FINE & SPECIALTY CHEMICALS

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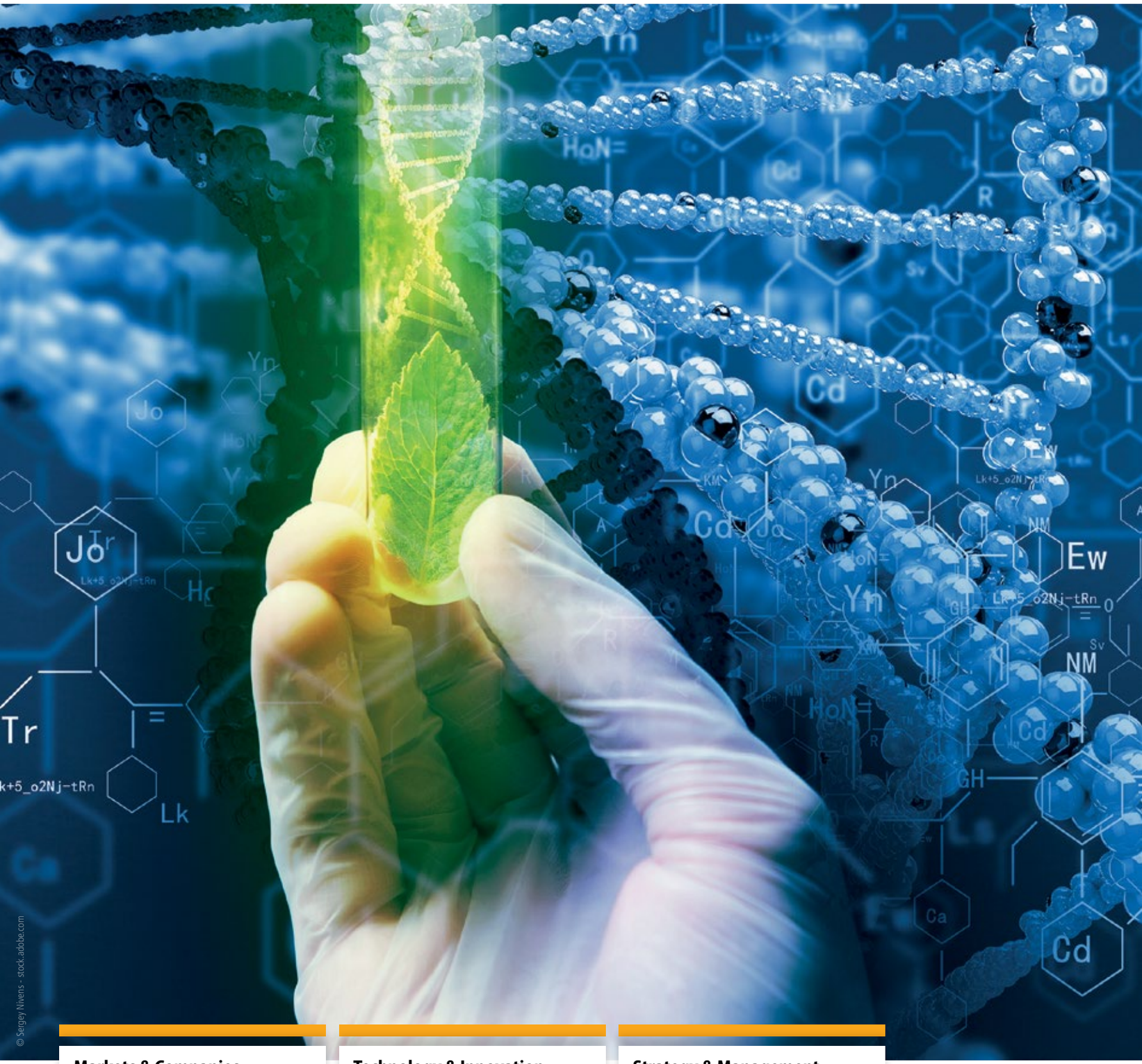

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Markets & Companies
Challenges for Growth in the European Chemical Industry, Final REACh Deadline, 2017 M&A Review, News & Opinions

Technology & Innovation
How to Tap the Full Potential of Biotechnology, Green Materials, Sustainable Chemical Production, Statements on Green Chemistry

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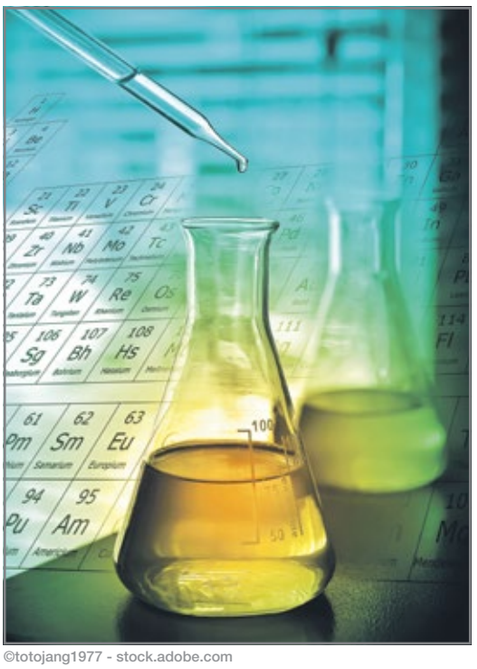

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Chemicals & Distribution

"Uncertainty in the Supply Chain Will Persist"

CEFIC's REACh Director Erwin Annys about the Chemicals Regulation in Europe

The European chemicals regulation REACh — the registration, evaluation, authorization and restriction of chemicals — not only aims to improve the protection of human health and the environment. Put into force in 2007, it also aims to enhance innovation and competitiveness of the EU chemicals industry. Eleven years into REACh and with the last registration deadline of May 31, 2018, but also the Brexit on the horizon, the European Commission has recently published the results of the second review of REACh. Michael Reubold asked Erwin Annys, REACh director of the European Chemical Industry Council CEFIC, about the status quo and the future of chemicals regulation in Europe.

CHEManager: Mr. Annys, a bit more than a decade since the launch of REACh, the final registration deadline is looming on the horizon for Europe's chemical companies. From June 1, 2018, only substances that have a valid registration — or are exempted from REACh — will be allowed on the EU market. Do you fear any substance shortages?

Erwin Annys: The message sent by our companies and national chemical industry associations are clear: they are working hard to get the job done in time, but they feel comfortable that the substances they want to keep on the market and those they are purchasing to make their products will be registered in time. As chemical industry we feel comfortable that we will make it. The predicted number of substances for the 2010 and 2013 deadline turned out to be fairly accurate, but the number of substances that will be registered by May 2018 will probably deviate from the 2003 estimates.

Downstream users are more concerned as they don't always know which substances are used in the mixtures they import. They are much more uncertain and don't have the confirmation that all mixtures and substances will still be on the market. This uncertainty is probably related as well to the fact that many substances and mixtures are imported from outside the EU and they fear last minute announcements that the imports will stop because foreign producers are not able to comply with REACh.

May 31 — the point of no return — is that it? Or do you expect ECHA to allow any extension period? What happens, for instance, if registration dossiers have been submitted but are incomplete?

E. Annys: There is no possibility to extend the deadline for the last registration deadline, and an extension will not solve the problem. Uncertainty in the supply chain as to whether particular imported substances will still be on the market will persist.

It is important to realize that these issues are discussed in the so called Directors' Contact Group, consisting of ECHA, The European Commission and European industry associations covering all concerned sectors. Just as in 2010 and 2013, the group is developing recommendations on how to handle last minute surprises and how to act in case substances and mixtures are no longer available.

What advice do you have today — if it is not too late — to help companies register successfully?

E. Annys: For 2018 registrants — concentrate on the work to be done: register. And for importers, list the substances and mixtures for which you don't have a confirmation yet and contact your suppliers to get the latest update. If they tell you now that it will not be available anymore, you still have time to change supplier or register as an importer yourself.

What happens after successfully registering all substances affected by REACh? Can manufacturers and their customers lean back then?

E. Annys: It has always been clear but is now even clearer after the publication of the REACh Review [by the European Commission on March 5, 2018] that May 2018 is absolutely not the end of the journey. The evaluation of existing dossiers and regulatory risk management will continue as the Commission wants improve the implementation. The focus on improving supply chain communication and communication on articles is also clearly mentioned in the REACh Review, which is closely linked to the alignment between REACh and Circular Economy Action Plan, where this kind of communication will become more important

Erwin Annys, REACh director, CEFIC

How is REACh affecting chemical innovation? Is there a risk that manufacturers develop new substances which could be prohibited in certain applications?

E. Annys: The legislation is clear on what are substances of very high concern, although you can never be 100% sure. Many innovative companies are using predictive methods — like QSARs and the CEFIC LRI Ambit project — to have a good idea about potential toxicity and eco-toxicity. Hence a general prohibition is less likely, but in certain application is possible. Industry has realized as well that the time needed for a harmonized classification or for identification as SVHC is clearly shorter compared to the past, which makes the early screening even more necessary.

Looking past REACh, how can Europe's legislative framework for chemical management be strengthened over the coming decades?

E. Annys: This will be done via a continued improved implementation of REACh, going hand in hand with enforcement. Many of the issues already covered by REACh are as well repeated and further explored under the 7th Environmental Action

Programme. The REACh Review, and we expect even more of it in the Fitness check on chemicals legislation excluding REACh, will lead to a more holistic approach to chemicals legislation in the European Union. The interactions between the various legislative frameworks will augment and the REACh information will be used for decision making in other Regulations and Directives related to chemicals.

As chemical industry, we believe that this should happen in a transparent way giving the industry an opportunity to contribute as this is done under REACh. A major challenge will be the evolution of science, covering much more complex endpoints than under the previous legislations. Thus, we will need much more joint scientific events involving industry, academia and authorities and integrate the results of this collaboration into regulatory risk management.

"May 2018 is absolutely not the end of the journey."

The 2018 registration deadline of REACh is not the only incision or caesura looming for Europe. The Brexit is also on the horizon. How can REACh be implemented into UK law? Will the copy-and-paste approach do?

E. Annys: CEFIC is in favor of the highest regulatory consistency between the EU and the UK after Brexit or the UK establishing its own regulatory regime similar to REACh, if they are not joining the REACh world. In fact the potential problems are not limited to REACh, but we have to find solutions as well for plant protection products, biocides, pharmaceuticals etc. CEFIC supports an approach of grandfathering, allowing a continued use of already registered substances without restrictive actions. What has been approved before Brexit via registrations and authorizations — depending on the specific terminology of the different legislations — should freely remain on the UK and EU market after Brexit. It is important to realize that a hard Brexit will not only have serious consequences for the UK, but also companies in EU Member States who have actively trade with the UK-based companies.

How do you see the future of REACh — or chemicals policy and trade in Europe — in a post-Brexit world?

E. Annys: The future of chemicals policy in the EU is already quite well fixed in the REACh Review and the Fitness checks and that will not be influenced by Brexit. The UK authorities and their agencies are presently very active in the EU decision making regarding chemicals. However, the EU negotiating guidelines for the future trade relationship with the UK exclude UK participation in EU agencies. This would mean that other authorities will have to take up that additional work and that will be very challenging, also in view of the Commission willing to further speed up. UK companies exporting to the EU obviously would need to meet REACh requirements.

www.cefic.org

Getting the Investment Mix Right

What European Chemicals Companies Should Do to Boost Growth

In both the specialty and chemicals segments, companies can spur growth by yield optimization, capacity expansions with longer-term focus and new business models along the entire value chain, investment in core business — and a more risk-taking investment mindset.

As emerging market rivals continue to gain market share from their European counterparts, chemicals companies in Europe need to sufficiently target all opportunities for growth that exist, such as new growth models, including circularity, and increased investment in their core business.

In the decade before 2016, European chemicals companies lost 4% in market share due to declining production capacities, and, at the same time, they have generated free cashflows at record levels, but have under-invested compared to their global peers.

In our view, European chemical companies are at risk of so-called "compressive disruption," or a slow decrease in absolute profits and market relevance, due to their investment patterns — and their mindset.

For instance, European companies often anticipate a payback on fresh investment in about eight years, while those in emerging markets like China, India or the Middle East, may be willing to wait 10 to 15 years for a return.

Similarly, many European companies focus on cash optimization, and they calculate with an asset lifecycle of 30 to 50 years. This leaves plants built in the 1960s still in operation, even though companies have strong cash reserves that could be invested. As a result, some companies should push for growth to avoid becoming candidates for takeover.

Compare this to the approach of emerging-market competitors who produce with newer and often world-scale plants. These players also tend to set ambitious growth targets, such as doubling capacity in a decade or building regional and even global positions.

For these reasons, European companies need to find the right mix of investment in new growth models, such as circularity, and in the core business; the where and the how will depend on the segment and the growth model.

Bernd Elser, Accenture Strategy

Eike Christian Eschenröder, Accenture Strategy

Specialty Chemicals — Ideas for Growth

In general, we see a potential for European companies to invest in capacity expansion, but for specialty chemicals, we see more potential for short to mid-term growth from chemical process optimization and innovation. Even increases in yield and/or small decreases in input costs can boost margins further. It comes down to the all-time classic growth approach of production optimization, which can be achieved in standard ways, such as process stabilization, optimization of operating points, lowering energy and other costs, or in less-standard ways, for instance with complete process redesign. All in all, we see significant opportunity to narrow the gap between best daily production and average production yields, which can range from 94 to 96% for continuous chemical processes.

Other specialty companies are embracing circular models by positioning themselves for more relevance in downstream applications, such as applications that make cars more lightweight and therefore more fuel efficient. Another example is materials that make cars more durable, for instance for car-sharing companies that expect substantial wear and tear on their vehicles.

Circularity in Specialty Chemicals

In the chemicals industry, we see two primary ways to apply circular economy business models. Like the examples described above, the first is enabling circular models in downstream applications. The second is recirculating actual molecules. Both are, in part, driven by regulatory and consumer pressure to reduce impact on the environment.

We see strong potential for growth from circular models and have even gone so far as to say that enabling circular models in downstream industries is the single most important growth opportunity for the chemicals industry in the years to come. But we stress that the impact will be starkly different on each market niche.

As indicated in the figure, enabling downstream applications will mean an increased need for specialized polymers, for instance in the automotive industry, as well as higher demand for high-performance specialty construction chemicals, including foams for insulation. Such chemicals will be needed in greater quantities for more energy efficient building.

In agrochemicals, however, we see circularity models potentially having the opposite impact on growth for specialty chemicals: When molecules can be recirculated, for instance when more phosphates can be recovered, demand will decline. Or, when reduced food waste and higher food utilization by large producers takes place downstream, demand for agrochemicals will stagnate or even decline.

Given the differing impacts, companies must face the challenge of finding — and investing in — the right circular niche.

To visualize opportunities, to better analyze the trends and to find niches to explore, it's important to think in terms of the entire value chain. Co-creation events are one possible format for fostering discussion with internal and external experts who represent the value chain. Bringing a company's own salespeople, startups, and academia into such exercises can deepen the inquiry as well.

Potential for growth from circular models in different chemical segments

	Circulating molecules	Enabling circulation in downstream applications
Basic chemicals	↓ High degree of circularity due to wide use	→ Limited "specialized" applications/ requirements
Intermediates	↘ Various applications/ uses for circulated materials	→ Limited change in diverse downstream use
Polymers	↘ Increased pressure to reuse polymers	↑ Increased need for specialized polymers (e.g. automotive)
Agrochemicals	↘ Increasing phosphate recovery	↘ Reduced food waste / increased food utilization
Construction chemicals	→ Currently limited possibilities for circulation	↗ Higher demand for high-performance specialties (e.g. insolations)

Demand development: ↓ significant decrease; ↘ moderate decrease; → limited impact; ↗ moderate increase; ↑ significant increase
Source: Accenture Analysis

Commodities — Growth Scenarios

In the commodities segment, the market continues to be driven by supply — demand balance and price. Many commodities seem to experience a peak in terms of profitability — a favorable supply-demand balance, faster than expected demand growth and selected outages and force majeures contributed to an expansion of profit margins.

Here companies in established markets need a clear mindset change about time horizons. As mentioned before, emerging market players often accept longer payback periods for their investments. Since established players are hesitant to wait out longer horizons, they often don't invest at all. It's a question of risk profiles. Generally speaking, established companies are more risk-averse in their investments close to home and in beneficial environments.

Our recommendation to European chemicals companies is to assess whether moving closer to the risk profiles of companies in emerging markets makes sense, even though doing so means standing up to shareholder short-termism. Companies will have to re-evaluate investment decisions and prioritize those that can have a strong impact from a global perspective, even if such decisions ruffle feathers on a local basis or require a re-think of resources committed to the pursuit of new molecules.

