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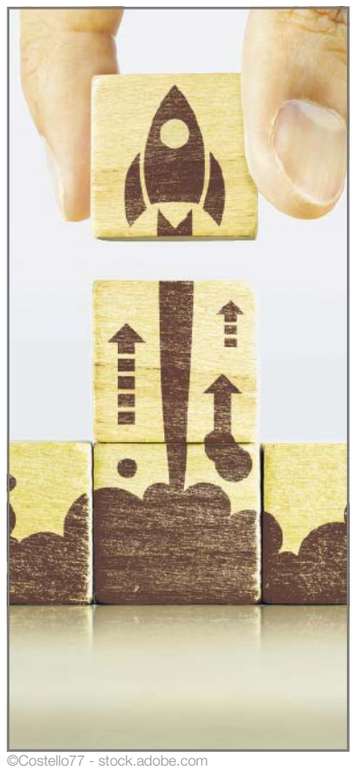

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Innovation

The Upswing of the Superstars

The Chemical Industry Has Shown Resilience to the Crisis — Now it Must Get Fit for the Future

Rising oil prices, the Covid-19 pandemic with its unprecedented drop in demand, and finally the supply shock — the recent crises have hit the chemical industry hard. Sales and profits plummeted, and share prices went into a tailspin. But the industry demonstrated unexpected resilience. The chemical sector was among the first to recover — an indicator of a general economic upturn in many regions.

Andreas Gocke, Boston Consulting Group

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For its annual report „Value Creation in Chemicals 2021 — Ten Years of Steady Growth — and a Few Superstars," the strategy consultancy Boston Consulting Group (BCG) examined the performance of leading international chemical companies from 2011 to 2020. The long-term perspective shows that the industry has mastered serious market downturns with astonishing confidence. For the 69 large-cap companies in the chemical industry — these are publicly traded companies with a market capitalization of more than $7 billion — the median annual total shareholder return (TSR) from 2011 to 2020 was 12%, while the median value for all sectors was 11%.

TSR accounts for the change in share price and any other effects on shareholders' net wealth, like dividends. It is driven by three factors: Firstly, by the combination of revenue growth and change in EBITDA margins as an indicator of a company's improvement in fundamental value. It uses secondly the change in the company's valuation multiple to account for the impact of investor expectations. Thirdly the model tracks the distribution of free cash flow to investors and debt holders in the form of dividends, share repurchases, and repayments of debt.

For the deep dive of the above-mentioned study, BCG once again significantly expanded the range of the investigation and examined the performance of 238 chemical companies with a market capitalization of more than $1 billion. Here, too, the result was impressive, with a median annual 10-year TSR of 9.1%.

However, the industry average is only partially representative of the companies as a whole. Since its first publication of the "Chemicals Value Creators Report" in 2012, a small group of companies has been at the top of the industry, including Croda from the UK, Pidilite from India, Sherwin-Williams from the USA, and the Swiss company Sika. Just 22 companies worldwide are among the consistent highflyers that have landed in the top quartile of annual TSR performance at least four times in ten years. There is a huge gap between the top performers and other companies; and even within the top group, the differences are considerable. India's PI Industries, for example, achieved a median annual TSR of 47% between 2011 and 2020, while US-based FMC came in at just 14% (see fig. 1). Overall, only slightly more than one-third of the surveyed companies were able to increase their value at an above-average rate. All others were far below average or even recorded a negative TSR.

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India-based Players Grow most Dynamically

Companies from India (10-year annual median 29%) and the US (13%) saw particularly high TSR growth, while Greater China underperformed with 4%. However, the figures may not fully represent the strength of Chinese companies within the industry, as the study excludes privately held and state-owned companies. Overall, however, the study does not provide any concrete evidence that geographic affiliation has a decisive influence on a company's suc-

cess. India is an exception: chemical companies there have been experiencing an enormous upswing since 2014, boosted both by government investment programs and the steadily growing middle class on the subcontinent. The median annual 10-year TSR in South Asia was 32%—the highest of any region and nearly four times the global TSR of 9%. Five of the top-performing companies, including TSR leaders PI Industries and Pidilite, are based in India.

Specialty Companies Dominate the Top Group

For further analysis, we group the surveyed companies into five subsectors: agrochemical and fertilizer, base chemicals and basic plastics, focused specialty, industrial gases, and multispecialty. More than half of the top 22 companies belong to the focused-specialty subsector. Looking at all the companies analyzed for the study, this subsector achieved the highest increase in value for shareholders, with a median annual 10-year TSR of 13%. Only the industrial gases subsector can boast a comparably good result. Nevertheless, no industrial gases company is among the top 22 performers.

Looking one level below the five subsectors, there are 20 product clusters, of which those belonging to the focused-specialty subsector have the highest TSR. Electronic chemicals players, who supply precursors for the manufacture of silicon wafers and semiconductor production, performed particularly well. Due to increasing digitalization, demand for these chemicals will continue to rise. Other product clusters, such as paints & coatings, are booming in lockstep with the construction industry. Mining & oilfield and agrochemicals in particular have lost significant importance over the past five years (see fig. 2).

However, belonging to a subsector or to a product cluster alone is no guarantee for sustainable value creation. The question arises as to what the top performers do differently and what value creation strategies they pursue. BCG's analysis has shown that the business model, the ability to innovate, and strategic acquisitions contribute significantly to value creation.

Consistent Alignment with the Market

Many of the top-value creating chemical companies pursue a market-based business model. This means that they consistently align their offerings and set-up to market requirements. They adapt to changes more quickly and adjust their business model more flexibly than their competitors. Of all the companies in this study, those with a market-oriented business model have a median annual TSR of around 14% over ten years. India's Berger Paints is consistently pursuing this business model. The company has adapted its offering to the changing needs of the Indian population. The paint and coatings manufacturer, a supplier to the automotive industry, maintains 40 training centers for painters and has trained more than 60,000 painters in the 2020 pandemic year. The number of retailers selling Berger products has doubled from 15,000 to 30,000 since 2015. Berger has also expanded its product range to include adjacent categories such as glass, wood, and metal coatings as well as construction chemicals. The company is constantly realigning itself to serve India's diverse customer base.

Many specialty chemical companies are pursuing technology-based business models. They compete through proprietary technologies and intellectual capital. This group includes suppliers of high-performance polymers, enzymes, and catalysts for industrial processes as well as electronic chemicals for semiconductor manufacturing. Such a business model typically requires a strong IP base and a unique offering—or one

Continued Page 6 ▶

Company Name	Subsector	Country	Median annual TSR, 2011 to 2020 (%)	Median annual TSR, 2016 to 2020 (%)	Number of years ranked in the top-quarter 2011 to 2020
PI Industries	Agrochemical and Fertilizer	India	47	28	4
Berger Paints	Focused specialty	India	36	32	4
Nippon Paint	Focused specialty	Japan	35	32	7
Pidilite	Focused specialty	India	29	27	8
Wanhua	Base chemicals and basic plastics	China	26	48	6
Lonza	Focused specialty	Switzerland	26	32	5
Asian Paints	Focused specialty	India	26	27	6
Sherwin-Williams	Focused specialty	US	26	24	7
Sika	Focused specialty	Switzerland	24	33	6
NOF Corp.	Multispecialty	Japan	23	26	5
Quaker Chemical	Focused specialty	US	22	28	5
Nissan Chemical	Multispecialty	Japan	22	21	5
EMS-Chemie	Focused specialty	Switzerland	22	17	6
Petkim Petrokimya	Base chemicals and basic plastics	Turkey	21	28	4
Chr. Hansen	Focused specialty	Denmark	21	10	5
Symrise	Focused specialty	Germany	20	13	4
Croda	Focused specialty	UK	18	19	10
Innospec	Focused specialty	US	18	12	4
Engro	Agrochemical and Fertilizer	Pakistan	17	12	4
UPL	Agrochemical and Fertilizer	India	16	11	5
Westlake	Base chemicals and basic plastics	UK	16	10	4
FMC	Agrochemical and Fertilizer	US	14	30	4

Sources: Company reports; S&P Capital IQ; BCG analysis.
Note: Companies are considered high-performing because of their inclusion in the top quartile of TSR performers for four or more years.

