CHEManager INTERNATIONAL 3/2022

©alphaspirit - stock.adobe.com

Markets & Economy

Evolution of Chemical Industry M&A, Rewriting the Rules for Chemical Distribution, Digital Transformation in the Chemical Sector, EU Energy Supply

Pharma & Biotech

The Future of Outsourcing, Carve-out as Transformational Opportunity for New CDMOs, AI Validation in the Pharmaceutical Industry

Innovation

Sustainable Industrial Wastewater Treatment with Ferrate(IV), Unique Continuous Reactor for Efficient and Sustainable Chemical Production

WILEY

From the Leader in Spectral Data

Accelerate Spectral Analysis with KnowItAll

Powerful Software. Quality Data. Results You Can Rely On.

KnowItAll Solutions for IR MS NMR Raman UV-Vis

Supports multiple techniques and instrument vendor formats to streamline your workflow.

KnowItAll offers solutions to **identify, analyze, and manage your data**.

Combined with the **world's largest spectral reference databases**, it provides one of the most advanced technologies available for fast, reliable spectral analysis.

And with the **NEW KnowItAll 2023**, Wiley continues to add even more tools to automate and accelerate analysis!

Learn more or get a trial
www.knowitall.com/chem2022

WILEY

©macgyverhh - stock.adobe.com


©Grispb - stock.adobe.com


©scharfsinn86 - stock.adobe.com


©Costello77 - stock.adobe.com

Markets & Economy

Pharma & Biotech

Innovation

The Evolution of Chemical Industry M&A

Chemical Companies Can Use Transactions to Reshape and Thrive in an Ever-Evolving Industry

©Parradee - stock.adobe.com

Every year, the chemical industry sees hundreds of mergers and acquisitions (M&A). This constant churn has meant that over the last decade, approximately 20% of industry revenue has changed ownership. Traditional M&A drivers, such as consolidation and portfolio extension, are still important, according to our research. But many transactions also show that the nature of M&A is evolving, as chemical companies look for ways to contend with ongoing volatility and move to a more sustainable future.

M&A is an important tool for change in the chemical industry. Like products, applications and processes, it is a source of growth and innovation for chemical companies as they seek to optimize their portfolios, adopt new business models and navigate their way through a constantly evolving industry.

A Snapshot of the Industry M&A Landscape

In recent years, the chemical industry has seen several exceptionally large transactions and several waves of consolidation. But beneath these high-profile spikes in activity lies a steady level of M&A that has continued, even through global economic slowdowns.

Most of these transactions, if we look at total deal value, have taken place within companies' home markets. For example, our research—the Accenture Chemical Industry M&A Study—revealed that deals where North American buyers targeted North American companies account for a significant percentage (75%) of their transactions. Similarly, deals with European buyers and sellers are in the majority (55%) in Europe. But there is some notable inter-regional activity. A large percentage (42%) of deals involved European buyers focused on North American companies, with roughly one-third (35%) of Chinese buyers fixed on European companies and about one-fourth (24%) of Japanese/South Korean buyers turning to North American targets (fig. 1)

So, what's behind these cross-regional transactions? It may relate to the benefits that can be accrued from extending into regions that have notable advantages. For example, it seems likely that companies in Japan and South Korea, which have mature chemical industries with a good technology base, are looking to North American targets to make further gains in their specialty positions. Chinese chemical companies, on the other hand, are often in need of more advanced technology, which likely drives their interest in European companies.

The Drivers of M&A

Our analysis of buyer rationales behind M&A transactions suggests that chemical companies are fairly risk-averse in their approach. With consolidation and portfolio extension cited by buyers as the rationale for a combined 67% of transactions, it seems that they are focusing largely on what they already know rather than looking to diversify into entirely new areas. Even the 11% of transactions where forward/backward integration was cited as the driver for buyers could reflect an interest in wanting to expand the existing business without taking significant risks.

For their part, sellers cited a range of reasons for their actions. More than half the transactions involved the sale of a whole company, with "investor exit" and "synergies" being the most common reasons. About one-fifth of the transactions involved the sale of a segment of the business to refocus the portfolio, or because the segment was underperforming or encountering financial or antitrust issues.

The research also uncovered two trends that are changing the nature of M&A in the industry: the increased participation of private equity firms, and the growing influence of greenhouse gas (GHG) emission requirements in M&A-related decisions.

Private Equity is Raising the Bar

Private equity is playing an increasingly active and prominent role in the M&A arena. In the last ten years, private equity has executed between $16 billion and $23 billion in transactions each year—a figure that accounts for 9% to 43% of total transaction value annually, and 23% of total transaction value on average over the entire period. Some of these deals have involved relatively small companies, but many have been in the multibillion-dollar range.

Private equity groups have proven to be highly effective players in chemical industry M&A. Frequently, they buy

Bernd Elser, Accenture

assets from chemical companies, increase their value over the course of a few years, and sell them for substantially more. In general, they tend to sell assets at higher multiples compared to chemical company sellers (fig. 2).

This suggests that chemical companies are missing out on higher multiples because they are foregoing opportunities to restructure and optimize businesses before selling them. Setting up lean and simplified organizational structures and cost-effective business platforms, business services and operating models typically enables sellers to capture more value in a transaction, especially if the improvements are documented and evident in the company's actual financial performance.

At times, chemical companies may believe that making those changes is too daunting a challenge. However, it is striking to see how quickly such changes can be implemented by new owners after a merger or acquisition—a clear demonstration that such value-creating changes are feasible and implementable. However,

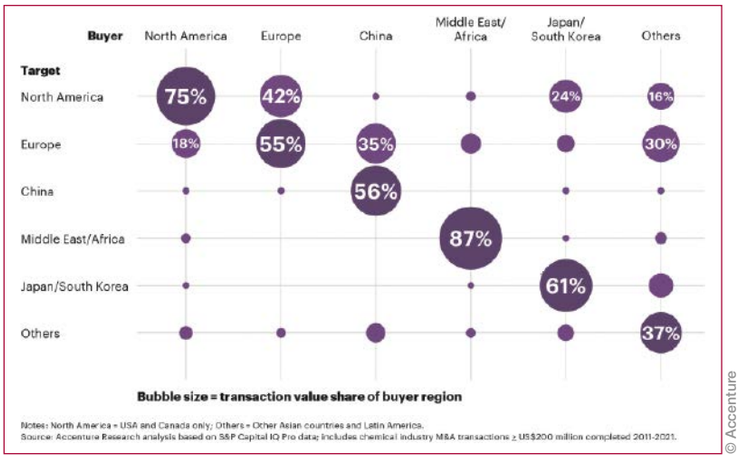


Fig. 1: Regional preferences in M&A

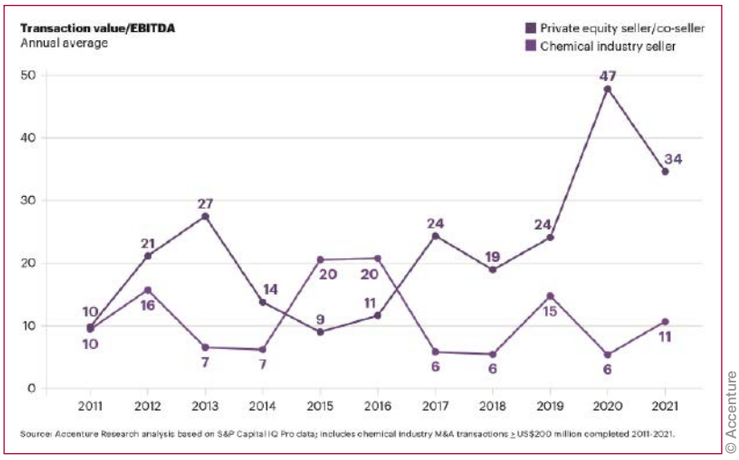


Fig. 2: Private equity vs. chemical company multiples in M&A

such efforts are often impaired by the seller organization's legacy mindsets and management attitudes. For chemical companies considering a sale, it is important to keep in mind the value that such efforts can bring. Typically, each million dollars in cost savings and profit improvement has the potential to create millions more in value, based on the transaction multiple.

Factoring in GHG Emissions

Reduction in GHG emissions—a major issue in the industry—appears to be emerging as an important factor in M&A decisions. In order to meet their net-zero goals, chemical companies will have to make significant capital investments in GHG emission-intensive businesses such as ammonia, ethylene and propylene production. In Europe, for example, according to research we conducted with NexantECA, achieving the EU Green Deal's 2050 net-zero GHG emissions goal will cost the industry about €1 trillion in direct improvements, the relocation of plants to be near green energy sources, the cost of downtime incurred through the transition, and so on.

Those demands appear to be playing a role in M&A. The research identified a pattern in which companies are selling businesses that produce both higher levels of GHG emissions and relatively lower financial returns. For example, one company divested a large fertilizer business that contributed 50% to its GHG emissions but only 5% to its EBITDA, while another divested a synthetic rubber business responsible for 25% of the company's emissions and just 9% of EBITDA.

For businesses looking at these costs, the question is whether to invest in reducing GHG emissions or to divest the GHG-intensive assets to get them off the books. In some cases, at least, they may be choosing the latter approach. It seems clear that GHG considerations, while not the sole driver of M&A activity, appear to be having a growing influence on the decisions being made.

What Chemical Companies Can Do

M&A has played a prominent role in the chemical industry over the last decade, and that can be expected to continue in the years to come. Understanding M&A trends and how to best approach these deals will be key to engaging in successful and value-creating transactions.

One important action is the deployment of technology as a value lever for M&A. This will allow companies to capture the benefits from insights, automation and future-ready platforms for divestments and to accelerate the integration of acquired businesses. On a related note, chemical companies should aim to complete restructuring efforts prior to a sale in order to reduce the chance of leaving value (in the form of increased multiples) on the table. They should also take a fact-based approach to assessing the impact that transactions will have on GHG emissions to avoid conducting "fire sales" of GHG-intensive businesses.

Given the importance of M&A in the industry, chemical companies should view M&A as a core capability with an end-to-end perspective that extends from well before transactions to well after. And they can't forget about people and culture, as effective change management is essential, particularly for the small but influential group of individuals in leadership positions. Such capabilities will be key to helping chemical companies use M&A to reshape themselves and thrive in a constantly evolving industry.

Bernd Elser, a Managing Director and Global Chemicals Lead, Accenture, Frankfurt am Main, Germany

- bernd.elser@accenture.com
- www.accenture.com

Rewriting the Rules for Chemical Distribution

Distributors Must Focus on the Needs of their Customers

The needs of chemical producers have changed significantly over the past few years. So, too, have the rules for distributors that wish to win in today's business environment. Unlike many industries, distributors have weathered the pandemic well and are poised for growth; they cannot be complacent. To make the most of the opportunity, they will need to deepen their capabilities significantly in some key areas.

©KPs Photography - stock.adobe.com

To better understand how chemical distributors have fared over the past six years and what their future looks like, we compiled performance data and surveyed their producer customers worldwide. 400 senior executives from commodity and specialty companies took part in the survey, with a representative sample from the Americas, Europe, the Middle East and Africa, and Asia Pacific. The study has eight key findings.

1. Covid-19 has Had Little Negative Impact on Chemicals Distributors

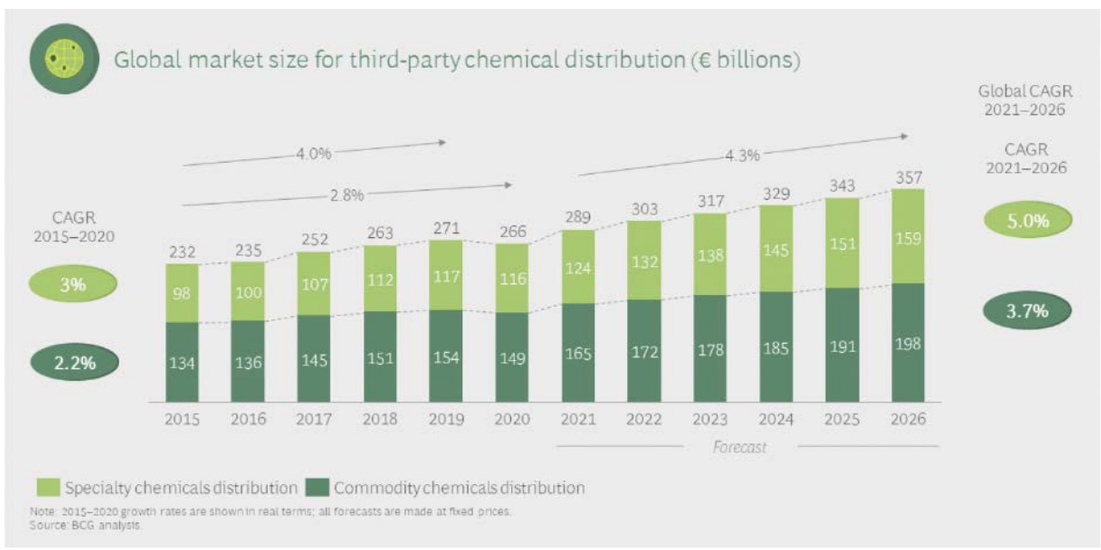
Between 2015 and 2020, the global chemical distribution market grew by a compound annual growth rate (CAGR) of approximately 3%, reaching nearly €270 billion (fig. 1). Surprisingly, in 2020, when the pandemic was in full force, the chemical distribution market shrank by only 2% to 3%; by contrast, manufacturing output declined by nearly 5%.

During the same five-year period, specialty distributors outperformed commodity distributors, with CAGRs of 3% and 2.2%, respectively. A few specialty distributors grew by more than 10% annually. Although both commodity and specialty segments contracted in 2020, the revenues of a few specialty distributors continued to grow by more than 30% year over year between 2019 and 2020.