We understand European companies face many internal barriers, but they have already shown their capacity for change. Previously they adapted their expectations about investment time horizons to make them shorter; now it's time to move in the other direction on that same continuum. We believe it's time for European chemicals companies to step up and take the opportunities for growth that are available to them, even if it takes longer to realize a return.

Over the long-term, these efforts need to be combined with business-model innovation that brings companies closer to their customers so they can become providers of solutions and services, and not just raw materials.

This links back to the idea of circularity. Since many commodity chemicals are solvents, we can imagine chemicals companies as providers of solvents "for rent" that they, in turn, reuse or recycle. Indeed, we estimate that up to 60% of the molecules provided by the European chemical industry to customer industries and end-users can be re-circulated if certain conditions are met. Yes, it's a move away from clearly established chemical uses, but the logic behind solution chemicals is compelling.

All in all, the biggest long-term gains are to be made in the commodity chemicals segment. We strongly encourage European companies to prepare to play out the circularity advantage in both commodity and specialty chemicals over the long-term — while also expanding capacity and innovating processes in specialty chemicals for a faster impact in the short and mid-term.

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References can be requested from the authors.

Along the Acquisition Trail

The Specialty Chemicals Sector is Abuzz with Activity

For the global specialty chemicals sector, the past two years have been among the most exciting of the young millennium. Many mergers and acquisitions were in the spotlight in 2017 and more have moved into it in 2018. The three biggest deals have now been completed, the $130 billion mega merger between US chemical giants Dow Chemical and DuPont, the takeover of Swiss agrochemicals major Syngenta by ChemChina for $43 billion and Bayer's $62.5 billion takeover of Monsanto. Two other transactions with potential to shake up the industry fizzled last year.

The Rocky Road to Mega-mergers

As March 2018 drew to a close, Bayer finally won EU approval for its $62.5 million acquisition of Monsanto. After pledging to sell seeds assets with sales of €1.3 billion to BASF for €5.9 billion to satisfy the European Commission, in a further concession the Leverkusen giant has proposed its former rival in Ludwigshafen as buyer of another asset package, believed to be worth around €1.5 billion. US approval was still out, and some thought Bayer might have to shed more assets. Others thought the EU had already made a clean sweep.

Spectacular deals that will not take place include the proposed takeover of AkzoNobel by US rival PPG and the merger of Clariant and Huntsman. After a protracted battle, the Dutch paints group successfully shook off PPG, which in the last round had offered $26.9 billion. The planned $20 billion fusion of the Swiss and US specialty chemicals producers ran aground on the opposition of an activist investor.

Beyond the "big bucks" transactions, the past 15 months have seen mergers and acquisitions of all sizes in specialty chemicals, agrochemicals and pharmaceuticals.

Specialty Chemicals

Done deals across the entire products spectrum

Germany's Lanxess sealed its purchase of US additives producer Chemtura for $2.5 billion. The buyout was the largest in the history of the company spun off from Bayer in 2004 and floated a year later. Lanxess also completed its acquisition of Solvay's €65 million phosphorus chemicals business, including the US production site at Charleston, South Carolina.

German specialty chemicals producer Altana acquired Solvay's formulated resins business for an undisclosed sum. Solvay had gained the assets with around $20 million in sales as part of its 2015 purchase of Cytec Industries.

US coatings group Axalta acquired Plascoat Systems, a UK-based leading supplier of thermoplastic powder coatings, from parent company International Process Technologies (IPT) for an undisclosed sum.

Axalta also picked up Valspar's North American wood coatings business for $420 million, after Valspar was bought by US market leader

AkzoNobel to Sell Specialty Chemicals for €10.1 Billion

Agreement with The Carlyle Group and GIC Concludes Dual-track Process

By inking an agreement with The Carlyle Group and GIC to take over the Specialty Chemicals business, AkzoNobel reached a key milestone in creating a focused paints and coatings company. On March 27, the Dutch chemical company announced the sale of 100% of its Specialty Chemicals business to The Carlyle Group and GIC for an enterprise value of €10.1 billion. The transaction creates two focused businesses — Paints and Coatings, and Specialty Chemicals — as part of its strategy announced in April 2017. The transaction, which is the outcome of a thorough dual-track process during which the boards of AkzoNobel considered both a legal demerger and a private sale, is expected to be completed before the end of 2018.

AkzoNobel's board of management and the supervisory board concluded that a private sale to The Carlyle Group and GIC is in the best interests of AkzoNobel, Specialty Chemicals and its respective stakeholders, including employees, shareholders and customers.

The Carlyle Group, a global alternative asset manager, has a global presence and the financial capacity to enable the Specialty Chemicals business achieve its full potential. Carlyle has extensive experience investing in chemicals, unlocking long-term potential and creating value in its portfolio companies. As a responsible investor Carlyle is focused on driving growth, job creation and long-term financial success. The firm also has a strong focus on Environmental, Social and Governance (ESG) aspects and building positive working relationships with wider stakeholders (employees, unions and local communities). GIC is a leading global investment firm established in 1981.

Thierry Vanlancker, CEO AkzoNobel, said: „We are very pleased to announce the sale of Specialty Chemicals to The Carlyle Group and GIC. We believe the business is well positioned to capture growth opportunities and further improve performance. Carlyle has significant experience in the chemicals industry and a proven track record when it comes to health, safety, innovation and sustainability."

Werner Fuhrmann, CEO of AkzoNobel Specialty Chemicals, added: „Specialty Chemicals is a strong and profitable business with highly skilled and motivated employees serving our customers every day with essential chemistry. As a focused chemicals company we will concentrate our efforts and resources to accelerate profitable growth. With this transaction, our business has an opportunity to achieve its full potential and we will continue to fulfil the current and future needs of our customers throughout the world."

Martin Sumner and Zeina Bain, Managing Directors at The Carlyle Group, added: „We are pleased to invest in the Specialty Chemicals business and proud to support a business with such a strong heritage. We are committed to growing the business, and building upon its innovation capability, high quality work force and asset base, as well as its world-class sustainability and environmental practices. We look forward to working with the management team to transition the business to a successful independent company." (mr)

Sherwin-Williams. In other coatings deals, AkzoNobel acquired the UK's Flexcrete Technologies and announced plans to buy French manufacturer Disa Technology (Disatech).

DSM of the Netherlands agreed to make an initial investment of $25 million in US industrial bioscience company Amyris, giving it an equity stake of about 12%. DSM also bought Amyris Brasil from Amyris for $58 million.

Israel Chemicals (ICL) agreed to sell its fire safety and oil additives businesses to South Korean private equity firm SK Capital for about $1 billion.

UK specialty chemicals company Croda made a cash offer for compatriot Plant Impact, a crop-enhancement specialist, for about £10 million. The acquisition was due to complete on Mar. 28. Croda also acquired Nautilus Biosciences Canada, a marine biotechnology company. Financial terms were not disclosed.

Belgian chemicals and plastics producer Domo Chemicals took an undisclosed stake in Group Michiels Advanced Materials (Group M.A.M.) as part of a partnership in specialty film coating.

In an all-US deal, Versum, the electronic materials spin-off of US gases producer Air Products, said it would acquire Dynaloy, a supplier of formulated cleaning solutions for the semiconductor industry.

AkzoNobel began negotiations with three or four potential buyers of its Specialty Chemicals division. The company has set an April 2018 deadline to sell or spin off the business employing around 9,000 people and accounting for about a third of its total sales and earnings. Buyers are said to include Dutch pension fund PGGM, private equity groups Carlyle, Bain and Advent.

PPG recently announced plans to buy Dutch wholesaler ProCoatings for an undisclosed sum after failing to buy AkzoNobel. ProCoatings sells a large portfolio of well-known professional paint brands. The deal was expected to close in the first quarter.

Agrochemicals

Many Seeds Sown in the Shadow of the Mega-mergers

In late 2017, Syngenta completed the acquisition of Nidera Seeds, the crop seeds business of Chinese grains trader COFCO International for an undisclosed sum. Nidera is an important player in South America.

Nutrien, formed last year through the merger of Canadian fertilizer giants Agrium and Potash Corp of Saskatchewan (PCS), agreed to acquire Agrichem, one of Brazil's largest fertilizer companies.

Pharmaceuticals

M&A Activity with a Distinct Biotech Focus

In pharmaceuticals, super-dimensioned M&A activity has been somewhat more modest. Many of the transactions have been between players in the biochemicals segment or conventional drugmakers who wanted to enter this sector.

In last year's biggest coup, US healthcare giant Johnson & Johnson scored with Swiss biotechnology firm Actelion, taking the prize for $30 billion after a fierce battle punctuated by a cameo appearance by French drugmaker Sanofi. As part of the agreement, J&J took an initial minority stake of 16% in the research arm spun off to Actelion's management.

US contract manufacturer Catalent agreed to buy contract development and manufacturing organization Cook Pharmica for $950 million, boosting its position in the fast-growing biologics area.

Swiss fine chemicals and biologics producer Lonza acquired Micro-Macinazione, a contract manufacturer providing micronization of active ingredients for the pharmaceutical and fine chemical industries. Lonza also completed its acquisition of Capsugel, paying US private equity investor KKR $5.5 billion for all assets of the US company regarded as one of the leading producers of capsules for delivery of drugs and food supplements.

US biopharmaceutical company Celgene said it would take a stake in China's BeiGene and help develop and commercialize that company's investigational treatment for tumor cancers. Later, BeiGene planned to acquire Celgene's operations in China and also license and assume commercial responsibility for the US company's approved therapies in China.

Fresenius Kabi agreed to acquire the biosimilars arm of Germany's Merck KGaA, which is divesting the business to focus on its pipeline of innovative medicines.

Sanofi announced it would buy Protein Sciences, a privately held vaccines biotechnology company based in Meriden, Connecticut, USA.

US Merck & Co unveiled plans to buy Germany-based Rigontec, a pioneer in accessing the retinoic acid-inducible gene I (RIG-I) pathway as a novel and distinct approach in cancer immunotherapy. A Merck subsidiary was to make an upfront cash payment of €115 million to Rigontec's shareholders, with additional contingent payments of up to €349 million.

Gilead Sciences offered almost $12 billion to acquire compatriot Kite Pharma and gain access to Car-T, Kite's cutting-edge chimeric antigen therapy treatment for cancer. The experimental treatment re-engineers white blood cells to attack cancer.

The UK's largest player, GlaxoSmithKline (GSK), took an additional 26% stake in its Saudi unit, lifting its overall share in Glaxo Saudi Arabia Limited (GSAL) to 75%.

US pharmaceutical giant Pfizer sold its 49% stake in Hisun-Pfizer Pharmaceuticals, its Chinese joint venture with Zhejiang Hisun Pharma. In return, Sapphire I Holdings, indirectly controlled by private equity firm Hillhouse Capital, will acquire Pfizer's shareholding.

Roche announced plans to buy San Diego, California-based US group Ignyta for around $1.7 billion in cash to expand the Swiss group's portfolio of cancer medicines. Ignyta is focused on precision oncology.

Distribution

One of the Most Proactive Sectors in M&A

The past year has been marked by a flood of M&A activity in distribution. German giant Brenntag announced plans to acquire all shares of specialty chemicals distributor Wellstar Enterprises (Hong Kong) and its three Chinese subsidiaries. Brenntag planned to take the majority stake of 51% immediately and the remaining 49% by 2021, operating the business in the interim as a joint venture.

Brenntag also acquired Medellin, Colombia-based Conquimica. The Latin American company mostly provides industrial and specialty chemicals to the coatings, food and cleaning industries and operates four warehouses in Colombia.

US distributor Univar acquired Paulinia, Sao Paolo-based distributor Tagma Brasil for an undisclosed sum, expanding its presence in the agricultural market. Tagma is a leading provider of custom formulation and packaging services for crop protection chemicals, including herbicides, insecticides, fungicides and surfactants.

AMVAC Netherlands, wholly owned by US specialty and agricultural products company American Vanguard, said it intended to acquire Grupo Ag-

ricenter, a Costa Rica-based distributor of crop protection products.

Dutch specialty chemicals distributor IMCD bought Bossco Industries, a supplier of products and technical solutions to all major industrial markets in the US Southwest. It also acquired Canadian and US specialty chemicals and ingredients distributor L.V. Lomas and Italian specialty chemicals distributor Neuvendis.

In Italy, performance additives producer Italmatch Chemicals boosted its presence in Latin America with the purchase of Sudamfos do Brasil, a leading Brazilian distributor specializing in phosphonates, phosphates and other specialty chemicals.

Luxembourg-based Azelis acquired Georges Walther, a family-owned specialty chemicals distributor in Pfäffikon, Switzerland, for an undisclosed sum. Most of the acquired firm's revenue is derived from cosmetic ingredients, essential oils and fragrances. It was Azelis' fourth buy in 2017, after US distributor Ross Organic, Denmark's LCH and Chemcolour, based in Australia and New Zealand.

In March of this year, Azelis agreed to take full ownership of Distralim, a Moroccan distributor of food ingredients. Based in Casablanca, Distralim supplies ingredients for confectionery, biscuits and ice cream as well as several non-food segments.

UK-based 2M Holdings, which comprises several companies active in chemical distribution and related services, acquired German specialty chemicals distributor Franken-Kosmetik-Chemiehandel for an undisclosed sum in February 2018. Based in Nuremberg, the family-owned company primarily serves the personal care, home care and food ingredients markets in Germany, Benelux, Croatia, Macedonia and Slovenia.

Dede Williams and Elaine Burridge, CHEManager

EU Objects to Tronox-Cristal Merger

The European Commission has issued a statement of objections to Tronox regarding its proposed $2.4 billion acquisition of Cristal's titanium dioxide (TiO_2) business. Tronox has to respond to the objections by early April.

"The statement of objections further details and clarifies the commission's position, and receipt of it establishes a defined framework to move forward," said Tronox CEO Jeffry Quinn. "We continue in constructive dialogue, and I am confident we can determine an appropriate and proportionate resolution to any valid concerns of the Commission."

The mining and inorganic chemicals company added that the statement of objections does not prejudge the outcome of the Commission's investigation nor the need to offer any particular remedy. (eb, rk)

Lundbeck to Acquire Prexton Therapeutics

Danish drugmaker Lundbeck has announced plans to buy Swiss drug developer Prexton Therapeutics in a deal worth up to €905 million.

The deal would give Lundbeck global rights to Prexton's foliglurax, a first-in-class experimental therapy for Parkinson's disease that is currently in Phase II trials. First data from the clinical Phase II program is expected to be available in mid-2019.

Foliglurax works by stimulating a specific glutamatergic target that actives a compensatory neuronal system in the brain. The aim is to treat the motor systems of Parkinson's, such as resting tremor and dyskinesia. Lundbeck said pre-clinical studies have demonstrated positive effects in models of the neurological condition, which affects around 6 million people worldwide. (eb, rk)

Ashland Explores Composites/BDO Options

US specialty chemicals company Ashland is exploring strategic alternatives for its composites business as well as its butanediol (BDO) production plant in Marl, Germany, and the related merchant intermediates and solvents products.

The move is part of the company's aim to create a more streamlined operation with a portfolio focused on specialty ingredients.

Ashland said it intends to evaluate all options for the assets, including a potential sale. The company noted, however, that it plans to retain its BDO plant in Lima, Ohio, USA, to ensure consistent supply for the group's internal needs.

The global composites business, which posted sales of $779 million in 2017, makes a range of unsaturated polyester and vinyl ester resins across 14 plants in the US, Brazil, China, Finland, France, Spain and Poland.

Should Ashland decide to sell the assets, it expects to sign an agreement by the end of 2018. The company has retained US investment bank Citi to assist in its strategic review. (eb, rk)

US Clears LyondellBasell's A. Schulman Buy

Petrochemicals giant LyondellBasell has received the go-ahead from the US Federal Trade Commission (FTC) to acquire A. Schulman, a manufacturer of high-performance plastic compounds, composites and powders, for $2.25 billion. The deal is scheduled to close in the second half of this year, subject to approval by Schulman's shareholders and the other required regulatory clearances and approvals.

The Texas-managed chemicals and plastics producer said the FTC has granted early termination of the waiting period under the Hart-Scott-Rodino Antitrust Improvements Act, one of the prerequisites for the transaction to go ahead.

LyondellBasell announced plans to buy A. Schulman in mid-February, after signing a definitive agreement with the Ohio-based compounder.