Fig. 1: These companies consistently lead the industry in total shareholder return (TSR).

that is difficult to imitate. The median annual TSR of this group is 12% over ten years.

The ability to successfully innovate is also a hallmark of top performers. Germany's Symrise, a leading manufacturer of flavors and fragrances, generates more than 20% of its sales from new products each year. Its organic growth since 2011 has been consistently higher compared to its competitors.

The top performers also pursue mergers and acquisitions strategically. Houston, US-based Westlake Chemical purchased Boral's North American building products business in 2021 to strengthen its position in the fast-growing North American construction market. Westlake is also positioning itself in the environmentally sustainable plastics market through acquisitions of, among others, Dimex, a leading manufacturer of recycled plastic and related environmentally friendly products. Westlake is now the second-largest producer of PVC in the world.

The Future of the Industry is Green

Even though the chemical industry has coped well with the current crisis, the pressure to adapt will increase in the future. Top companies will not be content with optimizing existing processes and increasing production volumes. They will use more digital technologies and collaborate intensively with their customers and a variety of partners in the ecosystem.

More than 50% of the chemicals growth in the near future will happen in China. Companies will shift their focus from upstream and base chemicals to downstream chemicals such as electronic chemicals and food ingredients.

Western chemical companies, on the other hand, will have to re-regionalize their supply chains to compensate for the vulnerability of global logistics and geopolitical hurdles, such as the US-China trade dispute or the heavily discussed European Union's carbon border tax. Decarbonization needs, in particular, will pose major new challenges for the industry in the coming years, but it will also open up new opportunities. The successful chemical companies of the future will pursue a net-zero carbon footprint using innovations such as e-crackers, chemical recycling, bio-based feedstocks and fermentation technologies. Overall, chemical products will contribute to sustainable applications: storing energy, isolating human habitats, and reducing materials' weight and carbon emissions. This way, the chemical sector has the potential to become a driving force for economic development in industries such as manufacturing, construction, agriculture, energy, or mobility.

Fig. 2: The top-performing product clusters are in focused specialties.

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The EU Goes Green

Costs and Benefits for European Chemical Companies

The EU Green Deal, which calls for a net-zero carbon Europe by 2050, sets a high bar for reducing greenhouse gas (GHG) emissions, and its impact will be felt across industries. But the chemical sector's unique nature means that it will be more deeply affected by the Green Deal than other industries — and more deeply involved in making net zero a reality, as well.

The cost to the chemical industry will be high. An in-depth analysis by Accenture and NexantECA shows that the Green Deal will require new technologies and processes, disrupt operations, bring changes to plant networks and ultimately, require heavy investments from the industry. But the Green Deal will bring more than compliance costs. It will also open the door to large increases in demand for innovative new chemical products and create significant new growth opportunities for chemical companies.

Sizing up the Challenge

To reach net zero by 2050, the chemical industry will need to cut GHG emissions dramatically. The industry is no stranger to that type of mandate—over the last three decades, it has reduced annual GHG emissions by 171 million tons. Much of this was accomplished through improvements in technologies and processes, but it was also driven by capacity reductions and plant shutdowns. From 1993 to 2020, the EU share of total global chemical production decreased from 31.6% to 14.4%. To a great extent, the past reductions in emissions were essentially the "easy" cuts. Making the next rounds of reductions needed to meet the Green Deal goals will be more difficult.

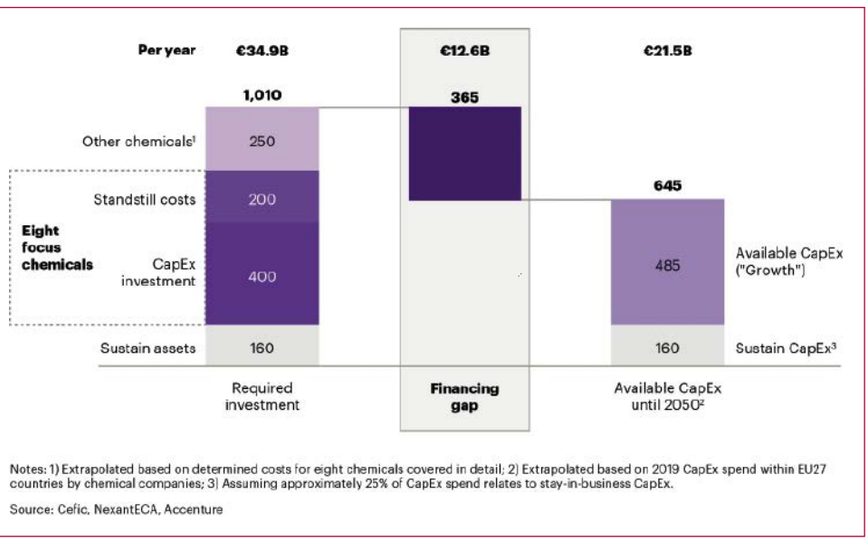
The Accenture/NexantECA research underscored the size of that challenge. It looked at the production of eight chemicals—ammonia, ethylene, propylene, nitric acid, carbon black, caprolactam, soda ash and fluorochemicals—that account for 75% of chemical industry greenhouse gas emissions. Based on that assessment, it found that the industry in Europe will have to reduce emissions by another 186 million tons a year by 2050. (That number is higher than some estimates, because it is based on both regulated and non-regulated plants, not just regulated plants.)

Those reductions will come with a very large price tag. Something between €400 billion and €600 billion in capital expenditures will be needed for core equipment and the design, construction and modification of facilities. Another €200 billion to €300 billion will be incurred as standstill costs—that is, the profits lost due to halted production as plants are retrofitted, improved or rebuilt. And changes to the production processes used for other chemicals beyond the key eight chemicals mentioned previously will require another €250 billion to €350 billion. Based on those figures, the overall mid-range estimated Green Deal "bill" for the chemical industry will be more than €1 trillion. To pay it, the industry will need to fill in a significant funding gap, compared to current capital spending, increasing capital investments by €12.6 billion a year over the next three decades (see figure).

The challenges ripple beyond those costs and the chemical industry itself. For example, making the necessary changes to plants and plant networks in a timely manner will require capacity expansions at equipment manufacturers and in the engineering, procurement and construction industries. Meanwhile, dramatic increases in renewable electricity will be critical to creating a net-zero chemical industry, requiring an additional 3.2 petawatt-hours (PWh) of renewable energy—about five times the amount generated in the EU today. Much of this will depend on the efforts of utilities and governments, but chemical companies will need to play a role in their planning because the power and chemical sectors are closely intertwined. The electrification of chemical plants will not reduce GHG emissions enough without using renewable energy, and the building of new renewable energy generation cannot be justified without the demand created by more electrification in plants.