Given that Covid-19 snarled supply chains across industries, why did the chemical distribution sector prove so resilient? Rising demand in underlying markets including food, pharmaceuticals, personal care, and livestock feed likely played a role. But the key reason for their resilience is the position chemical distributors hold in the value chain: they provide critical support services for producers and downstream customers alike.

Many distributors, for example, store manufacturers' excess output in local warehouses or pan-regional networks. During times of unpredictable end-user demand, we would expect the need for such storage facilities to be high. Specialized distributors also provide producers with industry expertise, as the rise in outsourcing demonstrates (see #3 below)

At the same time, distributors can provide the downstream customer with reliable sources of supply because they have deep, multi-source supply networks. If distributors cannot procure a particular product from the usual producer, they often have backup sources to draw on.



© BCG

Fig. 1: The outlook for chemical distributors is upbeat.

2. The Growth Trajectory for Chemical Distributors Remains Positive

According to our newly updated model, the CAGR of the global chemical distribution market will accelerate to approx. 4% for the next five years. The strong market fundamentals seen over the past few years are unlikely to change in the mid- and long term.

The APAC market will likely grow the most, with a 2021-26 CAGR of 5% to 6% due to increasing demand for chemical products in Asian markets, which is increasingly served by domestic producers as well as local chemical distributors. The North American and European markets are likely to experience lower growth, with a projected CAGR of 2% to 3%, which is on par with their GDP.

Specialty segments will continue expanding at a faster rate than com-

modity segments. According to our projections, the revenues of specialty and commodity distributors will grow at a CAGR of approximately 5% and 3.7%, respectively.

The pandemic did not slow the high pace of M&A. Chemical distributors continue to use M&A as a crucial way to drive growth.

3. Outsourcing Rates Differ by Region, Product Focus and Segment

More than 70% of survey participants intend to increase their use of third-party distributors globally. According to our respondents, third-party distributors help expand geographic reach; expand reach to smaller customers; enable producers to increase focus on core business; improve service for some end-customers; and reduce operational and overhead costs.

We expect that over the next five years the overall distribution outsourcing rate will continue growing slightly —0.5% p.a., down from more than 1% p.a. in the past. But it will vary substantially between regions, product focus, segments, and even sub-segments.

4. Diversification is Picking up Speed

For many years, producers consolidated their portfolios of distributors worldwide to reduce supply chain complexity and cut costs. That is no longer the case. More than 40% of our respondents on average said they diversified their portfolios of distributors over the past three years. Nearly 60% expect to do so over the next three (see fig. 2). The push to diversify is particularly strong in Europe.

As markets become more competitive and customer expectations rise, producers are realizing that no single distributor can be best in class in all regions. The key, rather, is to find distributors with top capabilities in the regional and local-segment combinations that contribute the most to the producer's bottom line. That means working with many different distribution companies—a trend at odds with efforts to reduce supply chain complexity. As the bar for relevant expertise rises, the shift to diversification is likely to continue.

5. Chemical Producers Switch to Different Distributors less Often

45% of producers worldwide said they were likely or very likely to switch distributors in 2018 (see fig. 3). By contrast, only about 17% said they are likely or very likely to switch currently. Nearly 35% said they are likely to change distributors in 2024. In times of crisis, producers look for stability and are loathe to switch partners. The numbers for switching are higher in Europe because companies there are looking for access to new regions and customers, distributors with better reputation, and compliance with new supply chain laws. We believe that 2021 is an outlier due to the pandemic, and that switching is on the wane: distribution partnerships have matured and become an essential part of doing business. The partners invest in each other when developing a relationship, esp. in specialty segments, making switching disruptive.

6. Distributors with a Strong Market Position and Expertise Score Highest

When asked to score distributors on a wide range of attributes, producers gave their highest scores to commodity distributors with a strong po-

Continued Page 8 ▶

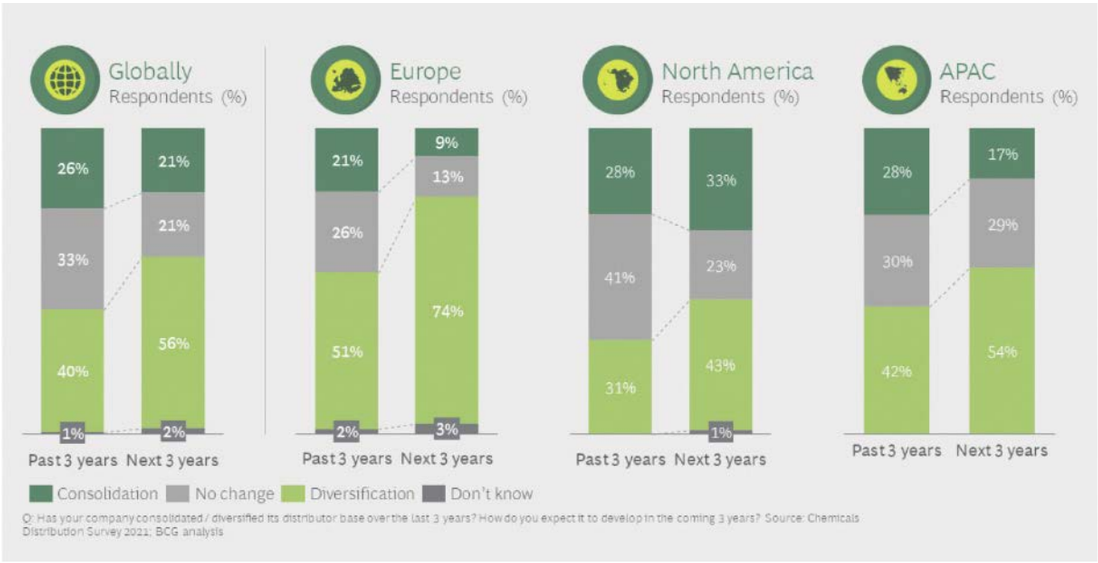


Fig. 2: Producers expect to diversify their distributor portfolio, especially in Europe.

Fig. 3: Producers are less likely to switch distributors over the long term.

sition in the market (see fig. 3). Both specialty and commodity distributors were considered equally strong for the attribute of next-highest importance – product and application expertise. Specialty distributors scored highest in the following dimensions of digital maturity/offering, global reach and sustainability performance.

These findings suggest that specialty distributors would be well served to improve their position and knowledge of local markets, while commodity distributors should think about improving their digital and sustainability capabilities as well as global reach.

7. ESG is now Part of Producers' Criteria for Selecting Distributors

Having become a key consideration for producers across the chemical industry, environmental, social, and corporate governance (ESG) is now playing a role in the distributor selection process. More than 90% of survey respondents said that they expect sustainability to be a major driver of distributor selection in the next three years. ESG considerations are especially critical in the specialty segment.

Some ESG criteria, such as low energy consumption and the fulfilment of highest government standards, will probably skyrocket in importance compared to other criteria. Capabilities in areas with KPIs such as emissions will also gain importance as producers look for ways to assess potential partners.

Emphasizing the urgency of sustainability in their product portfolios and brand positioning, many producers are increasingly looking for distributors that do the same.

Distributors that embrace sustainability over the next few years will be poised to differentiate themselves and capture market share.

8. Digital Skills Become Table-Stakes

Producers are increasingly looking for distributors who can collaborate digitally with them. Customer relationship management (CRM) has seen the largest increase, from less than 20% of producers in 2018 to more than 50% today.

Many producers were already working digitally with distributors when Covid-19 hit. The pandemic only accelerated the trend.

Digital collaboration will continue to grow over the next three years. By 2024, approx. 85% of producers will be working digitally with distributors across a wide range of areas, from technical customer support to automatic reordering and replenishment.

Three Focus Areas

First, as producers look for localized expertise, distributors will need to build expertise in the specific geographic-segment combinations. In the past, distributors tried to become "jack of all trades," with outstanding capabilities in all parts of the world, because that's what producers were looking for. But as producers increasingly look for regional-segment specialists, distributors need to change their sights accordingly.

Second, given the growing importance of ESG, distributors must embed sustainability into the products and services they provide customers. It was not long ago that distributors treated ESG capabilities as simply "nice to have." With the recent revelations about climate change, however, ESG expertise is now a "must have."

Equally important, as producers increasingly rely on digital collaboration to do business, distributors will need boost their digital capabilities – they are the only way to avoid disintermediation by producers looking to adopt a direct sales model.

Outlook

Having survived the pandemic so far in good condition, distributors are well positioned to grow, provided they understand how the rules for winning have changed. Distributors that keep their customers' needs front and center will be best positioned to succeed, regardless of what the future brings.

Tobias Mahnke, Managing Director and Partner, BCG, Munich, Germany
■ mahnke.tobias@bcg.com

Christian Hoffmann, Partner and Director, BCG, Munich, Germany
■ hoffmann.christian@bcg.com

Adam Rothman, Managing Director and Partner, BCG, Chicago, USA
■ rothman.adam@bcg.com

Robert Blaudeck, Lead Knowledge Analyst, BCG, Munich, Germany
■ blaudeck.robert@bcg.com

Yehia Amar, Project Leader, BCG, Frankfurt, Germany
■ amar.yehia@bcg.com

■ www.bcg.com

Due to Rising Energy Costs: Europe's Generic Drugmakers may Cut Output

As Reuters news agency reported at the end of September, European drugmakers have warned that they could stop producing some cheap generics due to rising electricity costs and are calling for a review of the pricing of these medicines. This is the latest industry response to the worsening energy crisis.

Generic industry lobby group Medicines for Europe, which represents companies such as Teva, Novartis' Sandoz and Fresenius' Kabi business, has sent an open letter to the energy and health ministers of EU member states.

The EU's 27 energy ministers met two days later to reach agreement on measures to ease Europe's energy crisis, with a levy on windfall profits from fossil fuel companies and a cap on gas prices under discussion.

A spokesman for the Czech EU presidency, which was responsible for preparing and chairing the meeting, confirmed receipt of the letter but said Friday's talks were intended to approve proposals from the European Commission. So far, these did not include solutions specifically aimed at drugmakers.

The letter was also addressed to the Commission, which said it would respond „in due course."

According to the letter, electricity prices for some drug factories in Europe have increased 10-fold and raw material costs have risen 50% to 160%, Reuters reports.

The letter's authors call for the pharmaceutical industry to be excluded from EU measures to reduce electricity consumption and for the off-patent medicines sector to be included in the relaxed rules on state aid to support the economy.

Generic drug associations in member states are also asking national health authorities for more flexibility in drug pricing, according to Medicines for Europe.

Medicines for Europe's director general Adrian Van Den Hoven told Reuters that higher energy costs were hitting a sector that was forced to consolidate due to price pressure, making the market more vulnerable to supply outages and shortages.

Standard infusions for hospitals are among the most energy intensive drugs to produce because they need to be heated and cooled for sterility. The same goes for the fermentation process behind commonly used antibiotics and therapeutic hormones, he said.

The issue centers on the pricing regime. Off-patent medicines are typically sold by low-cost drugmakers at prices set by national health agencies or insurers' associations, which frequently also cut prices.

Generics account for about 70% of all dispensed medicines in Europe, many of them to treat serious conditions such as infections or cancer but make up only 29% of the region's drug bills, according to the lobby group.

The surge in energy costs risks undermining a recent push to boost medicines production in Europe and make the region more self-sufficient after the Covid-19 pandemic exposed a dependence on suppliers abroad and led to a breakdown of certain supply routes. (rk)

EU Energy and Supply: What Will Happen Next?

The European Commission Proposes an Emergency Intervention in Europe's Energy Markets

The European Commission proposed last month (Sep. 14, 2022) an emergency intervention in Europe's energy markets to address recent dramatic price rises. The European Union (EU) is confronted with the effects of a severe mismatch between energy demand and supply. To ease the increased pressure this puts on European households and businesses, the Commission is taking a next step in tackling this issue by proposing exceptional electricity demand reduction measures, which are designed to help reduce the cost of electricity and that would redistribute the energy sector's surplus revenues to final customers.

This new proposal follows previously agreed measures on filling gas storage and reducing natural gas demand to prepare for the upcoming winter. The Commission is also continuing its work to improve liquidity for market operators, bring down the price of natural gas, and reform the electricity market design for the longer term.

First Measure: Reducing Electricity Consumption

The first measure proposed by the Commission to tackle high prices is to reduce demand. To target the most expensive hours of electricity consumption, when gas-fired power generation has a significant impact on prices, the Commission proposes an obligation on

Patricia Van Arnum, DCAT

EU member states to reduce electricity consumption by at least 5% during selected peak price hours. EU member states will also be required to identify the 10% of hours with the highest expected price and reduce demand during those peak hours. The Commission also proposes that EU member states reduce overall electricity demand by at least 10% until Mar. 31, 2023. They can choose the appropriate measures to achieve this demand reduction, which may include financial compensation. The Commission says that reducing demand at peak times would lead to a reduction of gas consumption by 1.2 billion cubic meters over the winter and that increasing energy efficiency is also a key part of meeting the EU's climate commitments under the European Green Deal.

Second Measure: Revenue Cap for Low-cost Power Generation

The Commission is also proposing a temporary revenue cap on "inframarginal" electricity producers, namely technologies with lower costs, such as renewables, nuclear and lignite, which are providing electricity to the grid at a cost below the price level set by the more expensive "marginal" producers. The wholesale market in the EU is a system of marginal pricing, where all electricity generators get the same price for the power they are selling at a given moment. Electricity producers establish their price according

to their production cost. Renewable energy sources are produced at zero cost and are therefore by definition always the cheapest. The bidding goes from the cheapest to the most expensive energy source. The Commission points out that these inframarginal producers have been making "exceptional" revenues, with relatively stable operational costs as expensive gas power plants have driven up the wholesale electricity price they receive. The Commission proposes to set the inframarginal revenue cap at €180/MWh. It says that this will allow producers to cover their investment and operating costs without impairing investment in new capacities in line with the EU's 2030 and 2050 energy and climate goals. Revenues above the cap will be collected by EU member state governments and used to help energy consumers reduce their bills. EU member states trading electricity are encouraged, in a spirit of solidarity, to conclude bilateral agreements to share part of the inframarginal revenues collected by the producing state for the benefit of end-users in the EU member states with low electricity generation. Such agreements are required to conclude by Dec. 1, 2022, where a member state's net imports of electricity from a neighboring country are at least 100%.