The petrochemicals group, which is officially headquartered in the Netherlands, said the acquisition will build on its existing platform and create what it called "a premier compounding business with broad geographic reach, leading technologies and a diverse product portfolio." (dw, rk)

Biotechnology Is about to Change Our Lives

Key Enabling Technology for Global Progress in Healthcare, Nutrition, Energy and Material Production

Biotechnology encompasses a broad range of technologies that employ living organisms or parts of them to make diverse products. For example, drugs and therapeutics, nutritional compounds, environmentally friendly chemicals and materials, biofuels, and novel functional materials can be produced through biotechnology. The World Economic Forum's Global Future Council on (the Future of) Biotechnologies — part of the WEF's Network of Global Future Councils — explores how developments in biotechnology could impact industry (especially agriculture, health, chemicals and materials), governments and society in the future. Sang Yup Lee, distinguished professor in the Department of Chemical and Biomolecular Engineering at the Korea Advanced Institute of Science and Technology (KAIST), is a co-chair of the Global Future Council on Biotechnologies. He explained to Ralf Kempf and Michael Reubold the potential of biotechnology to drive progress, solve problems and increase sustainability across all aspects of human life.

CHEManager: Professor Lee, what do you think are the big trends in the field of biotechnology right now?

Sang-Yup Lee: The trends are not very different from what they used to be. However, they are becoming more important in the fourth industrial revolution. There are so many exciting things happening thanks to the rapid advances in biotechnology. Considering the three fields of biotechnology — medical, agricultural and industrial — the big change nowadays is represented by a more sophisticated healthcare system, an agricultural sector that produces enough food and of higher nutritional value, and the sustainable production of materials and chemicals. These three fields will all play increasingly important roles in our everyday life. And, of course, environmental biotechnology is a major trend, because we are generating waste in many different forms and we must treat it in a responsible way. Biotechnology can be employed to degrade toxic or harmful chemicals and agents to solve environmental problems. There are sophisticated technologies being employed to advance biotechnology to levels that we have never seen before.

With technology becoming more sophisticated, can biotechnology help meet the rapidly growing demand for energy, food and healthcare while at the same time making the way we produce and consume products more sustainable?

S.-Y. Lee: Biotechnology could help address many global problems, such as climate change, an aging society, food scarcity, the growing need for energy, and infectious diseases, to name just a few. Because of the rapid development in a lot of the sub-technologies of biotechnology, all sectors are benefiting from this progress. And they are perfectly in agreement with the Fourth Industrial Revolution and the 17 United Nation Sustainable Development Goals. Growing concerns over limited fossil resources and associated environmental problems are motivating the development of sustainable processes to produce chemicals, fuels and materials from renewable non-food resources. Metabolic engineering and synthetic biology are advancing very rapidly. That has led to the production of many chemicals, fuels and materials from renewable biomass, rather than depending on fossil resources. Thus, they have become key enabling technologies for transforming microorganisms into efficient cell factories for these compounds.

> „Biotechnology will become as common as having a cellphone."

Sang Yup Lee, professor, Korea Advanced Institute of Science and Technology (KAIST)

Based on or driven by these developments, how is biotechnology about to change life for people especially?

S.-Y. Lee: Let's start with some numbers. The current average human life expectancy is about 73 years — and it

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is still increasing. There are close to 600 million people who are 65 years and older. Annual healthcare spending around the world in 2018 is expected to be about $8 trillion. As society continues to age, it will be clearly impossible to sustain the present healthcare system with the technologies available today. We must do something!

We are all aware of the social problems of an aging society and challenges associated with diseases like dementia or Alzheimer's disease. We have about 50 million Alzheimer's patients world-wide and every three seconds there is a new dementia patient. If you extrapolate this scenario, we are going to have about 140 million dementia patients worldwide by 2050. How much will that cost? The world economy will collapse because of the aging society. Thus, I think that it becomes more important to prevent diseases. How are we going to ensure that people stay healthier during their longer lifespan? Well, in addition to regular exercise and good health behaviors, nutrition becomes very important. This is where biotechnology should intervene and develop new ways of supplying food that is nutritionally balanced and able to prevent diseases.

Of course, biotechnology has always been delivering drugs for treating diseases, but linking it tightly to medicine, food and nutrition will be its future. And this must happen in the near future. We should act now — otherwise we will be in trouble.

The same applies to sustainable production and consumption. I include consumption for obvious reasons, because it does not make any sense when consumers do not participate. In terms of production, we cannot rely on fossil resources — not only because climate change is one of the biggest problems and a global risk. We should also admit that raw materials are finite natural products. So, for example, fossil oil is currently estimated to last for only another 51 years. Coal and natural gas are expected to last another 150 and 53 years, respectively. Some people argue that we will discover new sources for those raw materials, but the rate of consumption is much higher than the rate at which these raw materials are produced or formed. So, eventually they will run short. How are we going to make all these plastics and others, even though we replaced all the fuels with renewable energies, such as solar and wind? What about the chemicals and materials? No matter how long you look at the sun, it will not give you chemicals and materials. You need to make them. But with what? Obviously, it comes from renewable sources such as non-food biomass and ultimately from carbon dioxide and that's where biotech is already playing important roles but it will play increasingly important roles. We must consider those aspects.

Obviously, we can use fossil oil and natural gas for a much longer period by saving them to produce chemicals and materials, together much lower amount compared with fossil-derived fuels that can be replaced by renewable energy. Nonetheless, it is desirable to produce chemicals and materials from renewables as well to cope with climate change issue.

Do you think that biotechnology has the potential to revolutionize the

raw material base of organic chemistry or can it produce only some platform chemicals?

S.-Y. Lee: Absolutely. So, a lot of them being organic, obviously because raw material is organic, plant biomass, algal biomass, organic waste, and so on; however, it is not restricted to organic substances only. Ultimately, carbon dioxide will be a raw material. We can also produce inorganic products. For example, we have been reporting the results of making metal nanoparticles, using the reversal of the mechanism of metal iron detoxification by microorganisms. Of course, the cases are rare. At least the organic chemicals we use every day, including a lot of polymers, can be addressed by the biotechnology revolution.

But this revolution is not only a scientific or a technical challenge because science and technology, in many cases, are already there. To really make use of all the potential of biotechnology, it also requires some actions from governments, regulatory bodies and the mindset of our society has to change as well.

S.-Y. Lee: Right. Take France as an example: the country has enacted a ban on all plastic dishes, cups, and utensils which goes into effect in 2020. From that date on, all disposable utensils and dishes must be made of bio-based, rather than petroleum-based material. With a regulation like this imposed, the chemical industry cannot survive without changing. In the future, there will be more regulatory initiatives like this and when we have a more diverse portfolio of materials and chemicals, the bio-based chemical industry will blossom. That's the only option left for the existing petrochemicals-based industry.

One of the problems is that fossil raw materials are currently quite cheap, which makes it hard for bio-based materials to compete.

S.-Y. Lee: The reason why fossil raw materials are cheap is because we have been running this petrochemical industry for half a century or more. During that time period, obviously everything has been optimized and, of course, the raw material itself is not expensive either. The combination of that results in a relatively low price for chemicals and materials we use every day. But in the future, these will become scarce or run out eventually. But we need all these materials anyway. As biotechnology is further improving by using a lot of different tools and strategies, including systems metabolic engineering, production costs are being lowered significantly. Not all bio-based products are more expensive than the petrochemical route at this moment either; some are already competitive. But in the future bio-based routes will be the methods of choice — and maybe the only choice left to produce these chemicals.

What do you think are the most common prejudices of people who are sceptic about biotechnology that must be overcome? There are risks to some of the methods but of course the benefits that biotechnology can provide are much larger.

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S.-Y. Lee: The GMO debate is the best example that triggered this kind of public controversy. I think that people who are active in the field of biotechnology did not properly communicate with the public and all the stakeholders.

Just like other emerging technologies, biotechnology offers the potential of enormous benefits but also potential risks, which we cannot predict with absolute certainty. But we must admit the potential risks whenever we find them. All these risks and challenges need to be addressed through dialogues among stakeholders including policy makers, experts, the public, and NGOs to map the risks and solutions. That is one of the things the Global Future Council on Biotechnology is studying by employing diverse expertise of council members — including scientists, engineers, lawyers, regulatory bodies and representatives from civil society — and through dialogues with cross-council members and other stakeholders. We need to ensure safety and security through regulation, but at the same time make sure we do not put unnecessary hurdles in place which slow down progress. The fact that biotechnology is increasingly recognized in society as a technology to improve the quality of life in a sustainable manner is the result of intensive communication efforts.

What would be the next steps science and the industry must take to promote biotechnology processes and to fully realize the potential of bio-production?

S.-Y. Lee: As already discussed, many of the currently available bio-based products are not yet competitive with the petrochemical route. For bio-based chemical production to really take off, it must compete with conventional chemical production on both price and performance. This goal now seems within reach, thanks to advances in systems metabolic engineering, a discipline that tweaks the biochemistry of microbes so that more of their energy and resources go into synthesizing useful chemical products. A lot of different technologies are available to design and improve enzymes. This enables higher conversion efficiency or even different metabolic pathways so that the yield can be increased from the level that found in natural organisms. A lot of effort is being made by many different groups around the world and that will eventually lead to more cost-effective production of a diverse portfolio of chemicals and materials.

> *„Ultimately, carbon dioxide will be a raw material."*

With recent advances in synthetic biology, systems biology, and evolutionary engineering, metabolic engineers are now able to create biological systems that manufacture chemicals that are hard to produce by conventional means — and thus expensive.

The range of chemicals that can be made using metabolic engineering is widening every year. Although the technique is not likely to replicate all the products currently made from petrochemicals, it is likely to yield novel chemicals that could never be made affordably from fossil fuels.

But as biochemical production scales up to large industrial use, it will be important to avoid both competing with food production for land use and accidental releases of engineered organisms into the environment.

You spoke about the fourth industrial revolution and for many people this means Industry 4.0, digitization or digitalization, and artificial intelligence. But isn't the fourth industrial revolution not really a mix of all these technologies with biotechnology and chemistry?

S.-Y. Lee: Yes, indeed — they are heavily intertwined. Let me tell you about two different sectors. One is healthcare. If you talk about precision medicine, obviously you need to monitor one person's lifestyle in addition to analyze his or her genome sequence, map the microbiome, and so on. It is through IoT already and of course, the bed or even the toilet are equipped with different sensors and the data will be collected and then artificial intelligence and big data analysis will result in better suggestions to doctors. Thus, diseases can be treated in a better way. Artificial intelligence — or AI — is already playing roles in my group for monitoring of all the possible drug-drug and even drug-food component interactions. That will be drastically changing how we take and prescribe drugs during the drug development process. You can disregard some of the chemicals or drugs that have proven useful but not good with another drug if taken together. This kind of result is already emerging and would not have been

possible without using deep learning algorithms and today's computational power. In the production sector, similar approaches can be taken to optimize the microbial performance and production bioprocesses.

That is fascinating. I remember a little talk you gave about the combination of traditional Asian medicine, which is also about nutrition, and the combination of biotechnology. This seems to be a big resource of knowledge that you can tap and exploit with biotechnology.

S.-Y. Lee: In five thousand years of Korean history, various mixtures of plants and animals have been used to treat or prevent diseases on a trial-and-error-based clinical testing. This knowledge and experience has been compiled 405 years ago by a physician named Hur Jun. The main problem with Western doctors is that they really hate traditional oriental medicine. They think that the brewage made from boiling mixtures of plants contain a lot of toxins that can cause kidney and liver damage. Therefore, they prefer to prescribe well-defined drugs like aspirin, to name just one.

However, after intensive analysis of all known compounds from natural plant extracts, particularly their metabolites, we discovered that they have a higher structural similarity

> „Chemical industry cannot survive without changing."

to human metabolites than synthetic drugs. In additional studies we discovered synergistic combinations of compounds that showed a much higher efficiency to treat certain diseases. Traditional oriental medicine takes a multi-component multi-target-based approach, rather than the current single-target single-molecule type of therapy approved by Western regulatory bodies. The human body is a highly complex system and therefore it is nonsense to try to treat diseases with one single molecule. What was done for hundreds of years based on experience and observation in many different countries has been underestimated for its values. Thus, we are revisiting to identify multi-target, multi-component interactions at systems level, and this approach will change not only how we prescribe a medicine or mixture but also how to design better nutrition.

We spoke about the topic of sustainability. In terms of environmental sustainability, which is also covered in the UN Sustainable Development Goals, biotechnology can really revolutionize the way we live and produce materials. Do you have a vision of how — and when — biotechnology will become a given in our lives when we really tap into its full potential?

S.-Y. Lee: By 2030, I think it is realistic to say that biotechnology will become a part of our life, from drugs, medicine and therapeutics to environmentally friendly chemicals, fuels and materials. We have talked about the role of biotechnology in the sustainable production of materials and the treatment of waste. It is expected that an increasing number of chemicals and materials will be efficiently produced from renewable resources by microorganisms developed by systems metabolic engineering. Major systems metabolic engineering achievements in recent years include microbial production of not only amino acids and drugs, but also bulk chemicals like 1,4-butanediol, succinic acid, and polymers.

The human life-style generates a lot of waste. But the waste decay processes are neither done by humans nor machines; they are mostly performed by a collection of microorganisms. In my opinion, we need to better analyze the so-called waste treatment microbiome or at large the environmental microbiome, which can be different from one country to another. So, it should be locally analyzed depending on the particular waste stream. For these analyses an enormous amount of data needs to be monitored, because in every location the temperature is different, the nutritional content is different, everything is different. Today we are able to intervene and to accelerate a better design of the waste microbiome, to give just one example. If we combine all these efforts in the different sectors we would have a much cleaner environment.

Eventually, biotechnology will become as common as having a cellphone or going online. There is going to be an even larger number of biotech companies, both big and small, along with an increasing number of venture companies.

Many of the inventions of mankind made in the last couple of centuries have proven to be little sustainable. If you had a reset button or a time-machine, how far back in time would you travel to reverse some of these dead-end technologies?

S.-Y. Lee: You are asking this question to the wrong person because I do not want to go back in time. But to answer your question, I would say that I do not want to go to the era before the petrol chemical industry because even though we are sort of attacking the bad things resulting from petrochemical industry due to the climate change, etc., but without the petrochemical industry it would not have been possible to enjoy our current standard of living. The petrochemical industry has definitely revolutionized the human living style. However, now we have to look back. We did make some mistakes because we could have done much better. For example, we could have used only a limited amount of the earth's fossil resources while also using sustainable routes and we could have reduced or even prevented the environmental bad outcomes. I would go back to, say, about maybe thirty or forty years and then try to convince people to rebalance the system and make it much more sustainable.

Part of the progress we make and some of the resulting advantages come with a downside. Is it all about handling and managing disadvantages while making use of the advantages of science technology?

S.-Y. Lee: Right. And most importantly we all should try to be frugal. We are eating and wasting so much. I think being frugal is one of the key points which can address a lot of different problems including food shortage and even health. We waste about half our food eventually. Of course, it's not fault of science, it's because of insufficient logistics, but of course science can help to solve logistics issues as well — especially if using all the core technologies of the fourth industrial revolution.

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Quest for the "Holy Grail"

Which Will Be the Most Promising Bio-based Chemical?

Petroleum is a limited resource and if we keep using it global warming will accelerate. Since this realization has filtered in the quest for alternatives has begun. Shale gas and natural gas are only pseudo solutions as those supplies are finite and fossil, too. The only way out are fossil-free resources. Industry and academia are developing processes for bio-based feedstocks fervently and with the prerequisite that the products must not be more expensive than conventional ones. However, in late 2014 the price for crude oil dropped below $70 per barrel and has not recovered as of early 2018. The prices for the chemical building blocks ethylene and propylene have roughly halved from 2014 to 2016. The dismal prospects have made big players such as Braskem and Dow Chemical shelve their bio-based propylene development. Thyssen Krupp Industrial Solutions has sent its multipurpose plant for organic acid fermentation in Leuna, Germany into hibernation in 2015 until better times, selling it subsequently to EW Biotech.

However, at the current price for crude oil, bio-based chemicals can rarely compete with their fossil counterparts pricewise and cannot even play a trump card in the matter of climate change: the amount of "C" that ends up as part of products is marginal. Nonetheless, support for bio-based products is firmly anchored in the policies of many governments and the targets they have set are ambitious.

Bio-based Policies in Europe and the US

There is consensus in Europe and the US that guidelines on how to switch over to a bio-based economy need to be stipulated; the approaches to implement the change are quite different regarding the strategies of the different governments and the legislative conditions.

The European Union has agreed upon

- a 40% greenhouse gas reduction by 2030 (compared to 1990 levels)
- at least a 27% share of renewable energy consumption
- at least 27% energy savings

More explicitly 20% of the chemicals and materials in the European Union will be bio-based by 2020, rising to a quarter in 2030. In the United States the Biomass R&D board envisions a billion ton bioeconomy. By 2030 1 billion t of biomass is projected to be sustainably produced. It is supposed to be the base for emerging bioproducts industries, but mainly to target "a potential 30% penetration of biomass carbon into US transportation market by 2030". Plainly spoken this means biofuel in the forms of biodiesel or the addition of ethanol to gasoline.

Which is the Most Promising Bio-based Chemical?