Bernd Elser, Accenture

Fortunately, the Green Deal does not ignore these challenges. For example, it calls for the EU to provide more support for increased renewable energy generation, and for regulatory changes that will encourage more low-GHG products and solutions. It recognizes the need for programs that protect against "GHG leakage" by stopping the importing of non-compliant products. And it calls for sustainable financing to help companies fund their net-zero initiatives.



The chemical industry's EU Green Deal funding gap, 2021–2050 (€ billion)

What's the Upside for the Chemical Industry?

The chemical industry—whose products are the "ingredients" for virtually every sector—is in a unique position in regard to the Green Deal. Like other industries, it needs to make changes to its processes and systems in order to meet the 2050 goals. But it can also play a key role in helping other industries do the same—and that's where the huge growth opportunity lies.

Virtually every industry will be affected by the EU Green Deal, as well as the growing consumer sentiment that favors low-carbon products. With that in mind, companies in a variety of industries have already made public commitments to sustainability—and they will need to change many of the offerings they bring to market to meet these commitments.

Chemical products will be a big part of the solution for these customer industries. Chemical companies that focus on net-zero innovations and produce new materials that are lighter, lower-carbon, more sustainable and made with processes that result in lower GHG emissions will find expanding markets for their offerings. And this growth in demand will not be restricted to Europe—it will be global because so many global companies have made net-zero commitments that apply to their worldwide operations. As European chemical companies reshape themselves for the Green Deal, they are likely to gain a head start in the race to bring low-carbon, sustainable and circular economy-related solutions to market, giving them a competitive advantage in global markets.

Getting Ready

What can chemical companies do to prepare for this future? To begin, they should assess each plant's future competitiveness in a lower-carbon world. How can investments in a given plant lead to innovative offerings, such as net-zero or low GHG emission products? Will the plant's future production costs be competitive globally? The answers to such questions can help identify which plants should be closed, moved or modified.

For chemical companies, the changes needed to reach net zero will be massive, complex and enterprise wide. As a result, each company will need to develop its own detailed roadmap for moving forward—one that defines and integrates technology plans, business portfolio strategies, cost-efficiency initiatives and growth programs. In addition to guiding projects and initiatives, this roadmap will help investors be more comfortable with net-zero driven changes. That comfort will be key to future share prices and, ultimately, the ability to fund net-zero efforts.

That kind of planning will need to reach across company borders, as well. Achieving the Green Deal's goals will involve a variety of interdependent activities that touch on customers, suppliers and partners, and even players from other industries—witness the need to coordinate the design of the chemical plant network with the expansion of renewable energy production, as already discussed. Sectoral roadmaps will be needed to coordinate, sequence and synchronize the activities of these groups, and bring together public-private partnerships, renewable energy initiatives, customer commitments to sustainable products, innovation efforts and technology plans to form a comprehensive approach.

Chemical companies certainly face significant technical and financial challenges with the Green Deal. But by meeting those challenges, the industry can play a critical enabling role in helping the Green Deal succeed. As the "industry of industries," the chemical industry will be in position to help a tremendous range of companies around the world achieve their net-zero goals and contribute significantly to meeting the global challenge of climate change. And by doing so, it will create a very real opportunity to prosper and grow in a more sustainable, circular future.

References can be requested from the author.

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A Global Innovation Hub – Past, Present and Future

SCI (Society of Chemical Industry) Connects Science with Business in the UK

In November last year, SCI (Society of Chemical Industry) had the privilege of hosting a debate at COP26 in Glasgow on 'Combating Climate Change with Chemistry'. We staged a panel discussion of young industrial scientists working globally to address climate change. They included SME representatives from California's hard-tech start up C-Zero and Sphera in Durham, UK, as well as corporate partners GSK, Unilever and AstraZeneca.

The event coincided with SCI's 140th year. As a learned society and the place 'where science meets business', the debate showcased the unique role of SCI—working as a global innovation hub to support both SMEs and large corporates as they navigate global industry challenges, putting the customer and society first. SCI has truly come full circle—returning to the very reason it was founded and reminding members why collaboration across the international chemical using industries is critical if we are to accelerate the science out of the lab for full scale commercial use—and societal benefit in testing times.

Innovation Is Not New

Chemistry has been at the heart of innovation over the last 200 years, an integral part of the industrial revolution, and a vital supplier of society's needs. It provided the route to synthetic fibers for clothing and furniture—supplementing the stretched supplies of cotton and wool and developed materials for homes, factories, farms, the growing automotive and aerospace industries. Chemistry related science was the bedrock of the healthcare industry too—from the first soaps and disinfectants, through to early drugs and the sophisticated molecule we now use for therapy and disease prevention. This year, SCI is continuing this trajectory by showcasing the latest in medical thinking. In June, we will host the 'What's New in Immunotherapies 3' event. Small, drug like molecules can be effective modulators of immune response pathways and their molecular properties can be fine-tuned to enable excellent cell permeability and bioavailability. Our event will pose the possibility of treating cancer by harnessing the body's own immune system to fight tumors. SCI is passionate about brokering opportunities for debate and the adoption of science into industry at pace and scale for public good.

SCI was founded in 1881 by a group of prominent scientists, entrepreneurs and inventors. They were pioneers of the emerging chemical industry and often controlled their own industrial companies. Together, they helped catapult society into the 20th century. Key individuals included William Henry Perkin, SCI President 1884–85 who discovered the first synthetic organic dye, mauveine, Ludwig Mond, SCI President 1888-89, founder of Brunner Mond, one of the four companies that merged in 1926 to become Imperial Chemical Industries (ICI), which spawned businesses such as Ineos and AstraZeneca, William Lever of Lever Brothers (subsequently Unilever) and George Matthey, one of the founders of Johnson Matthey. There were 300 founding SCI members and 1,140 by the time of the first General Meeting covering sectors as diverse as food, energy, materials, mining and glass. The early members were global, coming together to work for societal good. European members included Professor August Wilhelm von Hofmann, co-founder of the German Chemical Society. The original membership fee was one guinea—or £400 today.

Sharon Todd, SCI (Society of Chemical Industry)

At the Forefront of Societal Challenges

Today, SCI is still in the frontline of society's efforts to stem and reverse climate change, provide enough food for a rapidly expanding population and drive to personalize therapy for both widespread and orphan diseases. To address these goals, chemists are working with engineers, biologists, economists and psychologists to ensure that the choice and implementation of solutions is optimal. SCI's themes address many of the industry issues in an uncertain post Brexit world of climate change emergency, global health concerns and thirst for innovative solutions. SCI's strength lies in its expansive network of industry pushing the boundaries of new technology around the world and disseminating knowledge quickly and effectively. We counsel our members on current industrial challenges, ensuring they have access to current thinking, debates and networking around topics such as decarbonization, digitalization and AI, future energy strategy, the supply chain and circular economy. Current SCI focus areas also include hydrogen strategy, green feedstocks and the need

