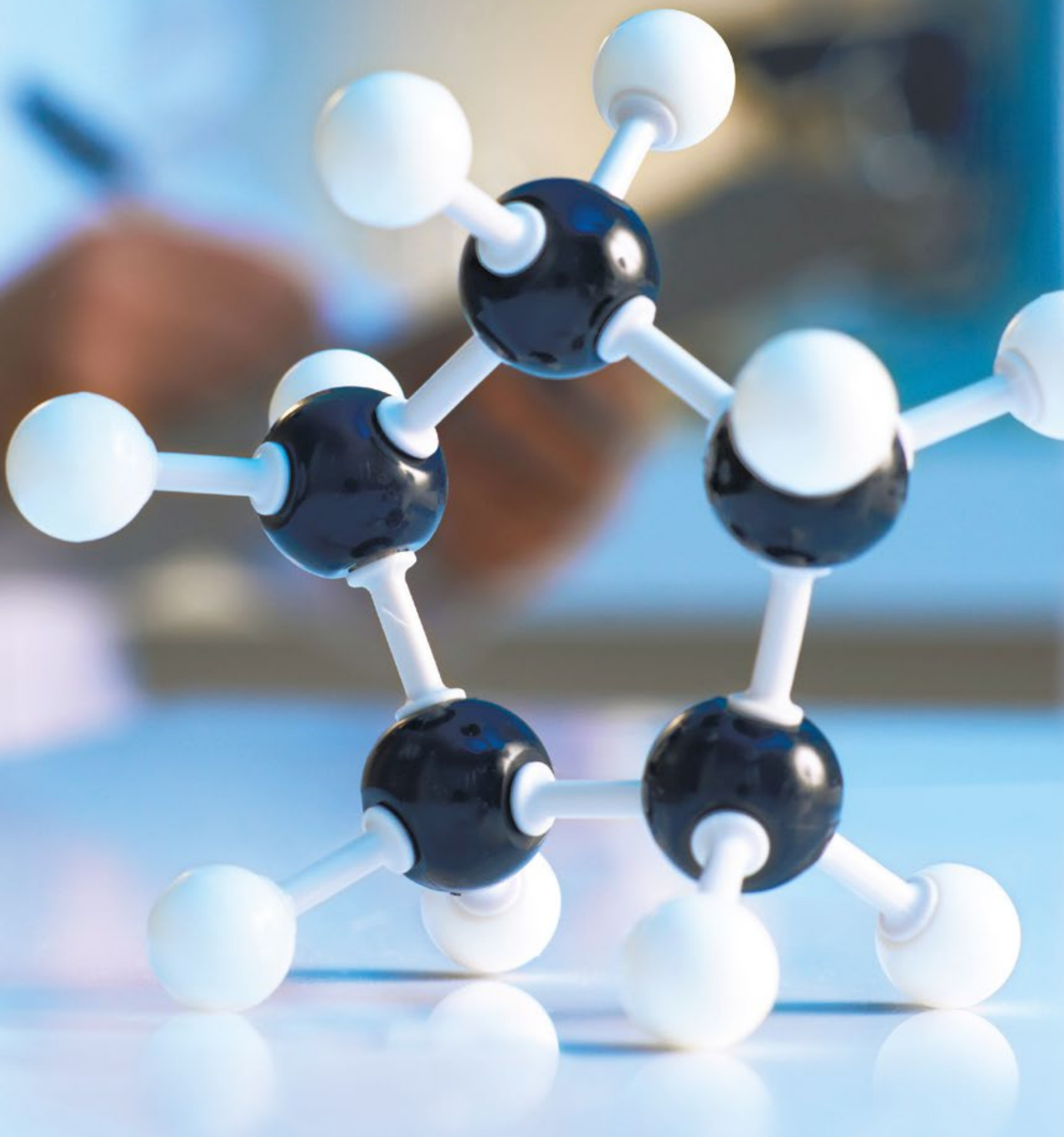


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