When new processes and products enter the market it is human nature to ask who does best in the competition. For the uninvolved observer it may be simple curiosity, for investors it's a matter of money — and lots of it — to decide whether to jump on the bio-based bandwagon and which car to take.

In 2004 the US National Renewable Energy Laboratory (NREL) has defined 12 top value added chemicals from biomass. These products seemed to be the most promising at that time but a lot has happened in the last decade. In the follow-up report of 2016 there is again a list of 12 promising chemicals. The overlap between the two lists is moderate and consists of glycerol, succinic acid and para-xylene.

The European Union, too, strives to identify the chemicals that are predestined to be made from biomass. RoadToBio is a EU-funded project set up in mid-2017 to deliver a roadmap by 2019 illustrating the 'sweet spots' for Europe's chemical industry. In a first step, a long list with 120 chemicals at technology readiness level of 6 (TRL 6) or higher was compiled that show potential for the chemicals market. In parallel, the value chains of 500 petrochemicals were analyzed from a purely technical point of view. 85% of the value chains offer entry points where a petrochemical could be replaced by a bio-based one. The chemicals that were cited most often as replaceable are ethylene, propylene and methanol.

Interface between Bio-based and Petrochemical

The NREL report and RoadToBio project have in common that they both examine products with a TRL 6 or greater meaning that the production process has reached pilot scale. Furthermore the studies so far both work along the value chain of petrochemical products. A typical product tree starts from a low value feedstock like ethylene and branches into many higher value intermediates like polyethylene, ethylene oxide and vinyl acetate. The intermediates again have multiple uses.

Whenever a chemical can in theory be replaced by a bio-based one this is called an entry point in RoadToBio. Overall, of the 120 chemicals identified in the long list for further analysis, only 49 have entry points into existing petrochemical value chains, while the other 71 are dedicated chemicals. Dedicated chemicals are those which have no fossil-based counterpart and thus offer unique production routes. Lactic acid as base for the bioplastic polylactic acid is a prominent example for a dedicated chemical. In contrast, drop-in chemicals are bio-based versions of existing chemicals. A third group, smart drop-

in chemicals, are also chemically identical to their fossil counterparts but provide an additional advantage compared to ordinary drop-ins. This can be a faster and simpler production pathway or less energy use.

Four chemicals that appear on both the top twelve NREL list and among the 49 RoadToBio chemicals with potential entry points are succinic acid, para-xylene, 1,2-propanediol and glycerol.

Succinic Acid

The current world market for the dicarboxylic acid is around 50,000 mt/y and intended as raw material for specialty chemicals. However, the projected market is large and that this projection is a very real thing is reflected in the production plants that are set up worldwide. Between the four of them and in various joint ventures Succinity, BioAmber, Myriant and Reverdia are building production capacities of more than 400,000 mt/y of succinic acid. Microorganisms used for the fermentation are B. succiniproducens, *E. coli* and *S. cerevisiae*. The companies count on succinic acid becoming a platform chemical, opening up a much broader product range. Hydrogenation of succinic acid to 1,4-butanediol and tetrahydrofuran could access another market of combined 2.4 million mt/y. If this becomes a reality your spandex clothing and polyurethane mattress can be bio-based, too, in the future.

Para-xylene

Para-xylene is used to produce both terephthalic acid and dimethyl terephthalate, the two constituents of polyethylene terephthalate (PET).

It is nearly exclusively used to manufacture polyesters with the majority destined for fibers and films. The 27% going into PET bottle resin, however, are the ones that got the most attention from bioeconomy media in the last few years. Major consumers of PET — the Coca-Cola Company, Ford, Heinz, Nike and Procter & Gamble — have funded research for the production of renewable PET. Virent has developed a hybrid biochemical and thermochemical process that converts biomass into a mixture of hydrocarbons. This can be treated just like petroleum-derived hydrocarbons. A 100% plant-based bottle was showcased at Expo Milan in 2015 (Lane 2015), made with para-xylene from a demonstration plant but commercial production is expected not before 2021. Micromidas and Annellotech base their chemo-catalytic processes on cellulosic feedstocks, too, while Biochemtex counts on lignin. The only company using fermentation is Gevo: sugars from biomass are converted by a yeast into isobutanol which is then chemically transformed into para-xylene.

For the time being none of the companies has the capacity to make a dent in the 65 million mt/y market.

1,2-Propanediol

1,2-propanediol has a myriad of uses ranging from pet food to polyester resins, resulting in a global market of around 2.5 million t/y.

It is also known as propylene glycol and is currently produced from propylene as a coproduct of petroleum cracking, therefore its price is closely connected to the petroleum price. Bio-based 1,2-propanediol is usually produced by hydrogenolysis of glycerin with mixed-metal catalysts with the catalyst formulation and reaction conditions being the variables. ADM has 100,000 t/y production capacity in the US and Oleon 20,000 mt/y in Belgium. Global BioChem operates a 200,000 mt/y plant in China using sorbitol from corn as feedstock. The sorbitol is hydrocracked into 1,2-propanediol, ethylene glycol and butanediol.

Glycerol

The sugar alcohol can be used in bodylotion as well as in marzipan, to keep both your skin and the almond paste soft and tender. Apart from that glycerol has more than 1,500 other uses. The petrochemical production route for glycerol starts from propene but plays only a minor role. The market is dominated by bio-based glycerol as a byproduct of biodiesel production. For this vegetable oil is transesterified with an alcohol; for every 10 t of biodiesel 1 t of glycerol is produced. With a yearly production of about 2 million t of glycerol worldwide the market is saturated, resulting in stable and historically low prices. Industry is therefore looking for ways to add value to glycerol. Use as a substrate for fermentation processes such as succinic acid, citric acid, 1,3-propanediol or biogas are in part commercially proven as is application as animal feed.

And the winner is…?

If predicting the success of a bio-based product were easy governments worldwide would not employ legions of scientists and commission studies to do so. Only time will tell which of the cited bio-based chemicals will become a blockbuster and whether RoadToBio will come to the same conclusions as the NREL study. The petroleum price and governmental interventions are only two of the more unpredictable factors in the multi-parameter matrix which determines the economic success of a bio-based product. One of the communalities of the four chemicals discussed above is that they are drop-in chemicals. They are chemically identical to their fossil counterparts and for further processing it doesn't play a role whether they are made from petroleum or from biomass.

On closer inspection the production processes of promising drop-in chemicals are an eclectic mix of chemical and biotechnological. Fermentation steps are followed by chemical transformations; whether a metal catalyst or an enzyme is used is just a matter of what works best. Anything goes as long it is technically feasible. A process is no longer either chemical or biotechnological, cooperation is the new normal. Winners in the quest for the holy grail of bio-based chemicals are definitely the scientists from all the different disciplines involved. They have learned to look past the rim of the teacup of their own sector and gained a whole new perspective in their neighbor's teacup.

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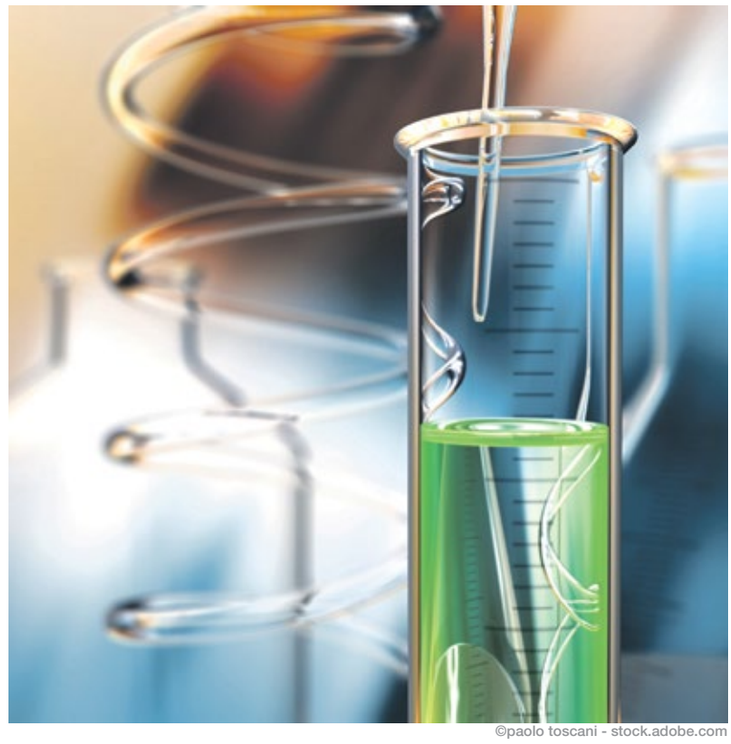
The article is based on a trend report commissioned by Dechema and written by international trade journalists. Dechema brings together experts from a wide range of disciplines, institutions and generations to stimulate scientific exchange in chemical engineering, process engineering and biotechnology.

How to Tap the Potential of Green Chemistry

Strategies to Cause Less Impact on the Environment

The challenges of sustainability are among the most complex and daunting ever faced by society. Green chemistry needs to be increasingly engaged in facing these challenges by addressing the intrinsic nature of materials and energy to make them more sustainable. While green chemistry may not yet be mainstream, the tools and approaches to getting there are evolving: cross-sectoral, value chain collaboration is growing; innovative new chemistries and materials are being developed; and education and awareness are progressing. By continuing to make improvements and breakthrough innovations, the chemical industry can create advanced product and process solutions that significantly accelerate the transition to a resource efficient, low-carbon and circular economy.



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In detail, we interviewed professionals ranging from CEOs to heads of R&D and process development about:

- What are the drivers, how would you rate the potential and where do you expect limitations of green chemistry?
- Which strategies do you consider central to accelerating innovation in and adoption of green chemistry?
- What does it need for green chemistry concepts to pay off not only environmentally but also economically? Can you give some examples?

Statement

The Journey Has Just Begun

Sonja Jost (DexLeChem):

Sonja Jost, CEO, DexLeChem

Green chemistry triggers innovations by helping us to leave our comfort zone. Things that we have been doing for decades in the same way are suddenly in the spotlight of scrutiny. By a pure change of perspective, we open the doors to a nearly untouched pool of innovations. If we look at the great inventions in human history, their momentum has always been created out of a need. Green chemistry and the underlying need for a more sustainable future is the need to restore our life on this planet. The momentum of the movement that drives this change is tremendous and unstoppable. And the good news is: there are no limitations to green chemistry, as there are no limitations to chemistry itself. There was chemistry before the age of oil and gas and there will be chemistry afterwards. Nature has taught us to which incredible results green chemistry can lead and researchers all over the world are diving deeper and deeper into this relatively young science. A lot of green chemistry concepts are already paying off compared to their predecessors. One nice example is the substitution of organic solvents based on crude oil through water in the production of chemicals. For a long time, this was considered a "no-go". However, knowledge develops and suddenly this altered approach offers significant competitive advantages: By using the unique properties of aqueous solutions a simple product/catalyst separation is possible that enables the re-use of the expensive catalysts for the first time while no chemical modification is necessary. In other words: up to 30% of the manufacturing costs of chemicals can nowadays be saved by applying water in the production. This example shows us that the art of designing new competitive advantages lies in taking totally new paths and not in merely trying to copy the former state-of-the-art. We have just begun the journey and there is no end in sight.

Statement

Biologization of Industries Is a Megatrend

Jürgen Eck (BRAIN):

Jürgen Eck, CEO, BRAIN

The transformation of society towards a bioeconomy is underway, with the aim of handling natural resources more efficiently and establishing sustainable manufacturing processes and products to tackle the challenges our times present. The biologization of entire industries constitutes a megatrend. Industrial biotechnology is the innovation motor and driver for new and attractive value creation, enabling product ideas that seemed inconceivable few years ago. Using microorganisms in our Green & Urban Mining BioXtractor for extracting gold or rare earths from ore or waste streams, or metabolizing CO_2 into precursor materials of bioplastics are just two examples developed by BRAIN.

As a cross-sector technology, industrial biotechnology integrates highly differing disciplines from natural and engineering sciences. Its "output" addresses multifaceted target markets in chemicals, energy or commodity and consumer goods industries addressing important tasks including providing healthier food by developing natural sugar or salt substitutes as in some of our programs.

Expectations for future bioeconomy markets are high. Business experts predict that sales from "green" chemicals will expand from around $140 billion to $610 billion over the 2010–2025 period, reflecting a compound annual growth rate (CAGR) of around 11%. Global financial markets also regard the bioeconomy as a megatrend, leading to capital reallocations with a greater focus on socially responsible investments. The aim of such "impact investing" is to integrate factors like environmental protection, social acceptance and human well-being into future financing strategies.

BRAIN plays an active role in shaping the change towards a sustainable bioeconomy by developing and marketing product and process innovations for various B2B markets focusing on bioactive natural compounds and enzymes as well as customized high-performance microorganisms.

Statement

The Best Way of Practicing Chemistry

Rakeshwar Bandichhor (Dr. Reddy's):

Rakeshwar Bandichhor, director API-R&D, Dr. Reddy's

Use of renewable raw materials, cost-effective operation and material production with respectable atom efficiency, environmental well-being with remarkably lower Process Mass intensity (PMI), health, safety and global sustainability are the green chemistry drivers. Minimizing or ideally eliminating waste by applying green chemistry by design is preferred over waste management. Green chemistry is basically the best way of practicing chemistries and executing processes either in the lab or at scale. Chemistry's contribution to society is well known and widely appreciated. Green chemistry now further elevates the importance of chemistry and enables a more sustainable society. In practice, the limitations of green chemistry are broadly due to several points: firstly, a lack of expertise in finding greener alternatives in a timely manner and secondly insufficient organizational incentivization of the excellent work done at the ground level by chemists and engineers. Traditional batch manufacturing is another limiting factor. Nevertheless, over the last decade a lot of technological advancement has taken place, and sophisticated tools are available to realize the green chemistry and engineering objectives at higher scales, e.g. continuous processing, bio-catalysis, etc. Supply chain partners to multinational companies are usually cost-driven and not adequately environmentally responsible.

Most industries believe – consciously or subconsciously — that high costs, unchartered time and efforts are involved in the adoption of green chemistry and engineering practices. However, this is not true. In order to maximize the benefits of this discipline and accelerate green innovation, a top down approach is required to build a culture of open innovation, effective training, learning and technical capabilities to ensure that structured and science-driven approaches are adopted.

Innovative green chemistry by design and structured science-driven approaches based on guidelines such as 12 green chemistry principles, green chemistry metrics (particularly, atom efficiency, PMI and reaction mass efficiency), and solvent selection guidelines are keys to safe and cost-effective operations. Pfizer has set a great example in this regard. By employing some of the above guidelines, the company won the US Presidential Green Chemistry Award for its outstanding work on Sertraline. They eventually doubled the overall yield by process intensification enabling the process to be more cost effective.

Statement

A Huge Business Opportunity

Christophe Le Ret (Umicore):

Christophe Le Ret, Global marketing dircetor, Umicore

To be better adopted (and pay off), green chemistry needs to be not only environmentally, but also economically advantageous. Simply because almost no consumer is ready to pay more for the same — in greener — features, even if a vast majority is conscious of the urgency of the environmental need.

Behind this common sense is actually a huge business opportunity: design recyclable, reduce and valorize wastes and use efficient reactions are three opportunities to generate new and sustainable businesses while protecting the planet.

Let's take olefin metathesis technology for instance, where Umicore has a strong competence: it is one of the most versatile and selective ways to build carbon-carbon bonds, the ultimate target of organic chemistry. It is also a way to transform non-edible feedstock into high performance materials and chemicals, to shorten the synthesis of complex pharmaceutical ingredients (and thus increase yields and reduce chemical wastes), to efficiently synthesize environmentally friendly pheromones, or as lately shown by Slugovc's and Abbas' teams, to potentially recycle natural rubber waste.

If "design recyclable" means to plan when creating a product how it can be (more) efficiently recycled, it can also apply to all the ingredients of a chemical synthesis: recycling the precious metal of a catalyst is generally more effective when thoroughly thought before process scale up. If solvents cannot be fully avoided, they may generate more value by being recycled or valorized than when being disposed.

We worked on such a case with a pharmaceutical customer using a palladium containing homogeneous catalyst. And designing a way to separate first the used catalyst from the end-product, then most of the ligand from the metal and to finally recycle both ligand and palladium appeared to be —albeit complex — sustainable and cost efficient at commercial scale.

Statement

Broad Opportunities for Economic Progress

Andreas Förster (ISC3):

Andreas Förster, director Innovation Hub, ISC3

Dechema manages the "Innovation Hub" of the International Sustainable Chemistry Collaborative Center ISC3, founded in 2017. Thus, we have become part of an international initiative to foster green and — reaching beyond the "12 principles" — sustainable chemistry. The chemical sector already plays an important role in solving key societal problems by using and developing innovative materials and products. This offers broad opportunities for economic progress especially in developing and emerging countries — whilst protecting health and the environment. Resource-efficient production does not only have a positive impact on natural resources, it can also reduce raw materials costs and costs for waste treatment and waste water disposal. Therefore, a sustainability-oriented chemical industry can make a major contribution to achieving the global Sustainable Development Goals (SDGs) of the UN. Business innovation is an integral part of the sustainable chemistry concept. Exchanging best practices around the globe can lead to new business ideas and value chains that are mutually beneficial and create employment at the same time as protecting the environment.