> *"Chemistry has been at the heart of innovation over the last 200 years."*

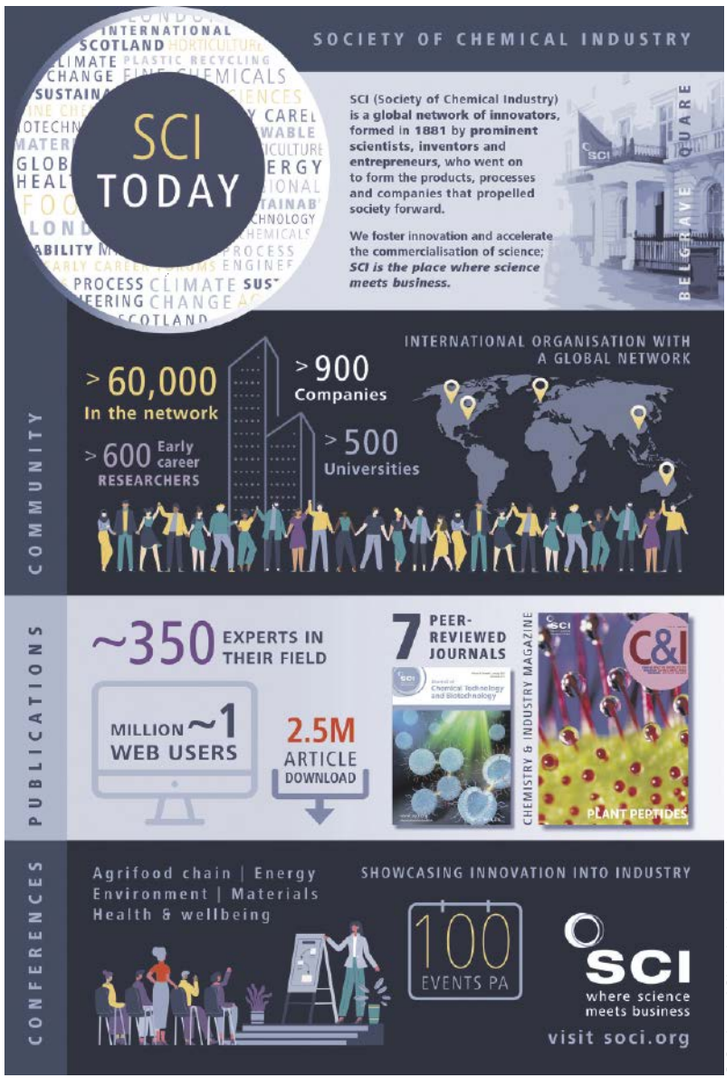
for sector collaboration to assemble the technologies needed to boost the recycling of materials for green industries.

In addition to innovation in the science, innovation is also required in supply chains, where many are needing to be rebuilt—driven both from a need for new greener feedstocks and a need for levels of transport which may be unacceptable as we strive to lower the carbon emissions from human activity. Countries and (global) companies are seeking a way of operating that makes supply chains more resilient and lowers the overall carbon footprint of essential products. We are pleased to be helping to facilitate those discussions.

Global Programs for Global Issues

SCI has developed a bespoke series of programs to meet member needs. SCI membership spans the globe and there is a China group as well as a presence in Canada, the United States and Australia. There are regional groups across the UK and SCI special interest groups span 24 technical and business interest groups as well as 17 international and regional ones. We work with companies up and down the supply chains (very few are not reliant on chemistry) to move away from fossil carbon feedstocks to sources of carbon which are sustainable and circular.

We collaborate with the automotive, aerospace and energy industries to ensure the materials which make batteries and fuel cells operate can be sourced efficiently at costs which will enable society to transition quickly to sources of energy that have significantly lower carbon emissions. We also work with the whole agrifood chain to achieve higher efficiencies at every step in the production of food and to seek sources of carbohydrates and proteins with lower carbon emissions. With our healthcare sector partners, we try to ensure that the chemical tools to enable the next generation of therapies can be made flexibly and cost effectively. We also champion the responsible use of chemicals in the environment, tapping the growing understanding of the interaction of chemicals and materials which have got into the environment, whether purposefully or accidentally, to minimize the impact on the biosphere.



The SCI (Society of Chemical Industry) at a glance.

Partnership

Corporate partners are a vital part of SCI's lifeblood. We work with them, leveraging their understanding of the chemistries they use and the supply chains they operate in to build a picture of both opportunities and challenges. We then cooperate with partners and governments to aim for the integration of regulatory and commercial strategies, to ensure that everyone understands the various points of view, but keeps a focus on the strategic goal of using chemistry and related sciences to serve society.

"Corporate partners are a vital part of SCI's lifeblood."

SCI is still London-based, close to Westminster, the heart of political decision making and commerce. In 1955, its global headquarters moved to 14–15 Belgrave Square, part of the historic Grosvenor Estate. It remains there today, and members value its central location with quiet areas for meeting and working. A fully equipped auditorium offers excellent conference and presentation facilities. There is also the haven of the terrace and science garden.

Publications and Events to Accelerate Scientific Research

Today, all SCI members receive a free copy of our journal C&I Magazine, the industry leading innovation publication, showcasing how new technologies are being used in industry. The publication's origins lie in one of the first journals in the UK to be dedicated to the subject of applied chemistry. The January 2022 edition included a leader piece around the fast-growing hydrogen market. As a not-for-profit publisher, SCI accelerates scientific research through the promotion, curation and publication of cutting-edge science through its portfolio of curated, peer reviewed journals.

"SCI was founded in 1881 by a group of prominent scientists, entrepreneurs and inventors."

Today, SCI has a vibrant events portfolio and during the Covid-19 pandemic, we continued to offer a full program of online webinars, talks and presentations. These have covered areas as diverse as soil erosion, electric vehicle batteries, anti-microbial resistance trends and Professor Neil Ferguson's talk on the pandemic itself. Members tell us they value these opportunities for networking, research, acquiring knowledge and continuing professional development. The global innovation landscape across the world is facing complex demands currently—whether regulatory, supply-chain and skills wise or politically—and all these core areas help equip companies with finding solutions.

SCI participates in the Chemistry Council with recent activity including calling for a specific sector plan to support the chemical industry in the UK. In 2022, we will continue this work and also expand our focus on climate change—an issue that affects us all. The more diverse our membership, the greater impact we will have. We believe there is hope in science. And so did our live COP26 audience. We asked "Do you believe that science is pivotal in providing climate change solutions?"—and 100% did.

We hope you consider joining the SCI community in 2022 so collaboration leads to a greater collective voice—and a louder, more impactful one.

Sharon Todd, CEO, SCI (Society of Chemical Industry), London, UK

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The Supply Chain Dilemma

Another "New Normal" that Will Have the Potential to Change the Chemical Industry Landscape

Since the middle of the 1980s, the supply chain of many chemicals has moved east. This was primarily driven by cheaper production costs in China or India, due to lower raw material prices, a cheaper asset base compared to plants in the West, and lower environmental and regulatory standards.

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This trend increased over the last three to four decades. The initially lower quality that ended in lower prices in the beginning changed to "good-enough quality" in many industries (e.g., pigments, surfactants, intermediates, additives, and a wide range of plastics and intermediates). The consequences had been drastic for most operations, especially in the West. It changed the process chain of nearly all products and with them the value chain. Plants were shut down, know-how moved abroad, and major parts of the supply chain moved to the East. China and India became the operational backbone for many products in the specialty chemicals and the agrochemicals as well as in the pharmaceutical industry—the latter especially in India.

While that change of the supply chain was a shock in the beginning it became the new normal at the end of the 1990s and many companies moved their assets to the East as well. The industry became used to Chinese and Indian competition by the beginning of the 21st century and so the chemical world faced more global competition. Over time, a certain balance was established:

- Chinese products improved and were marketed via traders in the west,
- Western companies built plants in the East to serve their global market,
- many intermediates that were able to "travel" were dominated by Chinese and Indian producers.

The chemical industry adapted its processes and businesses and initially started to play and later efficiently experience the global game.

Changes in the Logistics Landscape

In the past five years, changes took place that had a slow but constant impact on the supply chain of chemicals.