Third Measure: Solidarity Contribution from Fossil Fuel Companies

The Commission is also proposing a temporary solidarity contribution on excess profits generated from activities in the oil, gas, coal, and refinery sectors that are not covered by the inframarginal revenue cap. This time-limited contribution would maintain investment incentives for the green transition. It would be collected by EU member states on 2022 profits that are above a 20% increase on the average profits of the previous three years. The revenues would be collected by EU member states and redirected to energy consumers, in particular, hard-hit companies, energy-intensive industries, and vulnerable households. EU member states can also finance cross-border projects in line with the REPower EU objectives, a set of measures to reduce the EU's dependence on Russian fossil fuels while increasing the resilience of the energy system, or use part of the revenues for the common financing of measures protecting employment or promoting investments in renewables and energy efficiency.

In a further intervention in the electricity market rules, the Commission is also proposing to expand the Energy Prices Toolbox, a set of tools that the EU and its member states have to mitigate the effects of sudden price volatility in the energy market. The proposals would allow below-cost regulated electricity prices for the first time and expand regulated prices to also cover small and medium-sized enterprises.

Other Measures Proposed by the European Commission

As European Commission President von der Leyen announced on Sep. 7, 2022, the Commission will also continue to pursue other avenues to bring down prices for European consumers and industry and ease pressure on the market. The Commission says it will deepen its discussion with EU member states about the best ways to reduce gas prices, analyze various ideas for price caps, and enhance the role of the EU Energy Platform, a voluntary coordination mechanism supporting the purchase of gas and hydrogen for the EU, in facilitating lower price agreements with suppliers through voluntary joint purchasing. The Commission says it will also keep working on tools to improve liquidity on the market for energy utilities, and review the Temporary State aid Crisis Framework, designed to support the EU economy in the context of Russia's invasion of Ukraine, to ensure that it continues to enable member states to provide necessary and proportionate support to the economy. At the Extraordinary Energy Council Meeting on Sep. 9, 2022, Energy Ministers of EU member states endorsed the Commission's ongoing work in these areas.

Patricia Van Arnum,
Editorial Director, Drug, Chemical & Associated Technologies Association (DCAT)

- pvanarnum@dcat.org
- www.dcat.org

This article was published in the Sep. 15, 2022 edition of *DCAT Value Chain Insights* (www.dcatvci.org), an online publication covering the bio/pharmaceutical manufacturing value chain from the Drug, Chemical, & Associated Technologies Association (DCAT), and was edited and updated for publication in *CHEManager International.*

Welcome to the Future

DigiChem SurvEY Shows: Chemical Executives Say their Digital Transformation Is Now Two-thirds Complete

©Looker_Studio - stock.adobe.com

Many chemical executives say their companies have made significant progress in their digitalization efforts in the last two years — and they are even more excited about it now.

Ready for the future? In the chemical industry, it's getting very close. The average digital transformation is over two-thirds (68%) complete, according to respondents in the latest edition of the biennial DigiChem SurvEY 2022 of the global chemical industry—and a majority (56%) say that the speed of adoption at their company has accelerated in the past two years.

Experience often tempers excitement, but not this time around. If anything, industry executives are more optimistic about the value of digitalization than they were two years ago. Overall, the dial hasn't moved—in 2020, 66% expected to see a revolutionary or disruptive impact in the next three years, and in 2022, that number stayed nearly unchanged, at 65%. However, the share that envisions a disruption around the corner has grown. Fewer foresee a revolution ahead (35% vs. 46% in 2020), but more see disruption (30% vs. 20% in 2020), by which we mean an even more profound shift in the market.

In 2022, 637 executives from 35 countries participated in our survey, which was conducted by an independent market research institute.

More Gains Foreseen

As executives look back on their firm's digital progress in the past three years, they see a variety of gains. In this same time period, executives said, innovation and development (64%), processes and efficiency in the operational supply chain (57%), customer interface (57%) and sustainability scopes 1 and 2 (47%) were the areas where digitalization made the most progress in their firm.

More specifically, they saw better e-networking between suppliers and service providers (53%) and improved market and customer access (52%) as the top two benefits digitalization has already had for their firm, followed by a split between cost reduction (51%) and increased customer centricity (51%). Regionally, Europeans cited cost reduction as their top realized benefit (54%), while Americans pointed to better e-networking (54%), as did Asian-Pacific executives (62%). In the Middle East and Africa, however, executives saw new products and services as their biggest boon (60%).

"Digital is driving the chemical industry with ground-breaking innovations and new challenges."

Looking ahead, a majority of executives polled expected their firms to stay focused on applying digital technology to strengthen their R&D programs as well as their operational efficiency. Executives remain bullish on innovation and development (68%), supply chain technology (64%) and administrative functions (63%).

Roughly two-thirds of respondents believe their company's operational competitiveness will be enhanced over the next three years. In six of eight categories, digitalization will make a major difference, they predict. They see gains in supply chain planning (68%), sales and order management (67%), purchasing (67%), production and quality management (65%), customer service (65%) and logistics and distribution (65%). But even in the other two categories — sustainability scopes 1 and 2 and sustainability scope 3—the majority see gains (52% and 55% respectively).

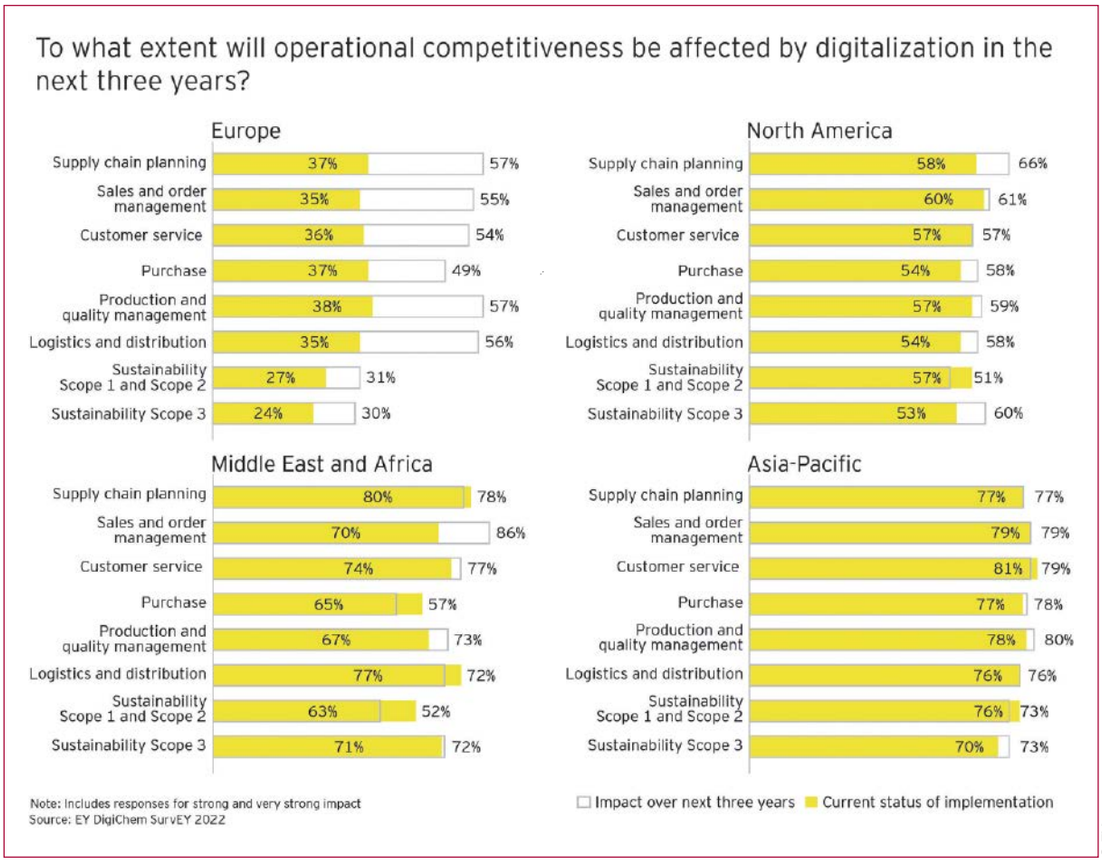
Regionally, North American, Asian-Pacific, and Middle Eastern and African companies don't foresee much change in the degree to which digitalization will affect their operational competitiveness—two years ago, the majority expected the transition to be challenging, and today, they still expect bumpy roads ahead.

In Europe, however, executives expect that operational competition will be heating up dramatically, with 10% and 20% jumps in the degree of operational competitiveness they now anticipate. For instance, 57% believe that digitalization will have a strong or very strong impact on supply chain planning, up from 37% two years ago. Sales and order management will be affected by digitalization too, in the view of 55%, up from 35% two years ago. Nor will logistics and distribution be left out, in the view of 56% of executives, up from 35% two years ago.

Frank Jenner, EY

"The average digital transformation for chemicals companies is over two-thirds complete."

Most executives are confident that these operational improvements will translate into substantial cost savings. In fact, they are even more confident now than when we asked them



A snapshot from EY's DigiChem SurvEY 2022.

two years ago: on average, respondents foresee 27% in cost savings, up from 22% in 2020, with the biggest companies seeing a 30% reduction ($2 billion–$10 billion companies) or even a 33% reduction ($10 billion+ companies).

A closer look, however, suggests that the news is not equally good for the entire industry.

Overall, executives of smaller companies are less optimistic about cost savings than they were two years ago. Firms of less than $100 million predict they can save 19%, down from 24% two years ago, while firms of $100 million–$2 billion predict 24% savings, compared with 25% in 2020.

Challenges Remain

Looking ahead, executives are concerned primarily with the nuts and bolts of the transformation. The biggest barriers? Technical infrastructure (40%), security concerns (38%), high investment requirements (38%), lack of qualified personnel (37%) and dearth of IT know-how (36%), with the top three concerns slightly higher than they were two years ago. Complaints about the lack of qualified personnel have fallen slightly (from 40% to 37%) but IT ignorance is as much a problem now as ever.

Executives also seem uncertain about which technologies they should invest in next. Asked to choose the three digitalization areas with the highest potential, they were relatively divided. Thirty-five percent picked data analytics, followed by 30% for data security, 29% for better data management and 29% for smart factory apps. Lowest on their list was the metaverse (13%), 3D printing and additive manufacturing (18%), digital market platforms (20%) and blockchain applications (20%).

"The speed of adoption has accelerated in the past two years as cited by 56% of survey respondents."

Somewhere in the middle of our checklist, and earning a resounding mediocre, came digital ecosystems, smart products and services, integration and optimization of processes and systems, and automation generally.

Interestingly, however, there is a great deal of regional variation in those priorities, with Europe seeing the most opportunity in data security (37%), North America in data analytics (39%), and the Middle East and Africa and Asia-Pacific executives focusing on digital ecosystems (37% and 33%, respectively).

What will it take to succeed? Executives say the top three factors are stable and secure digital solutions (41%), support from the entire leadership team (40%) and good interaction between the digitalization teams and the internal IT unit (39%).

Of course, success will depend as well on the firm's leadership, particularly with respect to meeting sustainability goals. Who's in charge here? 39% of respondents say their CEO is responsible for driving digitalization for better and faster implementation of sustainability goals, nearly double or triple the percentage who named another C-suite executive as their digitalization champion.

Conclusion: Believe the Hype

There is an old Wall Street saying that investors should buy on the rumor but sell on the fact. But the hype cycle doesn't seem to be functioning normally when it comes to digitalization in the chemical industry. Instead, something unusual seems to be going on: even as experience with digitalization grows, expectations are still rising, which is a good message in my view.

Frank Jenner, Managing Partner, Global Chemicals & Advanced Materials Industry Leader, EY, Mannheim, Germany

- frank.jenner@de.ey.com
- www.ey.com/de

Transition Pathways toward CO_2 Neutrality

Chemical Parks as Hot Spots of the Transition into a Fossil-free Chemical Industry

Chemical parks are locations of intensive value creation. They are a driver for sustainable development with a high economic, ecological and social impact. Major current challenges—short-term: implications of the war in Ukraine, mid-term: energy independency from Russia, and long-term: CO_2-neutrality by 2045/2050—all come together in chemical parks. But how do park operators handle these challenges? What initiatives are pursued to increase competitiveness and foster sustainable development in chemical parks across the globe?

Hannes Utikal, Provadis School of International Management and Technology

Marcel Loewert, Provadis School of International Management and Technology

These questions were the topic of a panel discussion with Joachim Kreysing, COO, Infraserv Höchst (Frankfurt, Germany); Tan Cheng Guan, Executive Vice President, Group CEO's office, Sembcorp Industries (Singapore); Martin Naundorf, Head of Sales and Business Development, InfraLeuna (Leuna, Germany); and Wouter Demenint, Commercial Manager Delta Corridor Project, Port of Rotterdam. The following text summarizes key results of the discussion, which was chaired by one of the authors, Hannes Utikal.