Haldor Topsoe Forms China R&D JV

Danish catalysis and technology company Haldor Topsoe has signed an agreement with Jiangsu Industrial Technology Research Institute (JITRI) and Xiangcheng Suzhou District to form a joint R&D company in Jiangsu province, China.

Topsoe will invest mainly technology and knowhow in return for a 60% share in the company. JITRI and Xiangcheng Suzhou District will own the remaining stakes and invest 80 million Chinese yuan ($12.6 million) over a five-year period.

The new company will focus on the fast commercialization of new technology and services, said Topsoe, with special attention paid to the needs of customers in Jiangsu and China.

The first project will be on developing more cost-effective lithium-nickel-cobalt-aluminum oxide (NCA) batteries for use in electric cars, for which China is the largest and fastest-growing market. The jv will also offer Chinese customers fast and efficient testing within hydroprocessing and emissions management (catalytic filtration) in a convenient location, Topsoe said.

Our decision is based on more than a year's talks with Haldor Topsoe, where we have been impressed by their high level of R&D work," said Liu Qing, JITRI's president. (eb, rk)

ExxonMobil, Synthetic Genomics Hike Algae Research

ExxonMobil and Synthetic Genomics are scaling up their joint research into using algae as a biofuel.

The companies believe that 10,000 bbl/d of algae biofuel could be produced by 2025, based on the research conducted to date along with emerging technical capability.

This new research phase includes an outdoor field study that will grow naturally occurring algae in several contained ponds in California, USA and, the companies said, enable them to better understand fundamental engineering parameters, including viscosity and flow, which cannot be easily replicated in a laboratory. More work will be required to advance larger-scale production. "The new outdoor phase is a critical next step in determining a path toward large-scale, commercial production," said Vijay Swarup, VP for research and development at ExxonMobil Research and Engineering, who added that the work with Synthetic Genomics continued to be an important part of its broader research into lower-emission technologies to combat climate change.

Last June, the partners announced that they had managed to modify an algae strain and more than double the algae's oil content from 20% to more than 40%, without significantly inhibiting growth. (eb, rk)

China's Anti-pollution Clampdown

Stricter Environmental Regulation Impacts Specialty Chemicals Production

Since late 2016, the Chinese government has conducted a series of environmental inspections of production companies. These inspections have typically led to short-term closures of a large share of plants. A report by the Ministry of Environment stated that 70% of all companies inspected failed to meet the standards for controlling air pollution. However, most of them were allowed to restart production after reducing their emissions.

Compared to previous government actions, these inspections are much stricter and conducted on a larger scale. They are an indication of much tighter implementation of environmental regulation at a time when the regulations themselves are also tightening. Since Jan. 2017, a number of government agencies, including the State Council and the Ministry of Environment have issued several policies mandating reduced energy consumption, lower carbon emissions and stricter pollution control. And the government puts a strong emphasis on implementation of these new regulations. For example, in Oct. 2017, 69 Hebei government officials were dismissed for failing to implement pollution controls, and an additional 154 officials were handed over to police for investigation. Similarly, changing the previous emission fee to an emission tax has shifted authority from local governments — which frequently favor local economic activity over the environment — to central tax authorities.

Kai Pflug, Management Consulting — Chemicals

Consequences for Chemical Producers

As China's president Xi Jinping has made reduction of environmental pollution one of his three top priorities for China, these developments are not likely to be reversed, even though some Chinese experts estimate that the campaign has decreased GDP growth in 2017 by 0.2%. It is therefore worthwhile for companies with chemical production in China — and for those doing business with them — to examine their direct and indirect consequences.

First of all, the environmental inspections have led and will lead to short-term production stops. In the

recent past, about 40% of all companies inspected were affected by such stops, which typically lasted 2 – 4 weeks. Generally, the polluting companies have to choose between upgrading their equipment to meet the environmental requirements and stopping production altogether.

Second, much longer production stops may result as a consequence of chemical companies being forced to relocate. Broadly speaking, the government wants to relocate all production of toxic chemicals into dedicated industrial parks. The timeframe depends on plant size. Small and mid-sized chemical plants (with up to about 1,000 employees and up to about €50 million of annual sales) need to start relocation in 2018 and have the relocation completed by 2020. For larger plants, relocation has to start by 2020 and be finished by the end of 2025. Of course, it will depend on the individual company whether such a production relocation will affect sales, or whether a sufficient buffer stock can be produced in advance to bridge the gap. Also, customers may not immediately be willing to buy from a new plant without first auditing the new production site, which will require an even larger buffer stock.

"The tightened environmental regulation will help bigger and technologically more advanced players."

The number of affected companies is quite large. For example, in Shandong province alone almost 200 chemical plants have been identified for relocation, though the majority of them have not yet started the process. Often this is due to a lack of funds for relocation.

Of course, an alternative to relocating production is to stop production altogether. This is particularly likely if the producing company is small, not very profitable and uses outdated technology. In such a case, local government will only give limited or no support, and as a consequence, a marginal producer may be forced to exit the market.

Third, it will take much longer to get permissions for new plants. A big and well connected local chemical company told the author that instead of the previous 6 months, the local authorities would now take about 18 months to give such a permission, primarily as the environmental due diligence will become more important in the approval process. As a consequence, markets for individual chemicals will take more time to adapt to demand increases.

Fourth, production costs will increase. Some examples of such cost increases include:

- **Costs for Volatile Organic Compounds (VOC) treatment:** In several industries including printing, ink production and flexible packaging, the installation of VOC treatment equipment becomes mandatory.
- **Costs for water treatment**: In one example known to the author, a specialty chemicals producer will have to reduce the emission of waste water by 90% after relocation, which will obviously require substantial additional investment.
- **Higher costs of raw materials**: Partly this is due to these raw materials being other chemicals, which will be affected by the same cost increases. However, it is also due to the restrictions on imports of materials for recycling, such as paper and plastics. For example, paper prices have already doubled within the last few months.
- **Environmental tax**: This tax will be higher than the current emission fees which it replaces, and implementation will be controlled by more powerful agencies.
- **Higher transportation costs**: According to some estimates, 80% of hazardous chemicals are being transported by road, and as measures to prevent accidents are implemented more strictly, the cost of such transportation may increase by up to 35%.
- **Chinese Chemical Industry Will Consolidate**

In the longer term, the aspects listed above will also have an impact on the overall structure of the chemical industry — an effect that is quite appreciated by the government. Many specialty chemicals segments in China are very fragmented and suffer from overcapacity. For example, there are more than 2,000 coatings producers, and the top 200 producers account for only about 60% of total industry sales. The tightened environmental regulation will lead to industry consolidation as the weakest and smallest players will not be able to afford the necessary production upgrades. This will also lead to a reduction in overall capacity along with the improvement in technological level.

Generally, the tightened environmental regulation will help bigger and technologically more advanced players. Indeed, these companies may benefit from higher prices as excess capacity is eliminated. This is good news for foreign players in China as they tend to have both a bigger average size and better technology, particularly with regard to emission control. In addition, the stricter implementation of regulation for all types of companies — whether foreign owned or local — corrects the previous trend of tighter control of foreign-owned ventures.

In terms of chemical segments, downstream and specialty segments will be more affected as they tend to be smaller and operate on a lower technological level. In particular, smaller plastics processors, adhesive producers and coatings producers were among the most affected so far. This is well aligned with the government target to either force such companies into chemical parks, where they can be controlled more easily, or to shut them down and thus improve both the industry structure and the environmental situation.

Western Companies Have to React

How should Western companies react? For companies producing in China, the key question is whether they are already located inside a chemical park or not. In the latter case, there will be intense pressure to relocate quickly. And of course, even inside a chemical park, they will need to strictly adhere to mandated emission control, though for most foreign companies, this is given already. However, this may be a good moment to recheck internal compliance policies and to promote a proactive approach to environmental protection.

"Companies with a stake in Chinese chemical production are advised to take a proactive approach."

How about sourcing from China?

Indeed, supply for a number of chemicals from China has temporarily dried up, leading to substantial price increases for specific dyes and agrochemical intermediates, and an increased investor interest in specialty chemicals producers in, e.g., India and Japan. However, given the huge importance of China for the global chemical market, and the high importance of the chemical industry for China, it is unlikely the chemical industry as a whole will suffer. Indeed, while chemical production growth has decreased to 3.9% in Q1 to Q3 of 2017 compared to 8.5% in the same period in 2016, it is still growing. As a consequence, it seems an overreaction to stop sourcing from China altogether. However, to reduce the supply risk, companies purchasing from China may consider a few measures such as:

- not relying too much on very small suppliers as these are particularly at risk of closure;
- instead, establishing strong relationships with a few suppliers, and monitoring their exposure to risk from environmental regulation (e.g., check whether they are already located in a chemical park, and whether they were recently affected by production closures; ask them for their internal audit procedures regarding compliance with environmental regulation);
- have at least two or three different suppliers for each chemical, preferably not all located in the same province. Ideally, one supplier would even be located outside of China.

In 2018, the program of environmental inspections is continuing, and thus will continue to cause supply disruptions. Given the political environment, additional legislation related to environmental protection of the chemical industry is likely as well. For example, the national emissions trading scheme, which initially will be restricted to power generation, may well be extended to chemicals. In this tightening environment, companies with a stake in Chinese chemical production are highly advised to take a proactive approach.

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China's Environmental Clean-up

How Western Chemical Companies Can Deal with Stricter Environmental Regulation in China

Since late 2016, the Chinese government has conducted a series of environmental inspections of production companies. Compared to previous actions, these inspections are much stricter and conducted on a larger scale. They are an indication of much tighter implementation of environmental regulation at a time when the regulations themselves are also tightening. It is therefore worthwhile for companies with chemical production in China — and for those doing business with them — to examine their direct and indirect consequences, e.g. production stops, relocation of plants to industrial parks, increase of production costs, and industry consolidation.

In detail, we interviewed some CEOs about:

- How does the stricter environmental regulation in China affect you or CMOs/CDMOs in general, e.g. does it create a necessity for shifting production to other countries?
- Which measures could companies with a stake in Chinese chemical production consider reducing a supply risk?
- How could foreign players in China benefit from this development?

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Statement

China's Competitive Advantage Could Decrease

Hendrik Baumann (Arevipharma):

Hendrik Baumann, CEO, Arevipharma

The China Safety Production law has been published first time in 2002 with amendments in 2009 and 2014. This law is the basis for all activities of the Chinese production industry, including the chemical and pharmaceutical industries. During the above-mentioned time period this law was spontaneously enforced, sometimes the local authorities made inspections of relevant production facilities and in some cases, they closed factories which were absolutely not acceptable or after an accident happened. Overall there was not a systematic law enforcement and therefore most of the chemical producers have ignored the law and its consequences. Probably the ignition for the change of the governments enforcement policy of the safety production law was the accident of August 2015 in Tianjin, were a series of explosions killed 173 people and injured hundreds of others at a container storage station.

Since 2015 we see a much stricter law enforcement, many closings of chemical manufacturing sites all over the country. We know from business partners that the local authorities perform onsite environmental audits on a more frequent basis, especially they check product lists against the production licenses, the waste and off-gas treatment systems (if available) or they require to install such systems. As a result, many companies have been closed and their products disappeared from the market without notice. Raw materials are no longer available, the number of producers have been reduced and prices increased subsequently.

For us as a chemical and pharmaceutical producer it is of importance having reliable suppliers, ideally from different countries, for each single raw material. Alternatively, we consider a restart of in-house production of critical raw materials. This sounds easier than it is, because the production know-how has been given up and must be re-accumulated, which means some of the processes must be developed and validated again.

Under the assumption that the European Union will not further tighten the current production and environmental laws, we see a high probability to get back market share and production from China. Pricewise and with regard to the production costs it is clear that the competitive advantage of China, with respect to overall production costs, will decrease within the next 5-10 years. We are convinced that European companies will then have a real "level playing" field with China and will be competitive. Consequently, it will also be possible in the future to export intermediates and API's to China.

Statement

Customers Expect an Uninterrupted Supply

Dimitris Kalias (VIO Chemicals):

Dimitris Kalias, CEO, VIO Chemicals

China's environmental clean-up has had a big impact on CDMOs and industrial competitiveness. While regulations governing environmental protection tighten up, the provincial fragmentation and lack of strong policy support present great challenges for small and medium chemical producers and their supply chain. The degree of strictness in the enforcement of the regulations can be different from province to province, depending on the management style of each chemical zone's administration and local government. Guidelines about tax collection and monitoring of pollutants are still under discussion, bringing uncertainty to an already fragmented regulatory landscape.

Not surprisingly, small and medium-sized companies find it very difficult to keep up-to-date with the ongoing regulatory changes and meet public audit requirements. As a result, they face long years of delays to get production licenses for new products or fail to get a license whatsoever. Small companies are even sometimes forced by the local authorities to merge with their neighboring manufacturing peers, e.g. pharma intermediate producers with agrochemical companies, without any economic criteria in consideration, only because their land is too small. Others just shut down.

And it won't stop there. There has been growing pressure for the installation of full automation systems as a process control mechanism to minimize risk. For CDMOs, automation solutions are invariably associated with IT infrastructure and purchase of software, such as ERP, PLC, DCS, etc. And although it may not be mandatory to have every system installed — it usually depends on the size of the factory and production pipelines — it is almost certain that conforming to process control standards can be very costly.

To us, it is crucial to secure an uninterrupted supply for our customers. Therefore, we at VIO Chemicals perform our own internal audits to gain a greater level of comfort prior to public control. We screen and assess our suppliers not only for environmental but also for quality, safety and regulatory compliance. Proactivity, anticipation, a strong local team and high investments in pollutants monitoring technology and process control solutions are fundamental to our competitiveness and reliability as a CDMO.

Statement

A Change of Global Supply Patterns

Torsten Derr (Saltigo):

Torsten Derr, CEO, Saltigo

All Saltigo plants are located in Germany. We have no assets in China and are not affected by the current changes there. In 2017/2018 Saltigo strengthened the German production network by an investment of €60 million to be prepared for an additional demand for molecules covering production losses from Chinese suppliers. This strategy is clearly paying off now.

Most of our customers reacted to the enforcement of environmental regulation in China by specific "China de-risking" strategies. For higher supply security some customers are willing to relocate complete supply chains or introduce a second supplier sourcing strategy, even at the cost of higher prices, if products originate from a western supply chain. As some of our customers could not cover their "contracted" raw material demand from Chinese suppliers, they are rediscovering the advantages of "made in Germany".

Some of our raw materials are procured in China. We experienced insecure supply situations in the last 6 months from a high number of Chinese suppliers and reacted in three manners: 1) backward integration into our own assets in Germany, 2) strengthening second supplier setup and 3) re-establishing supply agreements with western suppliers, especially in Europe.

Saltigo presumes that even after lifting the production restrictions, the cost level and local prices in China will not return to the competitive level of recent years. Chemical parks in China have to provide similar environmental standards as in Europe. The resulting environmental price tag will reduce the former Chinese competitive advantage. What we observe right now has the quality to permanently change global supply patterns in the CMO industry.

Statement

Environmental Protection Is Not for Free

Lukas von Hippel (Pharma Waldhof):

Lukas von Hippel, CEO, Pharma Waldhof

From my understanding, we see an evolutionary process on global scale. As a part of the globalization, we have seen in the late 90s of last century a trend moving supply chains east, mainly for cost reasons. Thus, quite some western companies suffered, some have not been able to change as quickly as necessary. Consequently, technologies disappeared in Europe to create a strong dependence from India or China. During this period, quite some colleagues tried to provide transparency on mechanism and consequences. CHEManager was one source of information discussing such effects, e.g. in the article "Zeit zum Handeln" that was published in March 2010.

While buying in Asia, a strong cash-flow to emerging markets was established, firstly creating jobs, and gaining economic wealth. Now, two decades later, environmental challenges become evident, and especially China reacts. First, in my opinion, it is a good development, since it shows there is no free lunch: Environmental protection is not for free, and the lever to global climate protection in these countries is bigger compared to other measures. As a next consequence, we see the shift of production as well to again cheaper countries, and discussion is going on which countries will be next, replacing hubs that get more expensive.

So, in general, the next step in an evolutionary process does not change the game, but effects cost structures and may force innovation. Companies who took their EHS policies in context to supply chains seriously may not be surprised by the development, and will not be affected by a development which has been known for years. However, everybody is getting additional work securing supply chain standards. Others who have not worked that diligent may face issues. So, it depends on the buying organization and the people acting how well supply chains are built up. Chance and risk may be used synonymously. Thus, it is wise to consider consequences before acting.