- No. 1: Over many years, SHE standards and regulatory control in China were low. In 2018 the Chinese government launched the Blue Sky Initiative which led to a government-driven closure of many small to midsize plants. Some larger producers had to shut down too but were able to upgrade facilities or due to their size were tolerated by authorities as long as they show improvements in the SHE field.
- No. 2: The trade war between the US and China showed limitations in exports from China at least to the US. Some of this supply was compensated by Western companies, but they suffered from the supply chain interruptions that took place due to the Blue Sky Initiative.
- No. 3: The significant increase in transportation costs primarily due to the lack of vessels and shipyards at the same time.
- No. 4: The rising costs in India and China due to regulatory and environmental changes as well as higher living standards (especially in China).
- No. 5: The change of many feedstocks toward renewables, driven by the visible climate changes that caused governmental initiatives and regulations to reduce the greenhouse gas emissions until 2030 by 40% in the EU.
- No. 6: The Covid reality that has impacted supply chains for two years.

All of those drivers are in place until today, might be partially mitigated—at higher costs–but will not disappear!

The change in the logistics landscape and availability of ships has and will have a significant impact on freight rates—they will not return to prices seen five years ago. Even more, the global reliability schedule dropped from >70% in 2018 to <50% in 2020 and to 30% in 2021. This is not only caused by the pandemic crisis but more linked to the limited availability of vessels and overbooking of capacities—it lasted in supply chain interruptions. This will not be an episode as the number of new ships produced to fulfill demand dropped from 117 in 2011 to 23 in 2021 and as each year nearly 50% of ships >100 tons of capacity have been decommissioned. The shutdown of shipyards in the last two decades will restrict a fast recovery of capacities that are crucial for the chemical industry.

Today, there are 450 million tons of carbon-containing chemicals, 85% of them are fossil-fuel-based, the rest is biomass- and recycling based. It is estimated that until 2050 this number will rise to 1,000 million tons, or in other words, the renewable-based carbon production has to rise by a factor of 15. Furthermore, it is estimated that by 2026 the plant-based materials market will count for $85 billion.

Uwe Nickel,
Proventis Partners

There are numerous projects running and many technologies either find their revival or new technologies based on well-known principles are in an early stage to convert bio-based feedstock into chemicals. One example is castor oil as a substitute—with 55% it has the highest oil content per unit. The market for its application is enormous, e.g., it is estimated that the global market for bio-based plastics reaches $28 billion at a CAGR of 26% by 2025. The problem is that it is only available from India and that the crop is very sensitive to climate changes. To use it on a broader scale for the chemical industry not only challenges like yield/unit have to be solved but also the availability in other regions. This will raise the need of easily accessible crop or side products which cannot be imported from far away but will be cultivated in the region in an efficient way to manage a changed supply chain for this kind of products to assure chemical products established in the markets.

Impact on M&A Activity

All of these supply chain implications and challenges will have an impact on companies and the market for transactions. The key changes will be:

- A change in worldwide operations—more companies will investigate alternatives to China and India.
- Distributors have to rethink their business models and need to diversify.
- Chemical companies have to revisit their supply chains regarding availability of renewables.
- Agricultural companies and farmers will have a different position in the future by becoming key suppliers and strategic partners.

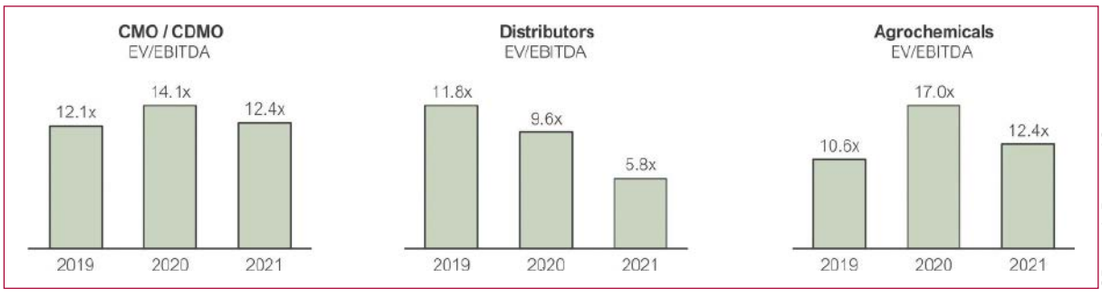

Fig.: Development of transaction multiples in relevant industries.

This will impact the whole of the chemical industry as well as the transportation and energy supply industry. In the chemical sector we will primarily experience consequences on the following players:

- Small to midsize companies, because they need to transform as fast as large companies but not having sufficient development resources or a diversified portfolio,
- CMOs/CDMOs as well as fine chemical and API producers, because they are very much focused on intermediates and operations in Asia.
- Distributors, because parts of their suppliers will be no longer competitive to generate margins on top.
- Farmers and agricultural companies, because they are becoming game changers and will tackle more downstream opportunities.

These supply chain changes will not only trigger the growth of circular chemistry but also the need to be more active in M&A especially for many sub sectors of the chemical industry. Furthermore, strategic partnerships of chemical companies to secure the supply with the limited volumes of renewables will be key to success and induce another transformation of the industry.

There have been a rising number of transactions in the last twelve to fourteen months in the relevant spaces. The multiples shown are only delivering a snapshot. We have analyzed these areas in more detail and the ranges are much broader than shown, especially in the area of chemical distributors where trading multiples for larger enterprises are above 10 times the enterprise value (EV)-to-EBITDA multiple. The acquisition of Caldic by Advent International, with a multiple of 15 paid, is still on the high side. Many companies are looking for opportunities through bolt-on acquisitions to move faster into the renewable space, and agricultural companies benefit from a growing demand due to a growing population and can further benefit due to the changed feedstock demand of the chemical industry.

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A list of sources and references is available from the author.

Dealing with Price Volatility

Analysis of Commodity Chemicals Price Developments in China

It sometimes seems that everyone running a business always thinks that times are tougher now than they used to be. For producers — and buyers — of commodity chemicals, this thinking will take the more specific form of concerns about increased price volatility. Have prices of commodity chemicals really become more volatile recently? And, if so, what does this mean for those dealing with them?

Kai Pflug, Management Consulting — Chemicals

Ralf-Roman Rietz, Strategic Advisor

Let us look at the first question — have the prices of commodity chemicals in China become more volatile in the past three years? To answer the question, we examined prices of 34 commodity chemicals from January 2019 to December 2021. The data is shown in the figure.