Chemical Parks: Focal Points of Current Management Challenges

Chemical parks exist all over the world in order to create value by process engineering. The majority of these industrial sites depends heavily on fossil energy and raw materials for production. One major concern of industrial parks in 2022 is the question on how to handle the current energy crisis with the high and very volatile prices for natural gas and electricity. In Europe, one major additional challenge is the pure availability of natural gas. Finding immediate substitutes for natural gas was named as the major challenge for chemical parks. Light oil was seen as a substitute for gas with regards to the generation of heat. Industrial park operators described operational flexibility as not fully gradual—at least 50% of the current natural gas supply in Germany would be necessary to keep the production system running—less natural gas would lead to a stop of the industrial production. The current energy crisis puts, thus, even more emphasis on the necessity to accelerate the transition to a fossil-free chemical production.

Transition Pathways are Site Specific

The development of a transition pathway starts with an analysis of the current resources and energy concept of a site. Local value chains and climate strategies of the producers on site need to be analyzed. One main challenge of a chemical site with multiple users such as the industrial parks in Frankfurt or Leuna is the regional coordination and alignment of the global climate strategies published by large global companies. Chemical parks need to translate companies' global CO_2 reduction targets to the regional context and they need to report a site's regional carbon footprint to the local community. In chemical parks, global climate strategies meet regional requirements and reporting duties.

Role of Industrial Park Operators

Industrial park operators play a crucial role in co-developing a defossilization strategy with their major clients. Together, they develop and implement the transition pathway. As park operators typically manage energy and material flows in chemical parks, they have access to emission data of different production facilities. This forms the starting point for developing a transition pathway. Depending on the governance structure of the industrial park operator, its role may vary: In a single- or major-user site, the status quo analysis is easier as less legal entities are involved in comparison with a multiple-user site consisting of a variety of stakeholders with specific interests. A transition pathway is characterized by the timing of investment in low carbon technologies and the balancing of economic and environmental considerations. Publicly owned industrial parks may focus more on CO_2 reduction targets and may need to focus less on the financial profitability of an investment than a privately owned industrial park. On the other hand, decision-making processes may take longer in publicly owned parks compared to privately owned entities.

© Infraserv Höchst

Geographic and National Context

The development of a transition pathway is heavily influenced by the geographical location, namely the availability of fossil-free feedstock (e.g., biomass) and energy (solar, wind, water, geothermal) on site or in the area. In addition, the current regional infrastructure, the availability of pipelines, roads and the energy grid at the right dimension are crucial context factors. But the transition is not only a technical, it is a socio-technical endeavor: National context factors such as a nation's institutional framework (e.g. national CO_2 reduction strategies, subsidies for low-carbon technologies, reliability of regulatory de-

12 Key levers for creating a CO_2-neutral industrial park Frankfurt-Höchst

1. Substitute natural gas
Green power Electrification of heat Synthetic methane from CO_2 (CCU) Carbon free burning gas (H_2, methane pyrolysis) Biogas / biogenic methane
2. Substitute fossil ethylene
Green ethylene from CO_2 (via ethanol) (CCU) Plastics recycling and cracking
3. Substitute fossil methanol
Synthetic methanol from CO_2 or biomass (CCU) Methanol via green ethanol
4. Substitute fossil acetic acid
Synthetic acetic acid from CO_2 (via methanol)
5. Further topics (applicable in many fields)
CCS Recycling

Source: Center for Industry and Sustainability, Provadis School of International Management and Technology

velopments) and a country's position in technology and innovation (e.g., low-carbon technologies, R&D investment, openness for new technologies) and human capital (qualified personnel; available upskilling and reskilling training) influence the transition pathway, too.

In addition, megatrends like a renewable hydrogen economy are locally driven undertakings and show a much higher availability in hot spots as of today. And finally, developments in the field of global trade and investments, the competitiveness of one nation in comparison with another with regards to local production and consumption, have to be taken into account when developing a transition pathway. It was mentioned in the discussion, that energy prices in Germany would be seven to nine times higher than in the US in August 2022. It was assumed that higher energy prices may persist in Europe over the next years leading to a competitive disadvantage of Europe with regards to energy-intensive production. These macro-economic developments are context factors for the local actors, they can only partially be influenced by park management or local stakeholders.

Green Ecosystems are Crucial

While chemical parks are the focal points of the transition, with park management and the major local producers being in charge of investments in low-carbon technology and using fossil-free feedstocks, they cannot realize the transition on their own account. They are part of ecosystems, which encompass complementary companies such as providers of low-carbon technologies and finance, actors from academia, policy making/regulation and civil society as well. Those different actors need to work together in order to create an effective transition pathway with economic, ecological and social benefits. While some of the necessary actors are in the region of a chemical park, especially the links in the fields of innovation go beyond the region in which a chemical park is located.

The port of Rotterdam in the Netherlands can serve as one example on how a multi-stakeholder ecosystem may be developed and managed to ramp up a green hydrogen economy. The effectiveness of public-private collaboration was seen as one key success factor in the transition to a fossil-free economy. As some of the technologies for a fossil free chemical industry are not yet fully developed and regulatory aspects (e.g., in the field of carbon capture and storage, CCS) are not yet clarified, a continuous public discourse on the requirements of a fossil-free chemical industry is needed to secure public acceptance of new technologies.

"Transform the European Process Industries"

In May 2022, an international expert workshop on transforming the process industry in Europe was held with more than 70 experts from industry and academia. The presentations and additional material are available at: bit.ly/Provadis-IPM2022

Case Study: Process4-Sustainability Cluster

In 2021, the cluster "Process4Sustainability: Cluster for climate-neutral process industries in Hesse" was founded in Frankfurt. It is funded by local companies, and the state of Hesse and the European Union alike, and managed by the Center for Industry and Sustainability at Provadis University of Applied Sciences. In addition to site operator Infraserv Höchst, the project's supporters include Sanofi, Clariant, Celanese, Kuraray and Bayer.

Goal of the cluster is to support companies in developing and implementing transition pathways toward CO_2 neutrality by 2045 at latest. In this context, suitable technical solutions for reducing CO_2 emissions are analyzed and opportunities for green growth are explored.

Key Levers to CO_2 Neutrality

The industrial park Frankfurt sees itself as an innovation campus, where low-carbon technologies can be tested and scaled up in an industrial setting. The project partners decide together about joint work packages and joint focal points. A first step was to identify the carbon footprint of the industrial park Höchst encompassing the production activities of all companies on site. The energy- and raw material-related CO_2 emissions were analyzed (over all three relevant scopes). The result: direct CO_2 emissions associated with energy production account for only one third of the total CO_2 emissions; roughly two-thirds of the emissions are associated with the fossil resources used in chemical production.

Together with the Society for Chemical Engineering and Biotechnology (Dechema), various transition pathways were analyzed for the industrial park. These include, to different degrees, the use of non-fossil raw materials (e.g., biomass), the use of green hydrogen, the use of green electricity, the electrification of heat and the use of CO_2 as a raw material in chemical production.

In a large number of expert discussions, 12 technological levers for CO_2 neutrality were identified (see table), which are now being examined in more detail together with innovation partners. Not every relevant technology embodies solution to the same degree or scale. The cluster Process4Sustainability seeks to partner up with relevant actors driving forward the transition toward a climate-neutral process industry.

Hannes Utikal, Head, Center for Industry and Sustainability, and Marcel Loewert, Business Development Manager, Center for Industry and Sustainability, Provadis School of International Management and Technology, Frankfurt, Germany

- hannes.utikal@provadis-hochschule.de
- marcel.loewert@provadis-hochschule.de
- www.process4sustainability.eu

The Future of Outsourcing

CPhI Report Predicts a Shift in Outsourcing Strategies

The increasing complexity in drug development and the highly competitive industry landscape are creating a dramatic shift in how pharmaceutical and biotech companies plan for and execute drug development and production. Speed, quality, and cost continue to be critical levers, but the challenge of achieving the right balance under the growing pressure to expedite development has made selecting the "right" outsourcing partners a strategic priority for pharmaceutical and biotech companies.

With increased market expectations and new and more stringent regulatory hurdles, these companies are also seeking advanced supply chain opportunities to optimize the development of their molecules. For many, establishing a partnership with a contract development and manufacturing organization (CDMO) is more cost effective than investing internally on infrastructure.

Outsourcing offers drug sponsors a variety of benefits, including access to a global network of cGMP facilities with high capacity and highly qualified experts across multiple disciplines. Having access to such vast industry expertise facilitates the seamless transition of projects through all phases of development.

This is especially critical for small and mid-size companies that don't have the in-house capabilities needed to support the capacity needs and time constraints, or the technical and regulatory knowledge or resources to successfully plan for and file an investigational new drug (IND)/ investigational medicinal product (IMPD) for their regional and global launches.

As precision medicine becomes more pervasive, the benefits of CDMO outsourcing are expanding by an order of magnitude for both small biotech companies and large pharma. The active pharmaceutical ingredients (APIs) and formulations developed for precision drug products are often drastically more complex and require specialized handling. While large pharmaceutical companies often have the capacity and knowledge to keep this work in-house, the small batch size requirements of precision therapies make it impractical.

To address these needs, more companies are turning to outsourcing all or part of their drug development and manufacturing projects.

A recent CPhI report entitled "The Future of Outsourcing—Strategies for Partner Selection" assessed these options as well as the overall market to see how outsourcing strategies are now evolving.

Outsourcing Strategies

The CDMO market continues to do extremely well and is growing significantly in all regions of the world. The Covid-19 pandemic and the consequential need to develop and manufacture new drugs, vaccines, and delivery platforms has further accelerated this growth. Yet running alongside Covid-driven growth, a record number of new drugs are entering development.

But how do both large pharmaceutical companies and, perhaps more importantly, the growing number of smaller innovators approach their outsourcing strategies?

Putting aside the option of in-house development, innovators must consider whether it is better to go for a two-CDMO strategy (i.e., one for drug substance and one for drug product), a larger full-service provider, or to work with a specialist integrated development partner earlier before re-reviewing their options in Phase I or II.

However, what is almost universally relevant to the situation biotechs encounter today is that they need to make and evaluate these decisions much earlier than before, as there is no guarantee there will be capacity immediately available when they need it.

Phase-Appropriate Development

With innovators increasingly turning to compressed timelines, development methods are shifting in response, the CPhI report states. For example, phase-appropriate development—whereby an innovator seeks to advance to just the next key milestone as quickly as possible—is still seen in the marketing of the majority of CDMOs.

Traditionally, outsourcing strategies were designed to help secure next stage funding, but many biotechs and small pharma companies are now entering development with more robust cash flows and the ability to plan further downstream and develop a product's roadmap from discovery to commercial launch.

Developing an IND strategy with the end submission in mind is how a drug sponsor shrinks their time to market and lowers program risk. Decisions made in early development have downstream implications and failing to plan for scale-up and commercialization can lead to time-intensive redoes and revalidation work.

At this stage the quality presentation often becomes the sticking point. Therefore, the report concludes, phase-appropriate development in accelerated development seems to be a thing of the past.

Asian Strategies

Another approach to emerge in recent years could be referred to as a hybrid Asian strategy, according to CPhI's experts. This hybrid model entails not only completing API development in Asia and the finished product in the US or Europe, but also the API component as well. This means essentially bringing in some of the cost advantages of Asian chemistry services and manufacturing, while completing later intermediate or final API steps in western markets.

A more traditional variant of the Asian model is to have discovery and integrated development until Phase I or II before transferring processes over.

©unlimit3d - stock.adobe.com

Biotechs Go Longer into Development than Before

Overall, biotechs are approaching CDMOs with a more fleshed-out roadmap and the intention of advancing further from the offset, as many life sciences venture investors recently raised new funds and have plenty of cash to put to use.

To this end, investors are becoming more involved in their biotech's development and outsourcing strategy, as this has fundamental implications for when and how they can exit. The report therefore anticipates that early-stage investors may start to bring in CMC consultants to map out the outsourcing approach as early as pre-clinical. A promising target is not enough on its own, it needs to be backed up by a robust development plan.

Alternative Partnering Strategies

The term CDMO covers quite a broad range of activities, with "D" taking dominance from the offset before "M" ultimately decides the long-term supply partner, the report states. One newer approach that is on the rise adds an additional process development partner, possibly a chemistry focused CRO, into this mix. Such a company might work with the innovator on chemistry and improvements, potentially even as far as commercial launch. This does mean adding an additional partner, but if the relationship is cooperative and information is shared, this could be a very strong triangle.

Biotech vs. Big Pharma

Large pharmaceutical companies generally have in-house CMC experience and options in terms of how they approach their outsourcing. Consequently, the greatest difference in outsourcing strategy between Big Pharma and biotechs is the role outsourcing plays in the company's business strategy. Where Big Pharma may only want to outsource a limited component, biotechs generally see outsourcing as a fundamental part of their business plan.

Not surprisingly, CPhI experts believe that the latter approach—which fosters deeper partnerships—will always have the most value for CDMOs.

For big pharma companies with multi-target programs, it is feasible to look at just the largest and most capable partners and select according to their needs. But for biotechs, securing the development capabilities they don't have is the highest priority, at least initially.

Is all Capacity Equal?

As already noted previously, capacity in the contract services space is constrained and has been for some time. Before the Covid-19 pandemic hit, contract organizations were already reporting long waiting lists for their services, particularly as clinical activity for cell and gene therapies surged. Now the industry is faced with pandemic-induced backlogs in addition to pre-existing constraints.

The small molecule market, the CPhI report says, experienced unprecedented growth in 2020, exacerbating capacity issues. However, due to the sheer number of CDMOs that offer small molecule services (according to the report 90% of all CDMOs worldwide are engaged in small molecule manufacturing), getting a place in the queue is generally easier than with other drug types.

Turning to large molecules, it is worth noting that the majority of development and manufacturing falls under the mammalian category, and outsourcing is common in this market segment. In addition to industry-wide capacity constraints, large molecule projects have been impacted by shortages of glass vials, syringes and stoppers, caused by the global Covid-19 vaccine push.