Billionaire-backed Biotech Plans Hong Kong IPO

A cancer detection startup backed by US billionaires Jeff Bezos and Bill Gates as well as China's biggest Internet company Tencent Holdings and several pharmaceutical companies is planning an initial public offering in Hong Kong this year.

The move is thought likely to bolster the Asian financial center's push to start attracting biotech listings after Hong Kong began applying new rules last year. Reports said the start-up, Menlo Park, California-based Grail, is working with advisers on the proposed share sale, which may seek to raise as much as $500 million.

Grail said in December 2017 that its first product, a screening test for a head and neck type of cancer prevalent in Southeast Asia and southern China would be launched this year in Hong Kong. The company's goal is to diagnose people at a very early stage even when they have no symptoms.

Backers of the start-up also include Bristol-Myers Squibb, Celgene, Johnson & Johnson Innovation and Merck & Co. (dw, rk)

Germany´s Merck Invests in Asian Biopharma

To support the growing demand for biopharmaceutical manufacturing capability in Asia, German pharmaceuticals and chemicals producer Merck plans to increase its spending on manufacturing and distribution in the region.

The company said it has budgeted an additional €40 million to build a "robust" platform in the region over a period of two years. This follows on a planned €80 million life science investment in Nantong, China, announced in November 2016.

To accelerate Merck's Mobius single-use manufacturing and address the growing biopharmaceutical demand in China, the German company is planning to open a single-use manufacturing site in Wuxi later this year. With the investment, it expects to reduce lead time by at least 50%.

China, which has a growing biosimilars market, is fast becoming a biotech powerhouse. Merck said, noting that single-use technologies provide increased flexibility and efficiency, which are critical for biosimilar development and manufacturing. (dw, rk)

Catalent Completes Expansion at Singapore Facility

Catalent Pharma Solutions has completed the $4.6 million expansion at its Singapore clinical supply facility, announced in Feb. 2016. The New Jersey, USA-based company said the expansion provides additional GMP space for secondary packaging, has doubled ambient storage, and quadrupled cold storage capacity at the site.

The facility is a key strategic hub in Catalent's Asia-Pacific network and global clinical supply business, supporting multinational customers' growing needs for full clinical supply services, while providing flexible solutions for local customers in the region.

According to Catalent the site has seen significant growth since opening in 1998, almost tripling in size, with headcount also tripling since 2012.

"We are particularly pleased to have completed the expansion in a year that marks the 20th anniversary of what was Catalent's first facility in the Asia-Pacific region," said Bernie Clark, VP marketing, Catalent Clinical Supply Services. (rk)

China's Environment Tax Comes due in April

In April of this year, more than 260,000 companies and organizations in China will have to begin paying an environment tax, as the government moves to restrict pollution and protect the environment.

The new Environmental Protection Tax Law (EPT law) went into effect on Jan. 1. As China mandates quarterly tax returns, the tax will have to be paid retroactively for the period January-March.

Under the plan, those that discharge listed pollutants directly into the environment will have to foot the bill for producing noise, air and water pollutants as well as solid waste. Tax obligations will accrue from the date of discharge.

China's first-ever tax directed at anchoring environmental protection in the corporation consciousness also is designed to help establish a "green' financial and taxation system and promote pollution control and treatment of pollutants.

With the introduction of the new tax, the government has ended the "pollutant discharge fee" it has collected since 1979. (dw, rk)

Addressing Challenges in Sterile Manufacturing

Biopharma Companies Seeking a CDMO Partner Need to Consider a Broad Range of Capabilities

With a market value of $62 billion in 2016, the contract development and manufacturing organization (CDMO) industry has a compound annual growth rate (CAGR) of 6–7 %, according to the study by EY "Consolidation of the CDMO industry: opportunities for current players and new entrants". This CAGR is slightly higher than the CAGR of 5–6 % seen by the pharmaceutical sector as a whole.

Stefano Chiaramonti, Patheon

Early clinical development of new products requires in-depth expertise. For example, large biotech molecules such as monoclonal antibodies and proteins are extremely sensitive, with high costs and limited availability of bulk material. Small molecules such as peptides are frequently poorly soluble, posing additional challenges from the process and analytical perspectives. In addition, the first GMP batch of clinical material has often not yet been manufactured at an industrial plant.

Formulation and Development

The work performed in the development laboratory is critical to ensure the success of a suitable formulation and development of a scalable process in an industrial facility. Examples of approaches used include the design of experiments (DOE) concept and risk management tools such as failure modes and effects analysis (FMEA). These may be applied even in the earliest clinical phases, with the goal of avoiding challenges at later stages, when the product is on the critical path to the clinic.

In addition, advanced technological tools may help improve product knowledge. For example, micro-flow imaging and other particle measuring techniques for detecting aggregates in solution can be very useful in aiding the formulation development of biopharmaceuticals; and cryomicroscopy and statistical models are helpful for the development of a lyophilization cycle.

The review of process parameters in each critical step at laboratory scale is key to managing risk during scale-up; it is vital to be able to work with very limited quantities of expensive APIs within a tight timeline.

Analytical Testing

In the analytical field, investigational skills are required when unexpected results occur, the causes of which can vary widely, for example unknown chromatographic peaks may be due to chromatographic conditions not being optimized, or to the presence of contaminants — the source of which can require a great deal of effort to pin down.

For early stage clinical trials, the analytical methods require a lower level of validation compared to the ICH requirements. However the "understanding" of the reliability of such methods is critical to ensure the reliability of analytical results, in particular when they are indicative of stability.

During early development, stability data at different temperatures generated by non-GMP lab-scale batches are needed to predict the behavior of the product. This is typically carried out at least three months before scale-up and confirmed with the data generated by the first GMP batch.

Compliance with Regulatory Requirements

Regulatory requirements for sterile manufacturing are becoming more stringent, with challenging expectations from a technology point of view. In a recent development, the European Commission issued a long-awaited draft of Annex 1 Manufacture of Sterile Medicinal Products on December 20, 2017. The revision is aimed at adding clarity, incorporating the principles of quality risk management (QRM) to enable inclusion of new technologies and processes, while ensuring that microbial, particulate and pyrogen contamination associated with microbes is prevented in the final medicinal product.

Compliance with these new requirements also facilitates a "fast track" approval from regulatory bodies, during a pre-approval inspection in particular, for products that have orphan indications or for which there is a currently unmet need.

Under these regulations, there is an expectation that the product will be fully characterized and evaluated at critical process steps. Data may come from freeze-thaw studies (where required), the establishment of a formulation design space, and additional process parameters such as holding times, process materials

compatibility studies, mixing, agitation, filtration and filling. Another key element is the robustness of the lyophilization cycle. Having this information helps to guarantee high quality and deep product knowledge by the time the registration and validation stages are reached.

Scale-up and Technology Transfer

The success of scale-up and technology transfer are key indicators of a CDMO's ability to develop and manufacture a product on time, meeting client expectations from both technical and quality standpoints. It is important to be able to tackle unexpected challenges during the development cycle of a sterile drug, such as lack of stability, generation of aggregates, or failure to meet product specifications.

Equipment in sterile facilities is also becoming increasingly automated, with greater use of restricted access barrier systems (RABS) or isolators, as well as automatic loading and unloading systems for lyophilizers, which increase sterility assurance effectiveness and minimize the risks of human contamination. CDMOs face increasing pressure to offer best-in-class technology to meet client and regulatory expectations, while retaining flexibility and pricing in line with market rates.

Operational Excellence and Skilled Workforce

Operational excellence is essential, enabling continuous improvement and helping to develop 'best-in-class' site cultures. Visual Management, Kaizen, Gemba walks and Value Stream Maps are among the tools that will help the CDMO to be ever-more efficient in responding to market requests.

A focus on developing a skilled workforce is also essential in this environment, particularly when science is equally as important as the ability to be a proactive communicator and a leader. These skills are needed to optimize speed and resolve issues on the client's behalf and, equally critical, to help with retention. The role of the manager to develop such talent through coaching and feedback is a clear goal.

„A CDMO's people are its most important asset."

In conclusion, a CDMO's people are its most important asset as it works to develop the high performance organization required to meet these various requirements. Flexibility, teamwork and passion should be in a CDMO's DNA — originating from individuals who are natural problem solvers and can think 'outside the box' in resolving product development challenges. Critical skills include the ability to apply technical and scientific expertise to drive the development of robust processes, particularly for large molecules that require lyophilization, or complex poorly soluble formulations for scale-up.

Biopharma companies seeking a CDMO partner should consider a broad range of capabilities in addition to cost, with reliability topping the list, followed by flexibility and expertise in troubleshooting. This partnership can work towards a shared mission of providing patients with timely access to needed therapies that are produced 'right first time.'

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References can be requested from the author.

"Benign-by-design"

Industry and Science Co-operate to Commercialize New Green Technology for Use in Organic Synthesis

PHT International, a full-service manufacturer of pharmaceutical and agrochemical intermediates, has partnered with Bruce Lipshutz, professor at the University of California, Santa Barbara, to commercialize new green technology for use in organic synthesis.

About 10 years ago, Lipshutz turned his passion to developing a greener and more sustainable chemistry in order to decrease the ever-expanding volume of organic solvent-containing waste. It has been said that over 85% of the world's organic waste consists of solvents. Several of these are toxic, flammable, and associated with other health risks such as reproductive damage, liver and kidney damage, respiratory impairment, and cancer. Much of this waste continues to be burned and/or buried as a means of disposal.

Lipshutz's thesis is simple: organic chemistry should follow the perfect model, Nature. The basics of the concept involves the use of a nonionic "designer" surfactant (TPGS-750-M) to form nanomicelles, in water at room temperature, instead of using traditional organic solvents. These serve as nanoreactors enabling all the necessary requirements of typical solvents for synthetic purposes. "Benign-by-design," these surfactants eliminate unwanted environmentally hazardous waste.

The development of new catalytic systems that are functional in water in the presence of surfactants will change the future of organic chemistry. This new technology will critically diminish the energy and resources needed for reactions, reduce the associated cost, improve yields and process performances, and substantially decrease the environmental footprint.

The Environmental Factor or E-Factor is a standard measurement used to capture the environmental impact of a synthetic reaction. E-Factors are calculated by the ratio of the total mass of waste to the total mass of the desired product. By examining the resulting E-Factor, the benefit of using this technology can be quantified. For example, in a typical pharmaceutical Suzuki-Miyaura coupling, the E-Factor, when using organic solvent, is typically 25-100 when aqueous is included. When using "designer" surfactant technology, E-Factors are notably reduced by an order of magnitude, before recycling.

"Organic chemists are doing great things for society; we're synthesizing, as examples, crucial pharmaceuticals and agrochemicals, making good use of a very sophisticated science," Dr. Lipshutz said. "But what about all the organic waste being created?"

Some of Lipshutz's most recent developments have focused on reagents that enable the use of precious metals as reaction catalysts in much lower concentrations. A new ligand, HandaPhos, has been developed. When this ligand is combined, in a 1:1 ratio, with $Pd(OAc)_2$, it forms a Pd-catalyst that enables Suzuki-Miyaura couplings to be run with Pd at parts per million (ppm) levels, using designer surfactants, in water, at room temperature. Other applications of the HandaPhos technology are Sonogashira couplings as well as for Au catalyzed reactions, while ongoing work continues to discover new applications.

The TPGS 750-M surfactant is currently being evaluated in various development programs within multiple pharmaceutical and agrochemical companies. In one example, the technology was evaluated in a commercial API process containing a traditional Suzuki coupling reaction with Pd/PPh3 catalyst. The green technology was able to provide improvements against the traditional process with a ~70% reduction in process costs (see table).

Comparison of Coupling Steps	Green Technology	Traditional Process
Process Yield	93%	63.9%
Purity	99.5%	97.8%
Impurity Levels	0.07%	0.5%
Catalyst Loading	400 ppm	5% (50000 ppm)

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Specialty Chemicals on the Upswing

Emerging Strategic Impact of Batch Analytics on a Company's Market Position

Recent significant investments by big chemical companies in a strong specialty chemicals portfolio indicate that the importance of these products and therefore of batch production is on the rise. Because of the value that data analytics could bring to their market position, forward-thinking companies have already moved ahead of the curve by digitalization of their production.

Artur Beyer, TrendMiner

Pioneers in the chemical market have used trends like self-service analytics to create an analytics-enabled workforce in order to strengthen their market position and create the most profitable factories of tomorrow. The reasons for this change are firmly based in financials, such as the better performance with respect to return on invested capital (ROIC) which represents a company's operating profitability.

Another important driver is to increase financial flexibility to safeguard the portfolio against commoditization, which can be done by getting as much out of the existing production capacity as possible. In a time where putting out new chemical compounds into the market is harder than ever before, sustainability is key. Next to an organizational strategy to build portfolios based on sustainable products based on known compounds, financial flexibility through operational excellence will be key for lasting success.

With plant-level process experts often tied up in a variety of tasks, ranging from maintenance planning over audits to frequent production meetings, the time to proactively investigate process performance issues is limited. Depending on the role in the organization, experience in the process industry has shown that the average time spent on data analytics is around 20%. In addition, data analysis as such is not a core competence taught during the standard education of a process expert. This leads to a skill gap that is hard to close in a short time, since rigorous data analysis and the needed algorithmic knowledge are not easy to learn.

Limitations in time available for data analysis and a likely data analysis skill gap often lead to priority-driven analysis in practice. The main focus is often on fire fighting and the more immediate history utilizing the tools that the historian systems and Microsoft Excel have to offer. Priority-driven analysis keeps the plant running but at the same time leads to missed opportunities in proactive process improvements. Those missed opportunities of improvement can be significant in value, ranging from $50.000 up to multi-million dollar savings per opportunity.

In general, batch production can be improved in the following areas:

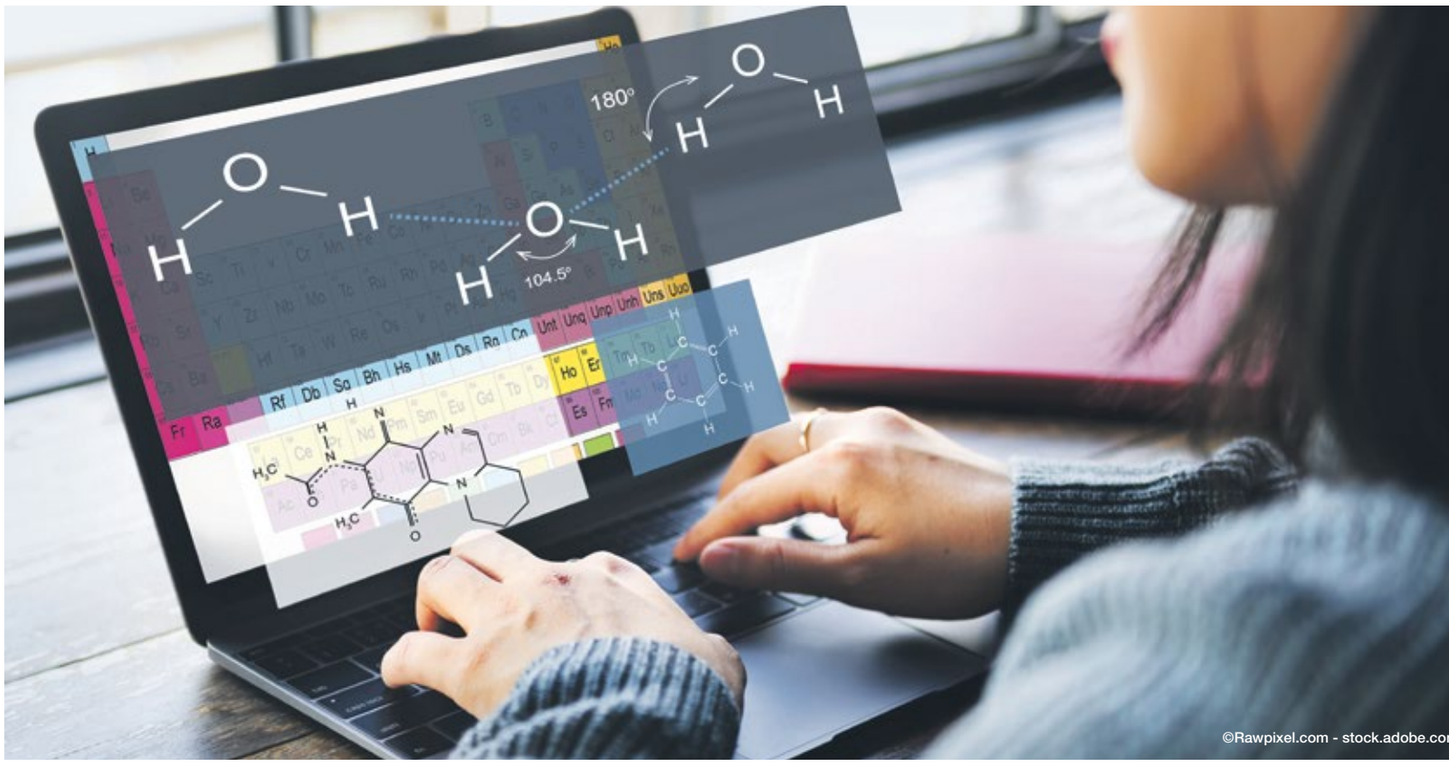
- cycle time reduction
- identification of bottlenecks
- reduction of unplanned downtime
- root cause analysis of quality deviations
- golden batch monitoring
- prediction batch evolution

Contributions in those areas will significantly boost overall profitability of the plants through increases in throughput and quality. This typically can be achieved without structural investments in new equipment or even in completely new plants.