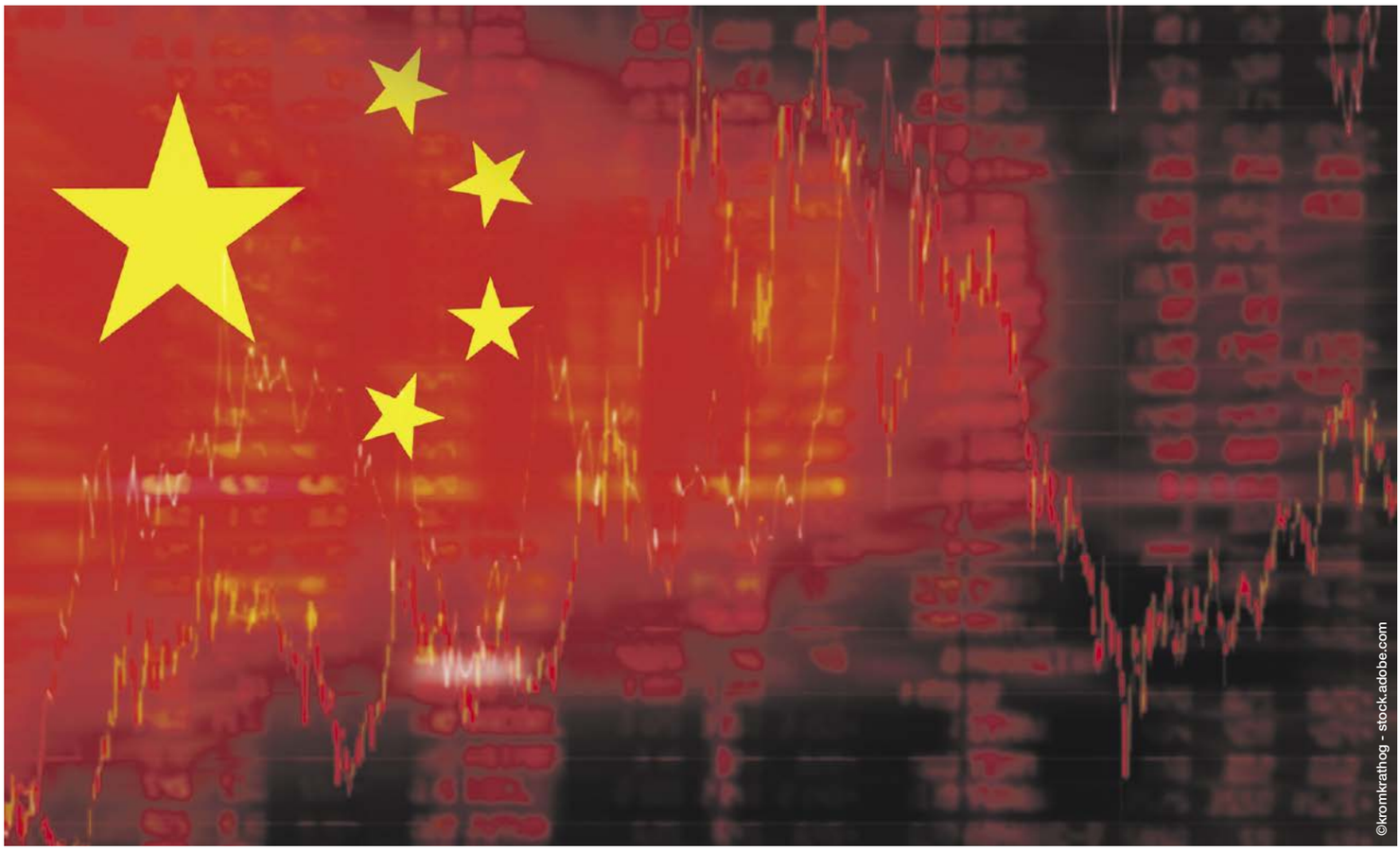
Analysis of Price Fluctuations

For the observation period from 2019 to 2021, the figure shows the price range for each year. It is immediately apparent that on average the price ranges for 2021 are wider than for the two previous years, indicating larger price fluctuations. Another observation is the general extent of the price fluctuations — some chemicals reach maximum prices more than three times the minimum ones.

In addition, the general trend here is a slight price decrease during 2019 followed by a more substantial price decrease in 2020 and a substantial increase in 2021. While this is partly due to aspects specific to each chemical, a broader rationale is the oil price development — the average annual oil price dropped from $57 per barrel in 2019 to $40 per barrel in 2020 and then increased to about $68 per barrel in average in 2021.

We also performed a separate analysis using the relative standard deviation as a measure of volatility. In 2019, this measure was comparatively low for almost all products. In 2020, volatility increased substantially for about one third of the products. Finally, in 2021 almost all products show increased price volatility. For individual products such as caustic soda — affected by production curbs as some chlor-alkali producers have been asked by local authorities to lower production rates as part of the country's dual control policy on energy consumption and intensity — the volatility increases are extreme.

So, it seems despite our initial skepticism about people always assuming things are worsening, they are probably right in this case. The volatility of the prices of basic chemicals in China has substantially increased recently. One reason for this increased volatility certainty is Covid-19. However, it is quite possible that increased price volatility is a longer-term trend that will stay with us even once Covid-19 is more or less under control.



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Impact for Chemical Companies

What does this mean for companies purchasing these chemicals? Obviously, dealing with chemicals with highly volatile prices brings specific challenges, which we will discuss below along with some potential solutions.

First of all, substantially varying input costs have a big impact on the pricing of chemical products. In order to obtain stable profit margins, this means both aiming to reduce the variations in the prices of the chemical raw materials and to pass on at least some of these variations to the end customers.

Long-term contracts for commodity chemicals based on a fixed price are one way of achieving such a stabilization. However, given the very high impact of oil price changes on basic organic chemicals, it may be difficult to find a producer of such basic chemicals willing to agree to fixed prices.

A more realistic proposition is hedging based on a proxy, such as crude oil. Such hedging with futures contracts is a financial tool to reduce the effects of fluctuating raw materials. As this allows the participation of financial players not involved in the production of chemicals themselves, the options offered will be much broader.

Upstream integration is another option, although more of a theoretical one. While in principle it reduces the exposure to relative volatility via increasing the share of value creation, it also puts a company much closer to the source of volatility.

Of course, volatile input prices are less of an issue if these can simply be passed on to end customers. This can be fairly straightforward for chemicals close to the ultimate raw material crude oil, as the price of crude oil is highly transparent, and it affects a large range of products, some of which having high visibility (e.g., petroleum prices at gas stations). Passing on these input costs can even be done on a formal basis, e.g., pricing based on an index. In an extreme case, a chemical company will only act as a toll producer, thus shifting the risk of varying raw materials entirely on the customer—though this will likely be accompanied by lower margins.

Other such options can broadly be summarized as increasing the overall share of value creation (which diminishes the relative fluctuation in raw materials costs). In practice, this can be achieved by integrating further steps downstream in the value chain, or similarly by offering more differentiated products. In both cases, as the overall value created by the chemical company increases, the relative impact of upstream price fluctuations decreases.