Finally, advanced therapy medicinal products (ATMPs) such as cell and gene therapy represent a much smaller share of CDMO activities. Contract organizations are immensely popular in this segment, with some reports showing a higher percentage of outsourcing in cell and gene therapy than any other field. In addition to industry giants, there are several specialty CDMOs carving out a niche in the cell and gene marketplace.

Most Effective Outsourcing Strategies

As explained before, the sector has been shifting away from phase-appropriate development in favor of a more forward-looking model. It should therefore come as no surprise that the industry experts involved in the CPhI report advise starting the search for an outsourcing partner early on and with a general roadmap in hand to narrow down the options.

Early engagement can be particularly beneficial for smaller companies who stand to benefit from the outsource partner's experience.

Multi-Vendor vs. Integrated Services

When considering potential CDMO partners, drug sponsors also need to decide whether to take a multi-vendor approach, where they work with more than one partner, opt for an integrated services solution that handles the process from start to finish, or just engage an outsource partner for a very limited part of the process. The suitability of each option will likely depend on a few factors, such as the size of the sponsor company, the type of expertise required, and the desired time to market.

Smaller CDMOs will likely have areas they specialize in—such as analytical method development or process characterization—while larger CDMOs can muster greater resources to support or lead key development activities. In the end the data must meet the expectations of the intended regulatory authority.

According to the CPhI report, for drug sponsors who lack experience managing CDMO relationships, selecting one vendor who can provide expertise across a range of services can simplify the process. In this case, sponsors are able to map out the entire product journey and if there is a delay in one phase, timelines can be easily adjusted.

This is more complicated with a multi-vendor approach, as the sponsor retains complete responsibility for keeping the project on track. In the case of a delay or unexpected change, the sponsor must communicate with multiple vendors, sometimes working in parallel, and adjust timelines across multiple projects.

The ability of a sponsor to communicate through one central channel is a significant benefit of the integrated services model. As integrated offerings may not be able to provide the same level of expertise across all stages of development, sponsors should consider whether capabilities or speed are more important to their individual project.

Mid-sized outsource partners may be a better fit for highly nimble biotechs who accept the added complexity of working with multiple vendors as a trade-off for quality and cultural alignment.

One CPhI expert states that there is a giant divide between the really small players and the really big ones. There's not a lot to bridge that gap, and this is causing a discontinuity in the market because the smaller players don't necessarily have integrated solutions and cannot provide a fully strategic outsourcing solution to their biotech and big pharma customers. However, culturally, they match up extremely well, particularly with the small, medium and virtual pharma companies. These smaller players tend to be entrepreneurial, fast paced, lack bureaucracy, and have a very strong depth of expertise, albeit in a very narrowly focused window. Therefore, it can be a very valuable proposition.

Outlook

Given the current level of demand, the CPhI report predicts that the CDMO market will continue on its current trajectory and the challenges addressed will not only remain relevant but will become even more critical. All CDMOs are expanding, and the CPhI experts foresee that perhaps some of today's niche players will quickly grow to become mid-sized CDMOs to fill the current major disparity in the overall market. (rk)

www.cphi.com

Ensuring API Supply Capacities for Europe and Beyond

EuroAPI: 150 Year of Heritage and Expertise, now Focused on Stand-alone Success

In early 2020 Sanofi announced plans to establish a new manufacturer of active pharmaceutical ingredients. The French drugmaker, in January 2021, named its new API company EuroAPI and in May 2022 listed it on the Euronext stock exchange in Paris. With around 3,350 employees, EuroAPI posted sales of about €900 million in 2021. The company is estimated to be the world's top manufacturer of small molecules and its second largest API maker in revenue terms. CHEManager asked Karl Rotthier, CEO of EuroAPI, about the start of the new CDMO, its vision for the future and current market trends in the API sector.

CHEManager: Mr. Rotthier, what was Sanofi's intent of spinning out its former Active Ingredient Solutions business and creating a stand-alone company?

Karl Rotthier: On February 24, 2020, Sanofi announced its plans to create a major leading European company dedicated to the production and marketing to third parties of active pharmaceutical ingredients (APIs), which are the essential molecules responsible for the beneficial effects used in the composition of any drug. At that time, Sanofi said that with increasing medicine shortages that critically impact patient care, the new entity would contribute to supporting and securing API manufacturing as well as supply capacities for Europe and beyond.

Sanofi still holds a stake in EuroAPI and has established a long-term customer relationship. How independent is EuroAPI in working with and for other, external customers?

K. Rotthier: EuroAPI is now fully independent. We have been operating as a stand-alone player since our listing on Euronext Paris, which occurred on May 6. This listing marks an exciting milestone for the development of our company as it will enable us to consolidate our leadership in the dynamic API market. As an independent company, we will gain flexibility and growth opportunities and, as announced, Sanofi will remain a long-term strategic partner.


© Grégoire Mahler

Karl Rotthier, CEO, EuroAPI

How is your portfolio made up, where do you see EuroAPI's core competence in terms of capabilities and technologies?

K. Rotthier: EuroAPI is the leading small molecules API company and the second largest API producer in the world with around 200 APIs in our portfolio. Our business is focused on two activities: a wide offering of APIs in our API Solutions segment and custom innovative projects for clients in our CDMO Services segment

We have a broad range of technologies: the Haverhill facility in UK specializes in flow chemistry and spray drying. In France, Saint-Aubin-lès-Elbeuf focuses on fermentation and vitamin B12, and Vertolaye on corticosteroids and solid chemistry. Our Frankfurt site is mainly dedicated to oligonucleotides and peptides while our Budapest facility focuses on prostaglandins. Last but not least, in Italy, our Brindisi site specializes on anti-infectives.

How does your map of manufacturing facilities look like? Do you plan investments in new facilities or any of the existing?

K. Rotthier: As you can see, all of our plants are located in Europe and each of our production sites specializes in different technology. As far as investments are concerned, we announced in July the initiation of a €24 million investment for the construction of a state-of-the-art biomass boiler at our Elbeuf site. This investment should enable us to support our vitamin B12 production capacity increase program, reduce our CO_2 emissions by almost 76% in 2026, compared to

2020 and support our strategy towards greater energy autonomy. Among planned enhancements, we can mention the construction of a new production capacity for highly active hormones in Vertolaye.

As a CDMO you are a leader in small molecules APIs. What are your plans to develop the R&D and manufacturing capabilities to accelerate your activities in complex molecule segments?

K. Rotthier: The number of small molecule drug approvals continues to rise, and there is a long pipeline of small molecule drugs in various stages of clinical trials. In terms of complex chemistry, our approach is to use modern organic chemistry, biocatalysts and flow chemistry techniques. Our development is guided by green chemistry principles for both improved sustainability and lower cost. We already have 330 scientists spread across our six sites today and our plans are to almost double this capacity by 2025.

Through Sanofi's experience in the field of oligonucleotides and peptides, EuroAPI can provide different classes of Tides. Do you have plans to grow this capability?

K. Rotthier: Regarding peptides and oligonucleotides, our production capacities give us a hedge in the biologics space, and we do have projects to grow in that field. Our plans are for example to debottleneck the downstream process in Frankfurt, enabling us to reach a yearly production capacity of more than 100 kg by 2024.

© EuroAPI

Overall, what do you think are the predominant trends in API/drug development?

K. Rotthier: The API market is dynamic, and I see three factors here: an increased access to medicine globally, consistent and sustainable outsourcing trends and favorable demographics due to an aging population. Excluding Covid years where the annual growth rate was approximately two percent, the growth rate is six to seven percent year over year and we are talking about a large, over €70 billion global market.

In terms of customer needs, where do you see market trends that you want to support and benefit from?

K. Rotthier: In our field, the quality of APIs and the reliability of supply are critical. At EuroAPI, all our offerings meet the latest regulatory and quality requirements through active monitoring and a reliable, high-performance supply chain. We have local regulatory expertise across Europe, the US and Japan and our industrial sites have health authority, GMP and ISO certifications.

Customers also require tailored solutions and that's what we are offering through our CDMO activity. The CDMO market is even more dynamic, benefitting from a seven to eight percent annual growth rate.

From the beginning of the pandemic on supply chain disruptions also affected the pharmaceutical industry, revealing the shortcomings of globalization. What role will EuroAPI play in ensuring API supply capacities for Europe in the future?

K. Rotthier: Thanks to our strengths, we can play a role in the repatriation of essential activities for the healthcare sector. We are well positioned due to the wide range of technologies and know-how, along with large production capacities and industrial footprint across Europe. Do not get me wrong: the idea is not to bring back high-volume, low-cost products, but to repatriate some of the APIs that are complex to make, as our focus is on high added value solutions.

■ www.euroapi.com

Investing in Growth Through Innovation

Arxada Addresses Customer Needs with Innovative and More Sustainable Solutions

Arxada was created in 2021 following the completion of the carve-out and sale of Lonza Specialty Ingredients to private equity firms Bain Capital and Cinven. The Swiss specialty chemicals company is active in three businesses: Consumer Microbial Control (CMC), Industrial Microbial Control (IMC) and Specialty Products Solutions (SPS). Following the carve-out, Arxada announced the acquisitions of Troy Corporation, a global leader in industrial preservation, and Enviro Tech Chemical Services, a category-leading manufacturer of proprietary and high-efficacy antimicrobial and biocidal products. CHEManager asked Marc Doyle, CEO of Arxada, about the start of the new company, its plans and vision for the future, and current CDMO market trends.

CHEManager: It has been a busy first year for Arxada. Will you maintain this pace for further acquisitions?

Marc Doyle: M&A is a critical growth lever for us. Given the highly fragmented market for the preservation of infrastructure, the environment and human health from microbiological threats, we see a number of potential opportunities to acquire new technologies or new products that tick these boxes.

What do the company's new owners, Bain Capital and Cinven, expect from you in terms of further development?

M. Doyle: Bain Capital and Cinven's strategy is to carve out good companies and make them great through strategic acquisitions and by investing in growth through innovation. They also have a strong focus on sustainability—part of the financing for the carve-out of Arxada included a sustainability-linked bond, which was the first of its kind for a private equity transaction. As a company, we are investing heavily in our sustainability strategy to help our customers adapt to long-term environmental and social change, and develop cleaner, greener solutions.

Arxada's roots go back more than 120 years. Does this longstanding heritage of innovation and technology still live on today?

M. Doyle: Arxada has an extremely strong track record in innovation, which spans beyond our history as part of Lonza. You can also trace Arxada's roots back to one of the biggest breakthroughs in the history of biocides: part of our history stems from Arch Chemicals through Avecia and Zeneca to ICI, who developed benzisothiazolinone—BIT—, which is still one of the most important antimicrobial chemicals in our industry today.

We acquired Troy Corporation in 2021, who again have a long history of innovation, the most notable being the invention of 3-iodo propynyl butyl carbamat—IPBC—, which is another major preservative chemistry still in use today.

Marc Doyle, CEO, Arxada

As well as developing these major classes of chemistry that we are still the leader in today, we continue to innovate and bring new products and chemicals to the market. For example, we created Tanasote, a more sustainable alternative to Creosote, which we are trying to make the industry standard in Europe. This forms part of our strategy of using our strength and heritage in innovation to develop more sustainable products.

Going forward with the Enviro Tech business we have been innovating around new uses of peracetic acid—PAA– to bring it to new applications to replace the use of chlorine and chlorinated chemicals.

What do the two companies—Troy and Enviro Tech—add to Arxada's offering?

M. Doyle: Both Troy and Enviro Tech brought us innovative technologies that enable us to keep abreast of regulatory trends. Troy is a leader in IPBC—a more sustainable fungicide—and we see a lot of ways in which we can harness our technologies to further evolve its use, for example by expanding our offering of controlled release formulations which reduce exposure to the active. With Enviro Tech, we saw a great opportunity for PAA to displace chlorinated chemicals given that it has a lower environ-

© Arxada

mental impact and is easy to work with—and we see further ways to use Enviro Tech's innovation capabilities to widen its use.

Are there any interesting trends or drivers you are seeing in the CDMO market? And what is your strategy as a CDMO to benefit from these trends?

M. Doyle: For the CDMO market as a whole, we are seeing three trends: more consolidation of a highly fragmented market, continued outsourcing and additional reshoring. These trends have been primarily driven by the agro and pharma end markets, which are the heaviest users of CDMO.

Our CDMO strategy has been to move into additional end markets which are increasingly using CDMO capabilities—such as nutritional ingredients, food and flavors and industrial biotech—where we see further opportunity to grow. At Arxada, we have CDMO capabilities both in traditional chemistry at our heritage site in Visp, Switzerland, and within the industrial biotechnology space at our Kouřim site in the Czech Republic, which puts us in a unique position within the market.

Which market sectors do you primarily address, and how is Arxada positioned in these markets in terms of portfolio range and core competences?

M. Doyle: The four core markets for Arxada are paints and coatings; home and personal care; professional hygiene and wood protection; in addition to industrials including energy, nutrition and mobility. One way of thinking about this is that we have a focused theme of addressing the need for more sustainable preservation across both human health and infrastructure related end markets through the breadth of our product offering, our technologies and our regulatory capabilities.

The Consumer Microbial Control side of our business primarily focuses on human health and protecting us from the threat of microorganisms. There is now a much greater awareness of the threats from bacteria, viruses, fungus and algae, in part because the increasing human population is bringing us more into contact with microorganisms, and also because global warming is leading to a proliferation of these microorganisms.

> *"When Arxada was carved out from Lonza it was a transformational opportunity for the business."*

Within our Industrial Microbial Control business, we leverage the same products, regulatory capabilities and technologies into the protection of infrastructure from microorganisms. Our businesses within microbial control are complemented by our work to protect human health through our Specialty Products Solutions business. We are a key supplier of vitamins and nutritional ingredients globally.

Do you plan to add certain capabilities or capacities in order to support demand growth?