Batch Analytics in Practice

While batch analytics holds a lot of potential for recurring improvements of production costs, there are some practical challenges along the way that need to be tackled in the right way to ensure lasting success.

From experience, the main practical challenges to overcome, are:



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- retrieval, analysis and monitoring of batch data with various expert systems across the value chain of analytics
- analyzing data across multiple assets
- leveraging (decentralized) knowledge about the process

Retrieval, Analysis and Monitoring of Batch Data

Analyzing process data starts with the availability of the relevant data. This is one of the biggest hurdles to overcome when attempting to start a data-driven analysis of a process issue. Data gathering usually takes a lot of time and effort and involves various historian systems and/or lab quality systems. Often data from both places needs to be combined. To solve this issue a live connection between the data analysis platform of choice and the various historian systems from different vendors across the organization is crucial. If the best practice of having the lab data available on the historian is not followed, the process expert also needs an easy way to connect to or at least upload data from the different lab systems that are out there. Now, the process engineer's time is focused on applying his/her knowledge rather than taking care of getting the needed data into place.

Once the relevant data is connected to the analysis platform, the first step of the analytics value chain needs to happen: analyze the data for new insights and diagnose the root cause of the problem. The focus of the analysis should not just be on the recent but on the complete history of process data recorded to unlock the true value of the data and making it available to the process experts.

Analyzing the process involves many interactions within the operation. This, as well as outside factors such as production loads and varied human interactions, means that diverse situations may be rare and scattered throughout the data historian. To solve this problem, there needs to be a search engine for the process data that enables the process expert to quickly retrieve and assess the comparability of the situations of interest across the entire production history. Achieving a direct and efficient connection between the complete data history and the expert knowledge of the workforce unlocks the true value of the process data and is the foundation of any diagnostic exercise.

Diagnostic exercises ideally are based on advanced analytics with easy interpretable results and fast iterations with the process expert. A pattern recognition-based, responsive and easy way to analyze process data is the key to bringing recent advancements where they matter: to the process experts.

Once the process expert solves the issue at hand, ideally a monitor is set up that represents the next step in the analytics value chain. This can be partially done using the capabilities of the historian systems by utilizing value-based alerts and/or calculations. This is not always desired due to:

- overflooding of possibly irrelevant performance monitors
- lack of permission to configure a performance monitor on a central system
- ineffectiveness of value based monitors for batch production
- performance monitoring is implemented on a different system, which creates a dispersed environment

The process expert should have the opportunity to create performance monitors based on his analysis to keep up with the process performance metrics relevant for his role. In addition, the warnings must extend beyond value-based options and enable other dimensions such as dynamic multivariate patterns or fingerprints. If the configured performance monitor is crucial for the operators it can be pushed towards a central system.

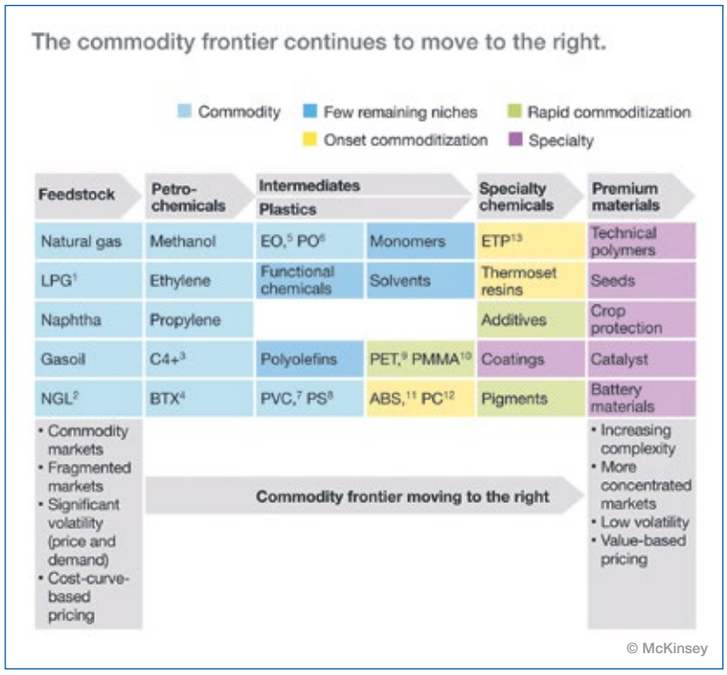

Fig. 1: Commoditization in chemicals

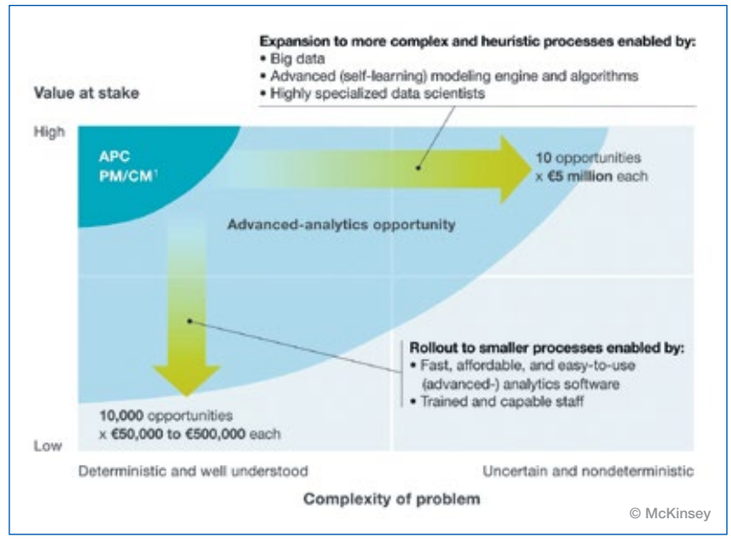

Fig. 2: Buried treasure – advanced analytics in process industries

The last step in the analytics value chain, which is currently rarely tackled, is prediction. As of today, the only way of predicting behavior of batches is the utilization of complex data models. Those models are hard to build, costly to maintain and the result is hard to interpret for the process experts. A solution is to enable predictive capabilities for the process experts. This leads to debottlenecking central data science departments and spreads the use of predictive analytics amongst process experts. For this to work, new ways of prediction beyond complex models, that are fast and iterative, easy to interpret, and robust need to be explored.

To achieve the above-mentioned prerequisites, new possibilities around pattern recognition emerge. Those techniques — which are fast, robust and visually accessible — enable predictions based on the current evolution of the relevant parameters and show the most probable evolution of the running batch based on how similar batches have evolved in the past.

Data Analysis across Multiple Assets

Production processes running multiple parallel lines are very common in batch production. Therefore, not just gathering data from all those production lines but also analyzing and monitoring across assets is a common challenge. Frequently data from identical plants around the world needs to be accessed, which increases the degree of difficulty even more. Gathering and analyzing data on such a scale is a huge time investment and is often neglected due to the restricted time of the process experts. Therefore, enabling all the capabilities mentioned in the previous section across various assets and plants on one platform is crucial to completely empower the organization's workforce in batch analytics.

Decentralized Knowledge about the Process

In a technology driven market the company's success in the segment of specialty chemicals is founded in technological advantages over the competitors. One of the biggest goals of every organization should be retaining knowledge and its availability for the relevant people in the organization. Usually, knowledge is not where it belongs; within a central knowledge base on top of the process data — providing the relevant context for the analysis to everyone who may need it. Hence, a process data analytics platform with an internal possibility of data contextualization or a connection to a central knowledge base is needed to overcome the challenge.

An Example across the Whole Value Chain of Analytics

There are many examples that both illustrate the challenges mentioned above as well as the validity of the proposed solutions. Here, a case of a global specialty chemical company is described, which ranges across the whole value chain of analyze, monitor and predict.

The reaction of a particular product had significant issues with cycle time and quality. Therefore, further investigation by the process experts was needed. Since the cooling behavior is known to be crucial for the outcome of the reaction, focus was first put here.

With immediate access to all the data stored in the historian there was no problem in getting the relevant process data ready for analysis. As the problem just occurred for one particular product, relevant production stretches have been isolated utilizing search queries. Further use of search capabilities resulted in a list of longer batches with quality problems. Statistical and visual comparison of those batches with previously isolated ideal runs clearly showed a signature cooling profile associated with a positive outcome of the batches. Based on those insights, a golden batch fingerprint has been created and used for monitoring and visual benchmarking. In addition, real-time predictions based on the dynamic patterns of the batch evolution have been used by the process experts to anticipate deviations from the ideal behavior.

The value gained from this analysis was a cycle-time reduction of three hours per batch and a significant reduction of quality deviations.

This case shows that empowering the process experts, to easily connect their expertise with the process data based on the solutions mentioned in the previous section (also known as self-service industrial analytics), is crucial to overcome the day-to-day challenges they face when analyzing process data of batch productions. Furthermore, it shows that the outcome is not only significant to reach production goals but also to strengthen the company's market position by decreasing production costs.

Conclusion

In an ever more dynamic market, characterized by rapidly changing environments, immediate financial flexibility is key for a sustainable market position. Operational excellence is a big lever to achieve this flexibility. Data-driven process analysis and improvement is at the heart of operational excellence. Since this puts the process experts of the organization at center stage, it leads to the need of their analytics empowerment on a global scale. Only if the information hidden in the data is efficiently connected to the knowledge in the minds of the process experts, the organization can move towards a proactive data driven process improvement strategy.

On a practical level there are various challenges that need to be solved in the area of data availability, analytics and performance monitoring. Ideally a self-service industrial analytics solution is used, that helps the workforce to overcome those challenges and integrate all process experts rather than working with dispersed knowledge across various systems.

Artur Beyer, industry principal Chemicals, TrendMiner, Hasselt, Belgium

www.trendminer.com

Joining Forces

Kolb Completes Acquisition of Elementis Specialties Netherlands

Kolb Distribution, wholly owned subsidiary of Kuala Lumpur Kepong Berhad (KLK), completed the acquisition of Elementis Specialties Netherlands (ESN), located in Delden, the Netherlands. As of Feb. 28, 2018, ESN is wholly owned by Kolb and renamed to KLK Kolb Specialties. The new business manufactures surfactants and further specialties and will expand the existing Kolb business portfolio in terms of product range and market coverage. The use of the Delden site as another hub for KLK's market penetration strategy will further accelerate growth in the group's downstream chemical specialties business in Europe. CHEManager asked Anja Vonderhagen, Kolb's executive business director, about the reasons for the acquisition of ESN and its further strategy.

CHEManager: Mrs. Vonderhagen, which advantages and/or synergies does Kolb expect from the acquisition of former ESN?

Anja Vonderhagen: KLK Kolb Specialties B.V.—which is the new legal entity name — adds unique capabilities to the KLK OLEO group which will offer additional value to our customers. Their product portfolio is a perfect fit to ours and they are very experienced in technologies which are new to the KLK OLEO group such as phospate esters and quats.

How will this deal expand the existing Kolb business portfolio in terms of product range and market coverage?

A. Vonderhagen: Together with KLK Kolb Specialties we will offer a broader surfactants portfolio and a unique production versatility with our three alkoxylation production sites under one roof. After the successful acquisition and integration of KLK Tensachem in 2014 we have now the fourth site in Europe manufacturing surfactants adding additional specialties to the group.

What will be the benefits of the deal for your customers?

A. Vonderhagen: We are known to our customers to offer solutions with high speed and flexibility.

KLK Kolb Specialties offers a new portfolio with the same mindset: customers first.

Together we can go to the market with a broader portfolio, proven flexibility and speed in working out solutions. Our customers will have access to the extended combination of assets, technologies and know-how to further develop our partnerships. The response from the market on our initial announcement on the planned acquisition back in December 2017 has been very positive. In the last months, we have been asked by some of our key customers to discuss projects involving the site in Delden.

What is Kolb's strategy to expand its market penetration and to further accelerate growth in the group's chemical specialties business?

A. Vonderhagen: This acquisition underlines the strategic expansion of KLK OLEO in Europe. We are committed to growth and will consequently seek to expand our portfolio to better serve our customers.

Kolb is integrated into the broad oleochemicals network of KLK OLEO. With additional technologies and production capabilities, we will continue serving exceptional customer needs.

What challenges are ahead of you integrating the KLK Kolb Specialties business?

A. Vonderhagen: We expect a fast integration and route to market as we did with KLK Tensachem.

In order to achieve this, we will look into the portfolio and production processes to improve efficiency to further strengthen our position in the market.

The Delden team is very enthusiastic as they are now central to the overall group's growth strategy. Nevertheless, we know that communication is key and we take this into account by close teamwork with our new colleagues.

Anja Vonderhagen, executive business director, Kolb

What will be the new branding of the acquired business?

A. Vonderhagen: KLK Kolb Specialties shows the link to KLK and Kolb, both well-known names in the chemical industry. The logo will be the same as for Kolb, the KLK OLEO logo.

The cultural element in M&A integration processes turns out to be a critical success factor. How do you look at that topic?

A. Vonderhagen: We acknowledge this point and are working on it actively. We analyzed the culture of the site in Delden and quickly identified that we have a lot in common. We transported this message to all employees, both from KLK Kolb Specialties and Kolb, focused on joining forces for a common future.

www.kolb.ch

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A Basket of Synergistic Products

How Specialty Distributors Help Customers and Suppliers Meet Market Requirements

In the past decade, specialty chemicals distributor Azelis *has transformed from a decentralized European business into an integrated group with a turnover of €1.8 billion and facilities in 42 countries worldwide.* The owners of the Antwerp, Belgium-based distributor, *private equity company Apax Partners, support Azelis' strategic focus on growing the business through continuously developing its product portfolio and extending its global reach. The expansion covers each of the major regions: Asia, Europe and in particular a transformation in Americas. However, Europe remains an important region for Azelis. Michael Reubold asked Anna Bertona, the company's chief executive officer Europe, Middle East, Africa (EMEA) about her strategy and approach to steer market teams in the region with a particular focus on the company's principal development activities.*

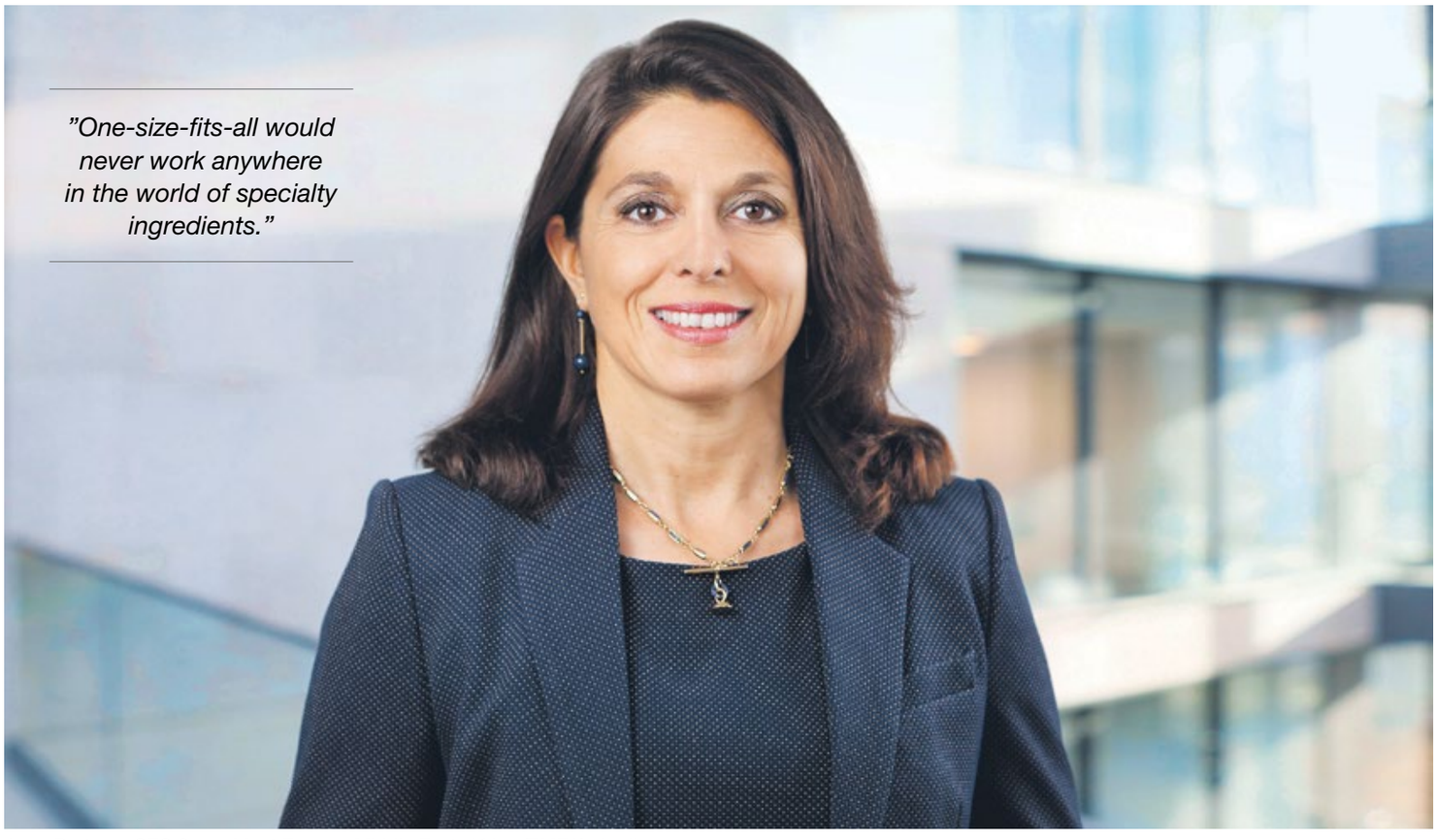
CHEManager: Ms. Bertona, the change of ownership in 2015 has seemingly accelerated the development of Azelis into a global distributor. What role is Europe still playing in the company's strategy?