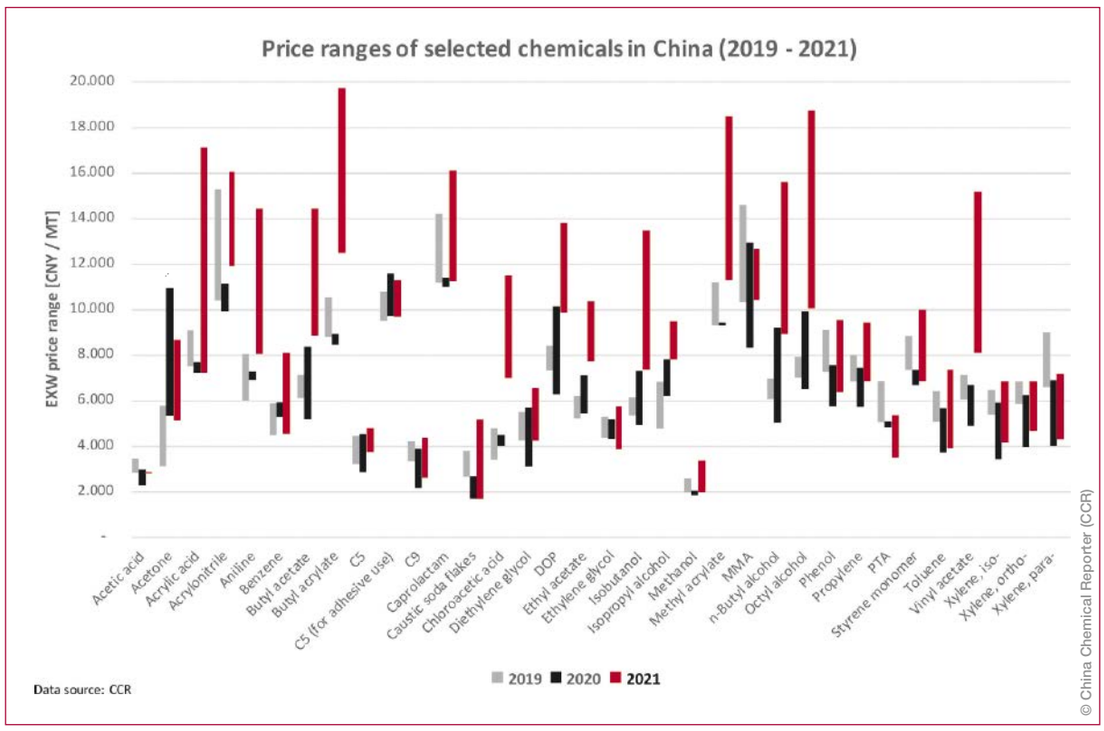

Fig. 1: Price ranges of selected chemicals in China

Stock Levels

Another issue affecting buyers of commodity chemicals with high price volatility is related to stock levels both of raw materials and of finished goods. Depending on the going market price of these materials, capital costs may vary substantially. This issue may be dealt with by periodically recalculating stock levels based on current prices of raw materials and finished products, thus identifying the net working capital that is the best compromise between capital costs and capability of delivering goods within the timeframe required by customers.

"The volatility of the prices of basic chemicals in China has substantially increased recently."

Related to this issue is the difficulty to do appropriate planning, as some of the main input variables for this planning are undergoing strong fluctuations. Depending on the price of main input materials, an expansion of production capacity may either be a highly sensible step or have negative effects on overall profits. This similarly applies to the economics of smaller process improvements, e.g., a capital investment that leads to a yield increase of an end product.

Scenario Planning

A sensible step is to define a few scenarios using different price levels as starting point. Based on the outcome of these scenario calculations along with an estimate of the likeliness of each scenario, a rational decision can be made. Considering scenarios—and updating them frequently—will also prepare a company for enacting changes more quickly should the overall situation change rapidly.

This issue is even more serious if the end product of a chemical manufacturer can be produced via different production processes using different raw materials. In this case, a change in the relative prices of the different raw materials may well lead to the currently employed production process becoming uncompetitive in the market. Again, scenario planning offers at least a partial solution. In rare cases, it may even be possible to establish several production processes based on different raw materials, thus giving the company options in case of diverging raw materials prices.

Unusual events like the current pandemic are less foreseeable, but market and macro-economic trends should be monitored to get early grasps of cyclic swings (e.g., chemical growth versus GDP, customer and end-use consumers purchasing behavior, international trade, capacity utilization and announced capital expenditures or lack of them).

As our analysis of recent commodity chemicals price developments in China shows, volatility of prices has been increasing recently, and it is far from clear whether this is only a temporary effect. As a consequence, companies requiring such commodity chemicals should examine options and strategies to deal with this volatility. This will allow them to stay profitable despite huge variations in the prices of their end products.

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After the Big Covid-19 Storm

A Look on Upcoming Highlights in the Pharmaceutical and Biotech Industry in 2022

The Covid-19 crisis has taken the pharmaceutical and biotech industry to a new level: Some companies played an important role in managing the pandemic and demonstrated their innovation potential.

Billions of euros and dollars have flowed into the industry. Their public reputation has improved greatly. Now the question is: What does 2022 hold for the biopharma industry? Which companies can play at the forefront in terms of products as well as business?

Covid-19 will continue to be a dominant topic, but other indications are also likely to come back into focus. Last but not least, things will be interesting on the financing side now that the pandemic bubble has burst, and the share prices of many biopharma companies have fallen sharply.

Looking ahead is always also looking into the crystal ball. It is based on an analysis of past developments, the current situation and assumptions. By its very nature, looking ahead cannot predict future developments by 100%. But it does give an idea of the developments that can be expected with a certain degree of probability.

Evaluate, an analysis and consulting firm specializing in pharmaceutical and biotech topics, has taken a look ahead for this industry with its Evaluate Vantage 2022 report. The study provides information for company managers and employees in the industry, for healthcare experts as well as for investors.

The Windfall of Covid-19

The report concludes that Covid-19 will still be a front-page story in 2022. "That spotlight should bring some benefits, largely in the shape of broad support—and a lot of money—from investors. But it also means heightened scrutiny, particularly for those that are making billions from successful pandemic vaccines and treatments."

According to the study findings, there is almost unanimous agreement among industry experts that vaccines against Covid-19 will continue to make billions this year for BioNTech, Pfizer and Moderna, with these firms' jabs expected to bring in at least $50 billion in combined revenue.

The huge success of Comirnaty will make the pharma giant Pfizer the world's biggest drug maker by prescription sales in 2022. The Covid-19 vaccine is expected to generate at least $29 billion in sales this year, accounting for almost half of the company's projected prescription sales.

This also means that BioNTech, the German biotech showcase company, will benefit significantly from Comirnaty. After revenues of up to €17 billion in 2021, the company expects sales of similar magnitude in 2022. This success has catapulted the Mainz-based company into the international top league within a very short time. By cooperating with Pfizer, the BioNTech management has taken a strategically important step. The collaboration made the expertise of a global corporation as well as global attention available to BioNTech. However, the Corona euphoria does not last forever, as can be seen from BioNTech's share price: since its high of €375, the valuation has more than halved. But management has proven that it is capable of developing and marketing innovative products in a structured manner. And the mRNA technology, that much is clear, offers numerous other potential applications.

The US counterpart in mRNA vaccine development, Moderna, is playing in a similar league. The Evaluate study indicates that the company took a while to get manufacturing ramped up, so 2022 sales of its vaccine are expected to surpass those booked in 2021. It´s Covid-19 vaccine Spikevax is the only reason the biotech is being featured in the analysis.

The Tübingen, Germany-based biotech company CureVac, on the other hand, plays no role in this analysis following the failure of its Covid-19 mRNA vaccine candidate. Although the company has been in existence for 22 years and has always proclaimed its pioneering role in mRNA technology, it has not yet brought a product to market. Already in 2017, CureVac had to admit the failure of an mRNA-based drug candidate against prostate cancer. All current pipeline candidates are at an early stage of development and thus still far from a potential market entry. The company's main focus now is on developing a next-generation Corona vaccine, but recent reports indicate that this project is also at risk of delays and the company may make a technology shift. In the meantime, the head of technology has left the company, while the CEO remains on board. Due to all these events, much trust has fallen by the wayside—the share price collapse speaks for itself.

In contrast, another Tübingen-based biotech company could emerge from the shadows in the future. Immatics announced in December 2021 that it has entered into a global license agreement for its TCR bispecific program IMA401 with Bristol Myers Squibb (BMS). The development pro-

Continued Page 18 ▶

Advanced Biotechnology Series

Biotechnology is a broad, interdisciplinary field of science, combining biological sciences and relevant engineering disciplines, that is becoming increasingly important as it benefits the environment and society as a whole. Recent years have seen substantial advances in all areas of biotechnology, resulting in the emergence of brand new fields.