M. Doyle: We've already significantly expanded our capacity over the past year: investing CHF 20 million in our industrial biotechnological plant in Kouřim, Czech Republic, which serves our CDMO business, and last month announcing a CHF 20 million expansion of our vitamin capacity to support our partner DSM.

Other recent projects include NOx abatement at Visp, Switzerland, quat expansion in Mapleton, IL, USA, increasing capacity for methoxyethyl cyanoacetate and butyl cyanoacetate in Conley, GA, USA, and Tanasote capacity expansion in Huddersfield, UK. We're expecting to make further investments in our operations over the next 12 to 18 months, not only to continue to support the growth of our business but also to make our business more sustainable.

In terms of customer needs, where do you see market trends that you want to support and benefit from?

M. Doyle: Increased regulatory pressures are driving transitions to new chemistries which better protect human health and the environment. We're helping to drive the preservation industry's transition to more sustainable and cleaner solutions through our investments in boosters, potentiators and controlled release technologies. There is a shift in the home and personal care market from hard preservatives, such as quats, to what are called soft preservatives such as our Geoguard technology. We strongly support this transition and work closely with customers to enable them to adapt their formulations to the new solutions available in this space.

Another trend we are able to support within our SPS business is the move towards 5G electronics applications. We recently entered a partnership with Novoset where we will develop, manufacture and commercialize a next generation hydrocarbon-based dielectric resin developed by Novoset which will find application within rigid circuit boards used for telecommunications and advanced semiconductor packaging markets.

We're also working to leverage our manufacturing process technology expertise to deliver more efficient manufacturing processes for some of our key chemistries that have lower CO_2 and greenhouse gas emissions.

What do you see for the company's future?

M. Doyle: When Arxada was carved out from Lonza it was a transformational opportunity for the business, allowing us to accelerate our growth strategy within the consumer and industrial microbial control area and in specialty chemicals markets with the strong, long-term support of our new owners.

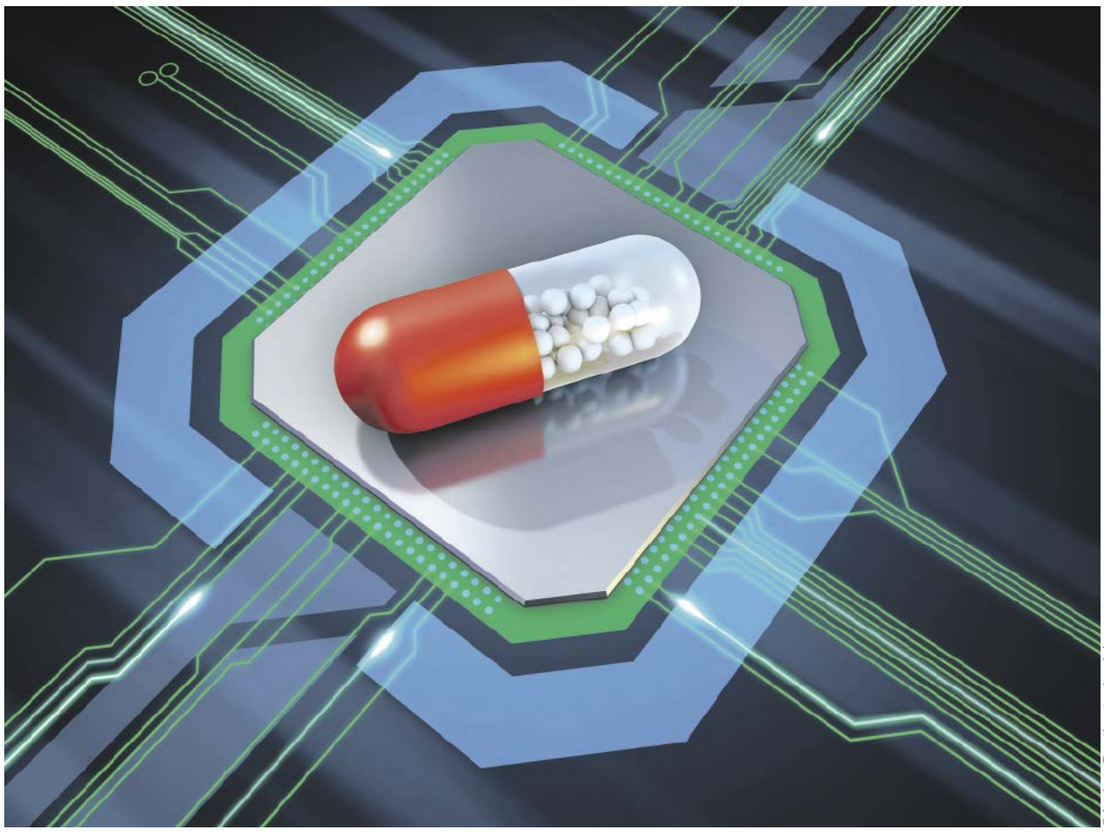
Independence is allowing Arxada to be a more responsive and agile business, developing unique, innovative solutions to help our customers protect their products from microbial spoilage, improve health and safety and reduce their environmental footprints. We look forward to supporting customers to better address their most difficult preservation challenges in a more sustainable manner.

■ www.arxada.com

AI Maturity Model for GxP Application

A Foundation for AI Validation in the Pharmaceutical Industry, Part 1

Artificial intelligence (AI) has become one of the supporting pillars for digitalization in many areas of the business world. The pharmaceutical industry and its GxP-regulated areas also want to use AI in a beneficial way. Several pharmaceutical companies are currently running digital pilots, but only a small fraction follows a systematic approach for the digitalization of their operations and validation. However, the assurance of integrity and quality of outputs via computerized system validation is essential for applications in GxP environments. If validation is not considered from the beginning, there is considerable risk for AI-based digital pilots to get stuck in the pilot phase and not move on to operations.



©Andrea Danti - stock.adobe.com

There is no specific regulatory guidance for the validation of AI applications that defines how to handle the specific characteristics of AI. The first milestone was the description of the importance and implications of data and data integrity on the software development life cycle and the process outcomes.

No life-science-specific classification is available for AI. There are currently only local, preliminary, general AI classifications that were recently published.

This lack of a validation concept can be seen as the greatest hurdle for successfully continuing digital products after the pilot phase. Nevertheless, AI validation concepts are being discussed by regulatory bodies, and first attempts at defining regulatory guidance have been undertaken. For example, in 2019 the US Food and Drug Administration published a draft guidance paper on the use of AI as part of software as a medical device, which demonstrates that the regulatory bodies have a positive attitude toward the application of AI in the regulated industries.

Introducing a Maturity Model

As part of our general effort to develop industry-specific guidance for the validation of applications that consider the characteristics of AI, the ISPE D/A/CH (Germany, Austria, and Switzerland) Affiliate Working Group on AI Validation recently defined an industry-specific AI maturity model (see figure). In general, we see the maturity model as the first step and the basis for developing further risk assessment and quality assurance activities. By AI system maturity, we mean the extent to which an AI system can take control and evolve based on its own mechanisms, subject to the constraints imposed on the system in the form of user or regulatory requirements.

Our maturity model is based on the control design, which is the capability of the system to take over controls that safeguard product quality and patient safety. It is also based on the autonomy of the system, which describes the feasibility of automatically performing updates and thereby facilitating improvements.

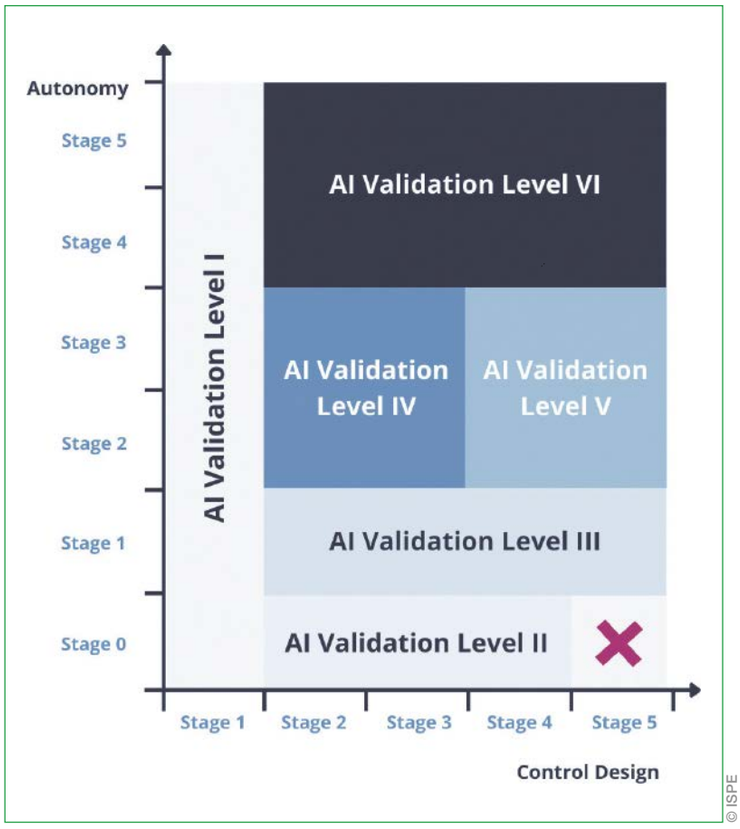
We think that the control design and the autonomy of an AI application cover critical dimensions in judging the application's ability to run in a GxP environment. We thus define maturity here in a two-dimensional matrix spanned by control design and autonomy and propose that the defined AI maturity can be used to identify the extent of validation activities.

Control Design

Control design is a five-stage process. In stage 1, the applications run in parallel to GxP processes and have no direct influence on decisions that can impact data integrity, product quality, or patient safety. This includes applications that run in the product-critical environment with actual data. The application may display recommendations to the operators. GxP-relevant information can be collected, and pilots for proof of concept are developed in this stage.

In stage 2, an application runs the process automatically but must be actively approved by the operator. If the application calculates more than one result, the operator should be able to select one of them. In terms of a 4-eye principle (i.e., independent suggestion for action on the one hand and check on the other hand), the system takes over one pair of eyes. It creates GxP-critical outputs that have to be accepted by a human operator. An example for a stage 2 application would be a natural language generation application creating a report that has to be approved by an operator.

In stage 3, the system runs the process automatically but can be interrupted and revised by the operator. In this stage, the operator should be able to influence the system output during operation, such as decid-



Industry-specific AI maturity model defined by the ISPE D/A/CH (Germany, Austria, and Switzerland) Affiliate Working Group on AI Validation.

ing to override an output provided by the AI application. A practical example would be to manually interrupt a process that was started automatically by an AI application.

In stage 4, the system runs automatically and controls itself. Technically, this can be realized by a confidence area, where a system can automatically control whether the input and output parameters are within the historical data range. If the input data are clearly outside a defined range, the system stops operation and requests input from the human operator. If the output data are of low confidence, retraining with new data should be requested.

In stage 5, the system runs automatically and corrects itself, so it not only controls the outputs but also initiates changes in the weighting of variables or by acquiring new data to generate outputs with a defined value of certainty.

To our knowledge, there are currently no systems in pharmaceutical production at level 4 or 5. Nevertheless, with more industry experience, we expect applications to evolve for applications at levels 4 and 5.

"Our maturity model is based on the control design, which is the capability of the system to take over controls that safeguard product quality and patient safety."

Autonomy

Autonomy is represented in six stages. In stage 0, there are AI applications with complex algorithms that are not based on machine learning (ML). These applications have fixed algorithms and do not rely on training data. In terms of validation, these applications can be handled similar to conventional applications.

In stage 1, the ML system is used in a so-called locked state. Updates are performed by manual retraining with new training data sets. As the system does not process any metadata of the produced results by which it could learn, the same data input always leads to the generation of the same output. This is currently by far the most common stage. The retraining of the model follows subjective assessment or is performed at a regular interval.

In stage 2, the system is still operating in a locked state, but updates are performed after indication by the system with a manual retraining. In this stage, the system is collecting metadata of the generated outputs or inputs and indicates to the system owner that a retraining is required or should be considered, e.g., in response to a certain shift in the distribution of input data.

In stage 3, the update cycles are partially or fully automated, leading to a semi-autonomous system. This can include the selection and weighting of training data. The only human input is the manual verification of the individual training data points or the approval of the training data sets.

In stage 4 and stage 5, the system is completely autonomous with reinforced ML independently based on the input data.

In stage 4, the system is fully automated and learns independently with a quantifiable optimization goal and clearly measurable metric. The goal can be defined by optimizing one variable or a set of variables. In production, the variables could be the optimization of the yield and selectivity of certain reactions.

In stage 5, the system learns independently without a clear metric, exclusively based on the input data, and can self-assess its task competency and strategy and express both in a human-understandable form. Examples could be a translation application that learns based on the feedback and correction of its user. If the user suddenly starts to correct the inputs in another language, in the long term, the system will provide translations to the new language.

Nico Erdmann, Manager, Deloitte, Germany;
Rolf Blumenthal, Senior Consultant, Körber Pharma Software;
Ingo Baumann, Partner, Head of Delivery, Thescon;
Markus Kaufmann, Global GMP Auditor, Novartis
■ https://ispe.org

This article, which is part 1 of an excerpt from a more in-depth article first published in the March/April 2022 issue of ISPE Pharmaceutical Engineering, was developed as part of a larger initiative regarding AI validation. The maturity model is the first step. In fact, many other topics such as data management or risk assessment have to be considered in the validation of AI. The basic maturity model will have an influence on the risk assessment of the AI application.

Bachem Innovates its Manufacturing Capabilities

Interest in oligonucleotide therapeutics has grown, as has the market demand, since their emergence as a new drug modality two decades ago. Initially focusing on rare diseases, oligonucleotide therapeutics are moving into more common chronic indications like asthma, diabetes, chronic renal failure, as well as cardiovascular and liver diseases.