Anna Bertona: Being a global business that is built on technical expertise and is very much diversified across multiple market segments in life science and industrial chemicals enables us to easily share and build upon this expertise. However, Europe remains important as it is our largest region in terms of sales, customers we serve and people we employ. In addition, it is where our roots lie, it is the region where Azelis was founded and where it is headquartered. Last but not least, Europe is where many of our partners and principals reside, and based upon our success with them in EMEA, many principals have extended their agreements with us to cover APAC.

EMEA is a dynamic market that is increasingly ready to innovate, probably much more so today than three years ago. Furthermore, Europe is the region where a lot happens that influences the rest of the world's economy; this is where competitive landscape is very dynamic, where some of the environmental and consumer trends originate from, where some of the important new legislation is passed on, to name only some. Having said that, it is important to remember that we all operate in the global economy today where one region cannot be seen independently from another. Being a truly global company, we closely follow all developments and we share learnings and best practices across all regions.

EMEA itself is a quite diverse region in terms of market size, maturity, and demands. Can you operate in this region with a one-size-fits-all approach?

A. Bertona: One-size-fits-all would never work here. As a matter of fact, it would not work anywhere in the world of specialty ingredients. We believe in a well-balanced mix between local and regional. Local autonomy in the countries is supported by regional marketing and infrastructure services. Remaining local is very important however as it enables us to stay close to our customers as well as continue to focus on country dynamics and developments. The local as-



"One-size-fits-all would never work anywhere in the world of specialty ingredients."

Anna Bertona, CEO & president Europe, Middle East, Africa (EMEA), Azelis

pect of our business is significant for different reasons. Not only do the languages and laws differ from one country to another, the implementation of legislation can be different too. Local tastes and needs are something we need to have solutions for, which we can do only when we have a true presence in each market. For example, bread in France is very different to bread in Sweden, and customers in Greece will need a very different range of skin protection products than customers in Norway. Remaining truly local throughout Europe is the only way to ensure we are the best local champion and have the right solution for that specific market.

How do you respect the differences of the geographic and market areas in your operating strategy?

A. Bertona: We benefit from our large scale as we can leverage the fact that we are present in a large number of countries in Europe. We coordinate lab activities across the regions, we share best practices and knowledge, and we complement one another's capabilities and skill sets. This often translates into solutions for our customers that otherwise would not have been possible.

What do you think are Azelis' strengths in the EMEA region?

A. Bertona: If I was to simply summarize Azelis' strengths in EMEA, I would say: highly educated people, large laboratory footprint, broad customer base and high customer satisfaction, excellent compliance and regulatory knowledge, and state of the art infrastructure.

Over time we have invested a lot in the laboratories across the whole group and in EMEA specifically. There are 24 labs in EMEA, each dedicated to a specific market segment that supports our customers and our principals. In addition, we have some of the best people in the industries we serve who have built a lot of knowledge and expertise and who are highly appreciated outside Azelis too. Furthermore, it is the lasting partnerships with our partners, quite a few of which have existed for 40+ years.

Our size is another one of our strengths. Over the years, we have built a solid pan-European presence, not only in Western Europe, but also all over Eastern Europe, a true foot on the ground in all the countries we serve. This gives us an opportunity to leverage prospects in various local markets, combined with the scale of the international organization.

And where do you see specific challenges of your business?

A. Bertona: We do all we can to ensure a high-quality, stable service to our partners however we do not always have all the factors in our hands. For example, from time to time there can be a raw material shortage, often as a result of macroeconomic movements or individual production issues of our suppliers, and this is something we need to manage when it happens. It is not good when it happens, as we do not want to disappoint our customers, but we try to have mechanisms in place that will minimize any potential negative effects of this.

Azelis' business philosophy is centered on technical services. What does it take to provide these services to your principals and customers on a high level?

A. Bertona: We need to have highly qualified people with the technical know-how to understand our customers' requirements and to provide solutions to their issues. All our sales force have solid technical backgrounds. They are dedicated to their market segments and typically have several years' experience in the segments they serve, helping them to understand better the issues our customers are facing. Our laboratories play a critical and dual role in all that. On one hand, we train our people in the laboratories, enabling them to stay up-to-date with innovations from our principals. On the other hand, we also give internal training on market trends and end-product manufacturing. All of this helps our people to understand our customers' issues better.

This strong technical expertise perfectly supports our lateral value chain approach. We want to be a full solution provider for our customers. We want to be able to provide our customers with the ingredient they need for their production process. If we identify an ingredient that is currently not in our portfolio, we will then identify suppliers of such ingredients and we will actively go after them in order to ensure that full and complete lateral value chain. Seeing that our customers value this only gives us more reassurance this is the best approach we can have.

Innovation is a key growth driver in the specialty chemicals market. How can distributors effectively trigger innovation on the supplier and the customer side?

A. Bertona: A specialty distributor has the advantage of offering a lateral value chain to its customers, a basket of synergistic products. We offer products from many different suppliers and also have the knowledge how these substances and ingredients interact best with each other, thus helping our customers to meet some of the most stringent market requirements. Closely following the market developments ourselves, we often proactively offer formulation solutions to our customers and this is highly appreciated as it shortens their R&D and time-to-market. Not only have we thought up something new, but we have already tried and tested it before offering to customers, which then makes their process much shorter and more efficient. The distributor makes new technology more accessible for smaller customers who would not normally be served by big suppliers directly.

Furthermore, distributors often serve the mid and smaller customers, which in some industries are more often the innovators compared to the larger accounts. This knowledge is not only valuable for the customers but also for principals as an input for their R&D. By feeding this market information back to our principals we keep them abreast of new needs and trends on the market.

www.azelis.com

Read the complete interview with Anna Bertone on CHEManager.com..

Solutions for the World of Tomorrow

With a Focus on the Automotive and Environmental Industries Asahi Kasei Takes on Europe

Following the founding of Asahi Kasei Europe (AKEU), based in Düsseldorf, Germany, and the opening of a European R&D center in Dormagen, Germany, the Japanese chemical company has built on its marketing and sales activities. The newly designed Asahi Kasei Europe exhibition center at the European headquarters demonstrates solutions for the world of tomorrow developed by Asahi Kasei and presents the materials manufacturer's products and technologies for the automotive, medicine and health, renewable energies and lifestyle markets. According to Asahi Kasei Europe president, Hideki Tsutsumi, the company aims to grow in Europe by providing value through collaboration and synergies.

CHEManager: Mr. Tsutsumi, Asahi Kasei Europe was launched in order to accelerate the business expansion in Europe. What is your ambition and what are your goals in Europe?

Hideki Tsutsumi: We are still setting up the base for expansion here in Europe. AKEU was established in April 2016 and is the operational headquarter for the business activities of the Asahi Kasei group in Europe. In 2016 we published our mid-term plan "C's for tomorrow 2018", where we decided to strengthen our activities on the European market. We are aiming at tripling the global turnover until 2025. To achieve that, the European market will play an important role.

The number of employees in our headquarters in Düsseldorf and at our R&D center in Dormagen has been increasing gradually and will further increase within 2018. We are now considering the set-up of a plastics production facility in Germany. This will enable us to react to our customers' needs more quickly and flexibly.

Where will be your main focus in Europe in terms of market sectors?

H. Tsutsumi: The main focus of our activities in Europe lies on the expansion in the European automotive industry. Asahi Kasei provides a broad range of products and technologies and we believe that our sustainable products perfectly match the needs of the European automotive industry. Besides the automotive industry, we also provide products and technologies for other industries, for example electronic products like sensors, fibers for the textile industry or electrolyzers for hydrogen production, a technology we expect to be in high demand in the coming years.

Hideki Tsutsumi, president, Asahi Kasei Europe

As Europe is a mature market with low one-digit growth rates, business expansion in most sectors means crowding out existing suppliers. This holds true also for the automotive industry. What is your strategy to expand this business?

H. Tsutsumi: Regarding the automotive industry, one key advantage Asahi Kasei has to offer is the broad range of highly innovative products and technologies, from lightweight, high-performance plastics and battery separators to rubber and sensors for tires and textiles for the car interior. So we are providing the whole package, all from one single supplier.

Besides that, the shift in powertrain technology to electric vehicles and also the CO_2 reduction targets the car manufacturers have to achieve in the coming years are already changing the market and its needs. Europe is also the most important market in terms of regulations for the environmental industry. We are a leading company in key technologies fitting these changing needs.

A customer could think about bringing a new materials' supplier in for several reasons, be it price, trust and reliability, quality, reputation or innovative strength. Where do you see AKEU's core competences and qualities?

H. Tsutsumi: Our strength is the combination of all these factors. Our goal

The concept car "AKXY" showcases a variety of Asahi Kasei's automotive products and technologies.

is to always strive for new innovations while worshipping our 96-year history. We are always thinking ahead, thinking of how we can provide the best solutions and advanced technologies to the markets, and we have proven that in the course of our history.

Research & Development is a cornerstone for innovation. In October 2017 Asahi Kasei opened a new R&D center in Dormagen. How will it support your growth strategy?

H. Tsutsumi: The main focus of our R&D center is strengthening the technical customer support in Europe. Besides that, we aim at developing new product grades and applications for the European market. We want to

> Asahi Kasei is an innovation-driven company.

achieve that by closely working together with European companies and universities and by continuously expanding our network.

How can Asahi Kasei compete with European chemical companies in terms of innovative capacity?

H. Tsutsumi: Asahi Kasei is an innovation-driven company. Our group slogan is: "Creating for tomorrow". We always aim at creating completely new products and technologies to contribute to society. Providing solutions to reduce energy consumption and CO_2 emission is our contribution. We can rely on a strong worldwide R&D network and are proud to say that we can look back on an impressive list of market changing revolutionary inventions, such as the lithium-ion battery and the electronic compass.

I believe that especially for the automotive industry we provide sustainable products that perfectly match the current and upcoming needs of the industry, such as eco-friendly, intelligent tires, which lead to CO_2 reduction and lower fuel consumption. We also provide engineering plastics for lightweight components as well as other components for electric cars, as for example battery separators for lithium ion batteries.

Besides the automotive industry, we provide our electrolyzer technology to produce hydrogen from electric power. Hydrogen can be used to store energy and can further be transformed into alternate fuels.

Asahi Kasei is working on many innovation projects like the AKXY concept car or the Hydrogen initiative. What are your plans and milestones regarding these projects?

H. Tsutsumi: The automotive and energy industries will be two main growth drivers for Asahi Kasei's business in Europe. With our concept car AKXY, which incorporates 27 products and technologies by Asahi Kasei, we show our cross-divisional strength and innovative power for the automotive industry. We are proceeding with the preparations to present AKXY to customers in Europe.

We started to intensify our activities in the hydrogen field and are aiming to expand this business. The field of environmental business needs high-level technology and we think that this is exactly our strength we can put to use. The hydrogen business is one promising solution to problems such as global warming and air pollution. That is why we are strengthening our activities in this business area.

Currently, we are proceeding with the set-up of an alkaline water electrolysis system demonstration plant within the Hydrogen Application Center in Herten, Germany. The plant is scheduled to start operation in April 2018, producing hydrogen from wind energy.

AKEU is participating in the three-year multi-partner ALIGN-CCUS project. What is the goal of this project and what will AKEU contribute?

H. Tsutsumi: The ALIGN-CCUS — short for: carbon capture, utilization and storage — project is a partnership project which runs from 2017 to 2020 and consists of 34 research institutes and industrial companies

> We are aiming at tripling the global turnover until 2025.

from five European countries. The project received €15 million funding from the European ERA-NET ACT fund and aims at transforming six European industrial regions into low-carbon centers, mainly by optimizing and reducing the costs of carbon capture technologies as well as developing the use of CO_2 in energy storage and conversion. Asahi Kasei participates in Work Package 4 for large-scale energy storage and conversion. We provide an alkaline water electrolysis equipment to produce hydrogen. Together with CO_2 captured at power plants the hydrogen can be transformed into fuels such as methanol and dimethyl ether. This system can be scaled-up and has high energy exchange efficiency.

Asahi Kasei has an operational strength to integrate different divisions. What is your special success factor regarding this?

H. Tsutsumi: Nowadays, interdisciplinary approaches are key factors for success. It is difficult to provide solutions to the customer just from one viewpoint. Asahi Kasei is active in a great variety of businesses. Bringing specialists from different fields together and let them develop an interdisciplinary solution to the customer's problem is our strength.

Your growth objectives for 2025 are quite ambitious: to triple your sales to more than €2 billion. What makes you confident that Asahi Kasei will reach this goal?

H. Tsutsumi: Surely, the automotive industry will be the main driver for us. The car manufacturers will have to apply new technologies to reduce the CO_2 emissions and to adapt new powertrains. Our solutions perfectly match these needs.

In the field of environmental technology Germany's drop-out of nuclear power will be a big step. Renewable energies and storage technologies will get more and more important. Our electrolyzer technology to produce green hydrogen perfectly addresses these changes.

www.asahi-kasei.eu

Chemspec Europe

Chemspec Europe is the key platform for manufacturers, suppliers and distributors of fine and speciality chemicals to showcase their products and services to a dedicated audience of professionals in the industry sector. The product portfolio of this international exhibition covers a maximum range of fine and speciality chemicals for various industries. Excellent networking opportunities and top conferences presenting the latest results of ongoing R&D projects round-off the show. **www.chemspeceurope.com**

CPhI Worldwide

CPhI Worldwide, together with co-located events ICSE, InnoPack, P-MEC and FDF, hosts 2,500+ exhibitors from more than 150 countries gather at the event to network and take advantage of free industry seminars. Every sector of the pharmaceutical market is represented under one roof. In 2018, CPhI Worldwide will launch a new bespoke and independently branded biopharma event, BioLive, which will provide visitors and exhibitors with additional capability to network and do business in dedicated areas. **www.cphi.com**

Specialty & Agro Chemicals America

Specialty & Agro Chemicals America focuses on the chemical products and technologies that have specific applications for the agrochemical and specialty chemical manufacturing markets. The event's mission and vision is to be a forum that narrows the focus and renews the value for chemical industry attendees. Participants cover a diverse range of chemical end-uses including adhesives & sealants, agriculture & crop protection, coatings & paints, cosmetics & personal care, flavors & fragrances, oilfield & lubricants, pharmaceuticals, plastics & composites, and water treatment. **www.chemicalsamerica.com**

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The largest USA-based API show attracts annually 700-800 chemists, business development personnel and buyers from the pharmaceutical, biotech, chemical, and chemistry services industries. It focuses on API development spanning early drug discovery through chemical development and commercial supply. Attendees are executive scientist "buyers" from pharmaceutical companies responsible for sourcing starting materials, intermediates, active ingredients, and commercial supply and experienced in working with Contract Research and Contract Manufacturing Organizations. **www.chemoutsourcing.com**

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