The need for large-scale manufacturing to support market requirements for oligonucleotides has never been so high and is coupled by the emergence of new challenges related to scalability, sustainability and cost. Bachem is the leading CDMO for oligonucleotide and peptide manufacturing and has been rising to these challenges in a number of ways to support the best their customers in drug development and commercialization.

Bachem's new oligonucleotide manufacturing facility provides innovative solutions for large-scale oligonucleotide API (active pharmaceutical ingredient) production.

Customizations, such as in-line mixing of dichloroacetic acid (DCA) solution—enabling the right amount of DCA to be transferred and avoids side reactions, ensure a more efficient process and results in a high-quality crude API. The production line is also equipped with the first MCSGP (Multi-column countercurrent solvent gradient purification) equipment for large-scale continuous chromatography. This set-up brings significant benefits such as time optimization, cost-efficiency, and lower solvent consumption during the purification step.

A focus on Industry 4.0, the automation and digitalization of traditional industrial processes through smart technology and integration, is a key industry trend. Bachem sees digitalization as an enabler to meet uncertain demands, compliance and ambitious timelines to deliver high-quality APIs. Within this concept, a "smart factory" is characterized by machines which are interconnected, and interoperable, and can process data autonomously. Such "smart factories" require only limited human decision-making or intervention and are therefore sometimes referred to as "intelligent automation". Entering Industry 4.0 and developing the Bachem "smart factory" represents a big step forward in providing their customers with more flexibility, consistency and speed in manufacturing.


© Bachem AG

Bachem has primarily been focused on automating and digitalizing solid phase peptide synthesis (SPPS). This improves the reliability of the process, reproducibility of results and safety, while significantly increasing the cost-effectiveness of operations. Major innovations, such as a robot-operator, called BALU (Bachem Amino acid Loading Unit), and Process Analytical Technology (PAT) have recently been rolled out.


© Bachem AG

BALU was designed and programmed to support commercial scale of SPPS. The robot handles the containers with the amino acid powders and can perform the powder transfer into the activator vessels for Bachem's 150L SPPS reactors without the involvement of an operator. BALU can perform other critical tasks, such as cleaning the amino acid transfer port to prevent cross-contamination. A barcode scanner that reads the labels placed on the amino acid containers ensures correct handling.

PAT performs inline analytics after key steps. PAT removes the need for manual In-Process Controls (IPC) and provides a better control of Critical Process Parameters (CPP). Additionally, this automated process enables data recording and analytics as well as paper-free cGMP documentation. Implementing PAT to their process control decreases human contributions and cost of goods. Manual tasks are no longer required, freeing resources for other tasks and projects. Furthermore, PAT leads to a higher reproducibility with minimized chemical side reactions.

Continuous innovation is key to transform oligonucleotide and peptide manufacturing and ensure a high-quality, sustainable, and cost-effective process. Investments in new production facilities and into automation of traditional processes enables companies to utilize assets more efficiently and streamline production scheduling for a higher capacity and flexibility. Bachem will continue to drive innovation, set high industry standards and expand their capabilities to help their customers in transforming patient's lives.

BACHEM

Bachem AG
Hauptstrasse 144
4416 Bubendorf
Switzerland
Tel.: +41 58 595 2020 (Sales department)
sales.ch@bachem.com
www.bachem.com

CHEManager INTERNATIONAL

INNOVATION PITCH

©Costello77 - stock.adobe.com

Green, Efficient and Circular
Sustainable Industrial Wastewater Treatment with Ferrate(VI)

Sustainable Production
Innovative Continuous Reactor for Chemical Manufacturing

WILEY

SPONSORED BY

HAFEN STRAUBING-SAND
BIOCAMPUS MULTIPILOT

GLOBAL ENTREPRENEURSHIP CENTRE
Scaling for impact

RUHR·IP PATENTANWÄLTE

Become a Premium Sponsor of CHEManager Innovation Pitch!
More information:
Tel. +49 6201-606 522 or +49 6201-606 730

Sustainable Industrial Wastewater Treatment

Ferrate(VI) Makes Water Treatment Green, Efficient and Circular

For decades, Ferrate(VI) has been known as the strongest oxidant in the world for the treatment of (industrial) wastewater. Unlike frequently used chemicals for water treatment, Ferrate(VI) is environmentally friendly. Producing Ferrate(VI) in a stable and preservable form has been impossible until now. Thanks to ground-breaking research, however, the founders of Dutch start-up Ferr-Tech have developed a patented method to do so successfully. The company is the first to provide Ferrate(VI) for industrial application. By purifying wastewater with Ferrate(VI), water treatment becomes more sustainable and energy efficient, while enabling reuse of the water in the industrial process. Judith le Fèvre, co-owner of Ferr-Tech and Director Marketing & Public Affairs, provides insight into the company's goals.

CHEManager: Mrs. le Févre, what motivated you to found Ferr-Tech?

Judith le Fèvre: Ferr-Tech was formed after co-founder Sina Samimi wrote his master's thesis on the tenability and stability of producing Ferrate(VI). "The problem with Ferrate(VI) in the past was that it had a shelf life of only a few seconds, making it unsuitable for industrial use", Judith explains. "Sina has developed a production process to make Ferrate(VI) tenable for two months. Now, as a Dutch start-up, we are the first in the world that can offer FerSol, Ferrate(VI) in solution for industrial use to the market."

What challenges did you face so far?

J. le Fèvre: One of the biggest challenges in circular business is that to be truly circular, you have to address the entire chain. Ferr-Tech is also working on this. "We separate clean water from sludge, the waste, but it would be ideal if the sludge could also be reused, for example as a raw material for fertilizer. This is not our core business, but it would be, of course, good to close the entire chain. That is why we are participating in a European project at a dairy giant, in which it is investigated, among other things, what the possibilities are with sludge."

In addition, Ferr-Tech is committed to further improving its own products. "We produce Ferrate(VI) in solution under the name FerSol. This product has a shelf life of two months and must be stored below 10 degrees. However, we are also developing Ferrate(VI) in cake and powder form. These products have an even longer shelf life, are even more powerful and require an even lower dosage than FerSol."

What were the most exciting experiences in Ferr-Tech's journey?

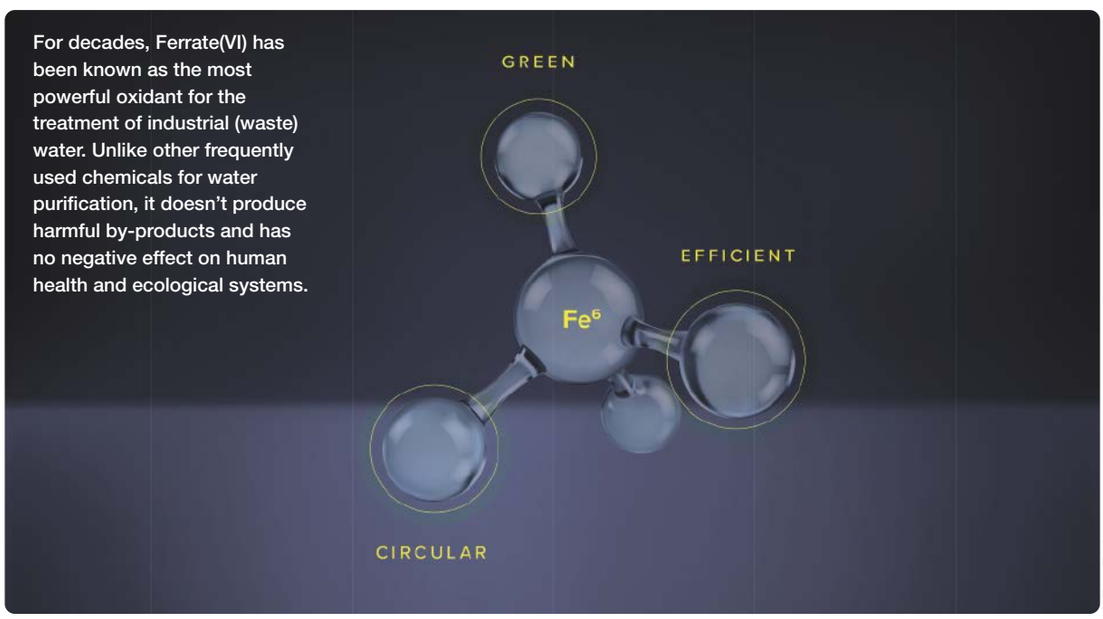
J. le Fèvre: For existing only two years, I think we got to experience a lot of exciting things already. However, in my opinion, winning the CES Innovation Award, is definitely on top of the list. The CES is the world's largest technology exhibit, located in Las Vegas. The CES Innovation Award, is one of the most prestigious awards a company in the field of technology can receive and for us, it also marks the start of conquering the US..

What are your plans for the future?

J. le Fèvre: Our goal is: clean and sufficient water for everyone. We're already doing projects in Spain, France, Norway, Germany, USA and of course our home country: The Netherlands. To reach the goal, we want to get to the entire world. Next on the agenda is the middle east. Over there, you have large desalination plants where fresh water is made from salt water. We improve the water to the Reverse Osmosis so the membranes last much longer. In this way, we multiply the sustainability of these kinds of plants and reduce the total cost of ownership.

However, meanwhile we are still a start-up, and the future is unknown to everyone. Yet, this doesn't keep us from innovating and trying to reach our goal.

Judith le Fèvre, Ferr-Tech



For decades, Ferrate(VI) has been known as the most powerful oxidant for the treatment of industrial (waste) water. Unlike other frequently used chemicals for water purification, it doesn't produce harmful by-products and has no negative effect on human health and ecological systems.

© Ferr-Tech

Personal Profile

Judith le Fèvre is co-owner of Ferr-Tech and a driven, innovative and internationally oriented entrepreneur. With a Master's degree in Business Administration, le Fèvre manages to develop and maintain Ferr-Tech's vast and strong network. She has many years of experience in Public Affairs & Lobby, and as an independent interim manager. On top of that she also has an eye for success and a preference for working with companies like Ferr-Tech with high societal value. She loves launching new undertakings and is one of the driving forces behind establishing Ferr-Tech as a household name in the industry.

Business Idea

Revolutionary Water Treatment

Ferrate(VI) is the strongest oxidant, alternative chemicals have a weaker oxidizing effect. The strength of this effect is expressed in the redox potential. The higher the value, the stronger the oxidant. Ferr-Tech's product, FerSol can be used for several essential processes in wastewater treatment and, as a result, saves a lot of energy. In addition, it reacts with dissolved substances, causing them to sink (coagulation). As a side effect it eliminates certain bacteria, fungi and viruses.

Many chemicals only have one functionality. Wastewater is treated through complex processes and installations, requiring various steps. A striking example can be found in the steel industry. Colour, iron ions and water hardness are treated by a 5-step purification process, including chlorine, metabisulfite, soda, ferrite and slaked lime (calcium hydroxide). FerSol enables a one-step purification process. By shortening these complex water treatment processes, we also reduce energy consumption.

Thanks to the powerful oxidation caused by Ferrate(VI), the particles of the residual product are strongly bound together. Thanks to this densification, less sludge is generated. This method simplifies sludge discharge and reduces costs, while decreasing energy consumption and CO_2 emissions.

FerSol has no harmful effects on people and the environment. as demonstrated with the Ames test and the FET test. It replaces chemicals that are difficult to remove from the water and makes processes more sustainable. From now on, when removing color, odor and oil, you can efficiently use a single green chemical: FerSol. In contrast, traditional methods require various harmful chemicals. Additional steps are often necessary, such as aeration or spreading.

The major advantages are:

- It is extremely powerful and has a three-in-one function, reducing the amount of chemicals needed;
- The residue of FerSol is environmentally and human friendly;
- The reduction in sludge also reduces the CO_2-footprint by lowering transport costs. In many cases, the sludge is 80% more concentrated than with other solutions;
- It enables residual water to be reused;
- As a side effect, it eliminates bacteria, fungi and viruses.

■ Ferr-Tech, Meppel, The Netherlands
https://ferr-tech.com

FERR-TECH
REVOLUTIONARY WATER TREATMENT

Elevator Pitch

Green. Efficient. Circular.

Ferr-Tech is, with their product FerSol, global market leader in the field of Ferrate(VI) applications for industrial (waste)water purification. Through a patented process, Ferr-Tech offers Ferrate(VI) in a liquid and stable form for use in the (waste)water industry. From their headquarters in Meppel, Ferr-Tech runs the water lab and handles high quality water tests, experiments and analyses for customers.

FerSol is the most powerful green oxidant for wastewater treatment. It is a chemical that is 63% stronger than chlorine and environmentally friendly. Ferr-Tech uses it to clean wastewater in the industry, to enable water reuse, as well as to clean crates in the Food & Beverage industry or plastic flakes in polymer recycling plants, for example.

Ferr-Tech feels the drive to contribute to the ever growing global problem of clean water scarcity and also to decrease the use of harmful chemicals.

Milestones

2020
- February: Ferr-Tech is founded.
- Sepember: the company's waterlab is ready for business.

2021
- Increased production with new production module starts in October.
- First aircargo delivery to the USA in November

2022
- Partnership VivoChem established in January
- Partnership with BÜFA Chemicals established in April
- Relocation to a bigger facility in July

Funding/Awards

2021
- August: VIA grant, EU funding
- October: MKB fund Drenthe
- October: CES Innovation Award

2022
- March: Nominee of WIS Award (outcome in September 2022)
- September: Winner of the WIS Award


© Ferr-Tech

As a Dutch start-up, we are the first company to provide Ferrate(VI) for industrial applications.


© Ferr-Tech

Breakthrough for Ferr-Tech is the ability to keep Ferrate(VI) oxidant stable and preservable as a liquid, distributed under the name FerSol.

Halving Chemical Manufacturing Costs

An Innovative Continuous Reactor for Efficient and Sustainable Chemical Production

Traditional batch chemistry is too inefficient for a sustainable future. Switching batch processing to continuous processing is inevitable if the world is to reach net zero. Stoli Chem, UK-based start-up company, has designed the SABRe (scalable agitated baffle reactor), a multipurpose scalable flow reactor. Established in 2016 as a Warwick University spin-out, the start-up team capitalizes on its expertise in heterogeneous catalysis and continuous process chemistry. The SABRe simplifies batch to flow conversion and unlocks the benefits of continuous processing. It can handle solids, rapid and slow processes and exhibits best-in-class mixing. The SABRe main applications are in the manufacture of pharmaceutical intermediates, fine and speciality chemicals. Nikolay Cherkasov, co-founder and & managing director of the company, explains Stoli Chem's technology and talks about the benefits of continuous manufacturing.

CHEManager: Mr. Cherkasov, what was your motivation for founding Stoli Chem?

Nikolay Cherkasov: I have spent many years in academia in chemistry and engineering having published 50+ research papers. With this experience, I was looking to share it for the benefit of manufacturing companies. Ideas must work. Today we have a multinational team centered on our site in Wellesbourne just south of Birmingham in the heart of the UK.

You and your team invented and developed the SABRe flow reactor. What problem does this technology solve?

N. Cherkasov: Traditionally batch processes are used for chemical production. Processes run in batch are limited by the discontinuous nature: processes are starting and then being taken to completion, then prepped ready for the next. The SABRe converts batch to flow. In flow chemistry, the process runs 24/7, meaning you generate more products and value.

Continuous chemistry opens up more opportunities for the processing of chemistries as well as the more dangerous chemistries such as explosives and highly exothermic reactions. Smaller volume intensified reactors prevent runaway with far more control.

What have been the most exciting projects so far?

N. Cherkasov: We have had both exciting and challenging projects. One recently was with corrosive sulfur chemistry, and another using viscous slurries certainly proved challenging but were successful in showing the versatility of the reactor. Perhaps the most exciting are our recent projects involving light and allowing photochemistry to be undertaken in our glass reactor. The future is certainly bright!

© Stoli Chem

What are the benefits of converting batch processes to flow?

N. Cherkasov: The main benefits of converting to flow come from exceptional heat transfer meaning that the reaction temperature is better controlled. Along with this, the SABRe has the best-in-class mixing capabilities. This high mixing capability allows for high mass transfer and means that the reactants are homogenized thoroughly.

The SABRe utilizes a series of CSTR (continuous stirred tank reactors) which are in essence a series of batch reactors stacked on top of one another. The reactants move from one tank to another throughout the process. The unique design of the SABRe allows for additional reagents to be added at any stage of the process offering complete control.

One of the case study examples using the SABRe highlighted that in an enzymatic esterification there was a ten-fold throughput increase compared to batch. Everyone can see the value in those types of increases!

What makes your flow reactor unique?

N. Cherkasov: The mixing is independent of the fluid flow rates. This means that scale-up is simpler and broadens opportunities to undertake a wider range of chemical reactions.

The unique sparging tubes that run along the inside of the reactor allow the addition of reagents or in-line sampling.

The configuration of our reactor allows precise reaction control, alongside best-in-class mixing.

Our reactor is also easy to use and is offered in a variety of materials to ensure chemical compatibility. The reactor can also handle combinations of liquids, solids, and gases.

Nikolay Cherkasov, Stoli Chem

Personal Profile

Nikolay Cherkasov is an experienced researcher and entrepreneur. He has extensive knowledge in heterogeneous catalysis having 50+ scientific publications and securing £2.5 million grant funding from various sources. He is a member of IchemE, a graduate of Innovate UK's ICURe program and won an Enterprise Fellowship from the Royal Academy of Engineering. He leads the company's day-to-day operations and business development.

Which application sectors do you focus on mostly?

N. Cherkasov: Many of our customers are in fine chemicals, speciality chemicals, and pharmaceuticals. Although our technology can be applied to any fluid process.

What will be your next steps in technology and business development?

N. Cherkasov: Our main priority now is scaling up our reactor, to help as many businesses as possible switch to flow chemistry.

Business Idea

Revolutionizing Chemical Industries

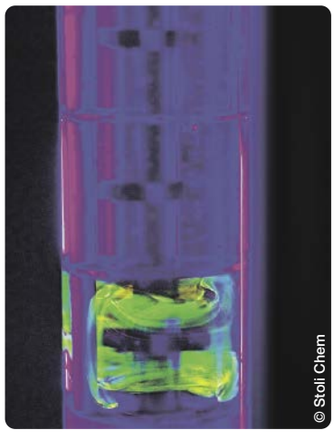
Stoli Chem's vision is to save the chemical industry millions in costs by increasing chemical processes' efficiency, safety, and sustainability. The fine chemicals industries are using processes which have not changed in centuries. Most of these chemical processes are carried out in batch reactors for simplicity. An alternative to batch processing is processing in flow (or continuous chemistry). The SABRe allows for scalable (flow) chemistry from lab to production scale.

Batch manufacturing has inherent flaws. By definition, batch is a start-stop process. After each batch cycle there is a cleaning and prepping period before a new batch can start. This is unproductive downtime. In GMP pharma, a fully utilized batch reactor produces chemicals 10% of the time at most.

Flow, by definition, is continuous. The SABRe utilizes a series of continuous stirred tank reactors (CSTRs), ten in total. These CSTRs can be viewed as small batch reactors with the reactants moving from one tank to another. This similarity to batch means that conversion from batch to flow processing is easier. In each tank an impeller rotates up to 1,300 rpm ensuring that the reactants are homogenized.

Uniquely, reagents can be added to any process stage to allow for optimum conversions to the valuable products. Temperature is controlled via a jacket surrounding the reactor, and stirring is controlled by a stirrer head connected magnetically to the reactor stirring shaft.

Flow reactors have a smaller footprint than batch reactors and can often produce as much. Hence, the same manufacturing size allows for superior and more efficient production.



■ Stoli Chem, Wellesbourne, UK
https://stolichem.com

Elevator Pitch

Sustainable Chemical Production

Sustainability does not require a premium price. At least in chemical production, sustainability could be economical. The keys are efficiency and scalability. Current batch production practices are scalable but neither efficient nor sustainable. On the other hand, continuous manufacturing is hugely more cost-, energy-, and material-efficient; yet is not scalable without multi-million investments. Stoli Chem provides tools for scalable and sustainable continuous chemical production.

Based on the experience of the academic founders, they have developed a technology that breaks and overcomes the standard dilemmas in flow. In most flow processes, the mixing speed, pressure drop, residence time, and fluid feed rates are inter-dependent. If the process is altered or scaled up, everything changes requiring extensive (and expensive) R&D work to regain and ensure process control.

In the SABRe system, mixing is decoupled from the flow rates. This design opens tremendous flexibility — the processes could be changed or scaled up while maintaining exceptional process control. The system opens the possibility of accelerating and intensifying multiphase (including solids!) processes that are a scourge of standard flow systems.

The future for Stoli Chem is promising. The flagship SABRe is proving popular for R&D chemists and engineers alike. Stoli Chem is currently working on scaling up and opening photochemical applications.

Milestones

2016
- Foundation of Stoli Chem as a Warwick University spin-out

2018
- Competitive Horizon 2020, SME Instruments project started to scale up the technology from 1 to 100 kg/day chemical synthesis

2021
- Lab-scale SABRe reactors available

2022
- A project started aiming to scale up and demonstrate 1,000 *t*/y chemical manufacture

Road Map

2022
- Launch of a kilo-scale photochemical reactor

2024
- Launch of a 10 L SABRe system for kiloton production

Fig. 1: Mixing in action in the SABRe highlighting the capability of the reactor.

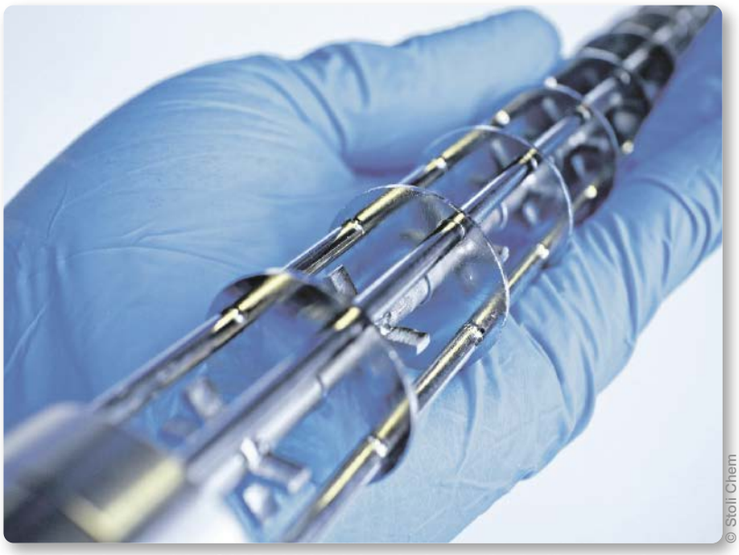


Fig. 2: The insert of the SABRe highlighting the innovative baffles and stirrer configuration.

CPhI Worldwide 2022

CPhI Worldwide, taking place in Frankfurt, Germany, on November 1–3, 2022, is dedicated to pharmaceutical developments, trends, products and services. Exhibitors include providers of contract research and synthesis services, suppliers of APIs, excipients, ingredients, intermediates and finished dosage forms, as well as producers of pharma manufacturing and packaging equipment. The event offers additional online networking opportunities and content.

■ www.cphi.com

Advanced Recycling Conference (ARC) 2022

On November 14–15, 2022, the Advanced Recycling Conference (ARC) takes place in Cologne, Germany, focusing on available recycling technologies for various streams of different plastics wastes as well as into political topics and environmental impacts. The hybrid event targets technology providers, related industries, waste management companies, plastic manufacturers, and investors as well as policy makers and scientists active in the field of recycling.

■ www.advanced-recycling.eu

European Coatings Show 2023

The European Coatings Show (ECS) covers all aspects of the production of paints, coatings, sealants, construction chemicals and adhesives on March 28–30, 2023, in Nuremberg, Germany. The demands placed on paint and coatings are constantly growing. Therefore, the coatings industry faces great challenges. ECS gives them the opportunity to meet innovation leaders and discuss the latest developments in tmaterials as well as technologies and equipment.

■ www.european-coatings-show.com

Chemspec Europe 2023

Chemspec Europe is to take place on May 24–25, 2023, in Basel, Switzerland. The event is the key platform for manufacturers, suppliers and distributors of fine and specialty chemicals to showcase their products and services to a dedicated audience of professionals in the industry sector. The product portfolio of this event covers fine and specialty chemicals for various industries. Conferences presenting the latest results of ongoing R&D projects round-off the show.

■ www.chemspeceurope.com

Index

Imprint

Publisher
Wiley-VCH GmbH
Boschstr. 12, 69469 Weinheim, Germany
Tel.: +49 6201 606 0

General Managers
Sabine Haag
Dr. Guido F. Herrmann

Publishing Director
Dr. Heiko Baumgartner

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

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

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

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

Stefan Schwartze
Tel.: +49 6201 606 491
stefan.schwartze@wiley.com

Production Managers
Jörg Stenger
Melanie Radtke (Advertising)
Oliver Haja (Layout)
Ramona Scheirich (Litho)

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

Lisa Colavito
Tel.: +49 6201 606 018
lisa.colavito@wiley.com

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

Wiley Reader Service
65341 Eltville
Tel.: +49 6123 9238 246
Fax: +49 6123 9238 244
E-Mail: WileyGIT@vuservice.de

Original Articles:
Specially identified contributions are the responsibility of the author. Manuscripts should be addressed to the editorial office. Instructions for authors may be requested from the publishing company. We assume no liability for unsolicited, submitted manuscripts.

Printed by: DSW GmbH & Co. KG, Ludwigshafen, Printed in Germany

WILEY

WILEY

CHEManager.com

International Issues

Your Business 2022 in the Spotlight

FEATURES:
PROCESS TECHNOLOGY, PHARMA & BIOTECH
APRIL

FEATURES:
FINE & SPECIALTY CHEMICALS, DISTRIBUTION & LOGISTICS
MAY

FEATURES:
PHARMA & BIOTECH, INNOVATION
OCTOBER

FEATURES:
REGIONS & LOCATIONS, CIRCULAR ECONOMY
DECEMBER

Editorial
Dr. Michael Reubold
Publishing Manager
Tel.: +49 (0) 6201 606 745
mreubold@wiley.com

Dr. Ralf Kempf
Managing Editor
Tel.: +49 (0) 6201 606 755
rkempf@wiley.com

Sales
Thorsten Kritzer
Head of Advertising
Tel.: +49 (0) 6201 606 730
tkritzer@wiley.com

Jan Kaeppler
Media Consultant
Tel.: +49 (0) 6201 606 522
jkaeppler@wiley.com

The most modern fleet, shaping a sustainable future

Passing the famous Castle "Pfalz", since six centuries safe in the waters of the River Rhine, one of Europe´s busiest waterways – the new gastanker M/T "Slot Dover" from GEFO. Four new sister vessels in 2022 and 2023: Slot York, Schloss Imola, Schloss Quedlinburg, Schloss Tramontana. All five new gastankers with Stage V engines according to new EU-standards and SCR-Catalysts. Most modern technology sets new benchmarks in their class by reducing hydrocarbons by 81 %, nitrogen oxides by 97 % and particulate matters by 95 %.

One tanker of the fleet of 150 tankers belonging to GEFO. 26 new build to reduce pollutant emissions. Which tanker will sail for you?

GEFO

www.gefo.com