To reflect this progress, Sang Yup Lee (KAIST, South Korea), Jens Nielsen (Chalmers University, Sweden), and Gregory Stephanopoulos (MIT, USA) have joined forces as the editors of the Advanced Biotechnology book series. It covers all pertinent aspects of the field and each volume is prepared by eminent scientists who are experts on the topic in question.

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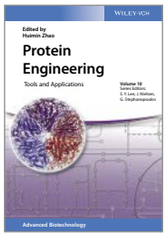

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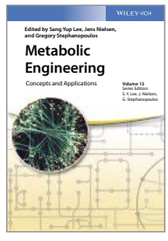

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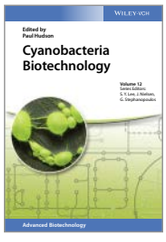

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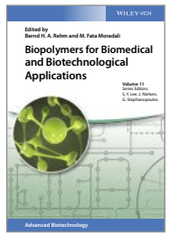

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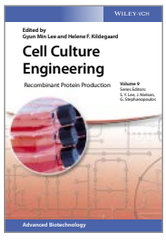

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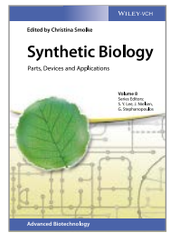

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gram targets a highly prevalent antigen in multiple solid tumors and activates T cells. In preclinical studies, IMA401 has shown anti-tumor activity with complete remissions.

World's Biggest-selling Drugs

Outside of pandemic-related products, the Evaluate report forecasts Humira to cling on its crown as the biggest selling drug. However, 2022 will be the last year of largesse for AbbVie's anti-rheumatic, with biosimilars due to arrive in the US in 2023. This will hand pole position to Keytruda. The fact that Merck & Co's cancer antibody is still generating billions of dollars in new sales each year is a testament to the company's success in in broadening the drug's label. In addition, Revlimid, an immunomodulator for the treatment of multiple myeloma, and Opdivo, a checkpoint inhibitor for the treatment of various tumors, will continue to be mega blockbuster brands.

Among the few European companies expected to play a significant role in the current year, Sanofi appears in the analysis along with its US cooperation partner Regeneron. The companies can continue to rely on revenues from Dupixent, a treatment for severe dermatitis. Furthermore, recent sales drivers include the European companies Novo Nordisk with Ozempic and AstraZeneca with Tagrisso.

Products and Indications

In addition, there are a number of potential new products that could be ready to launch this year and generate high sales in the medium term, with Alzheimer's disease poised to provide plenty of regulatory news. Lilly and Roche are striving to join Biogen on the market with their respective projects. With two big hopes in the pipeline for approval next year, BMS is under pressure to convince investors that it can avoid the fast-approaching patent cliff on Revlimid.

For Germany, the Association of Research-Based Pharmaceutical Companies (VFA) expects more than 45 drugs with a new active ingredient coming on the market this year. This means that 2022 is also likely to be another record year. More than a quarter of the new therapies will be directed against infectious diseases, another quarter against cancers. New treatments are also expected for rare genetic defects.

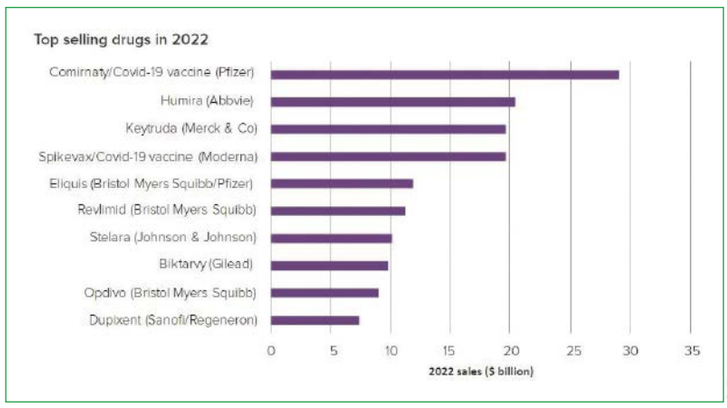

Fig. 1: Top selling drugs in 2022; 2022 sales ($ billion)

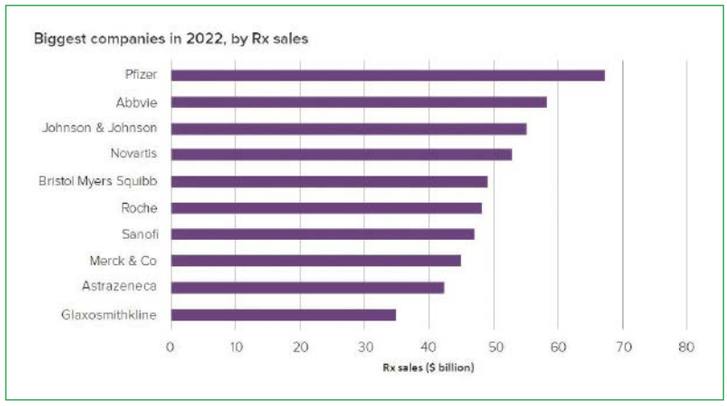

Fig. 2: Biggest companies in 2022, by Rx sales; Rx sales ($ billion)

The Costs of Research

Another way to identify the projects that are likely to be in focus is to look at biopharma's most costly development programs.

According to the report, disease areas that require vast and lengthy cardiovascular outcome trials to prove a drug's safety will always come out on top in this sort of analysis. Hence the appearance of Lilly's Tirzepatide and Novartis's Pelacarsen; whether any interim readout will happen for the latter project remains a topic of interest for the Swiss pharma giant's investors.

Roche has run a larger program with Gantenerumab than other amyloid-beta mAb (monoclonal antibody) developers and, therefore, has more to lose in terms of costs incurred than competitors should the winds of Alzheimer's disease shift.

Islatravir is Merck & Co's big bet in the long-acting HIV antiviral space, though safety concerns emerged in late 2021. Elsewhere, success in respiratory syncytial virus infections (RSV) is hugely important for GlaxoSmithKline (GSK), which is struggling to revive investor support.

"That spotlight should bring some benefits, largely in the shape of broad support — and a lot of money — from investors. But it also means heightened scrutiny."

Evaluate Vantage 2022 report

Hurdles and Trends

To get this financing on track, however, the industry must overcome a number of hurdles. In this regard, pharmaceutical information service Informa Markets points out that supply chain problems in the biopharma sector will continue to plague the industry in 2022. There will also be increasingly compressed timelines for technical transfers, and European pharma policy revisions could probably be in a pivotal year.

Moreover, the Covid-19 pandemic has forced pharma companies to become more agile and open-minded in approaching drug discovery and development, including managing evolving clinical trials. In this context, Sujay Jadhav, CEO of Verana Health, points out that the adoption of artificial intelligence (AI) in the pharmaceutical industry has long been in its nascent stages. But in 2022, the industry will benefit from new insights in understanding patients and diseases thanks to advances in AI.

Jane Z. Reed, director life sciences at Linguamatics, an IQVIA company, adds, that 2021 proved to be a pivotal year for the adoption of data science in the pharmaceutical industry for drug discovery and development. And Jim Robbins, senior vice president of life sciences at Arcadia, a healthcare data and software company, points out that life science researchers will be investing more in pharmacogenomics in 2022 because genetic mutations play an important role in many diseases.

How to Invest all the Money

Covid-19 and the billions in sales some companies are making from pandemic products raise the question of what companies intend to spend those windfall profits on in 2022. Based on the Evaluate report many biopharma watchers are expecting an uptick in M&A this year. Another likely trigger for these transactions is lower valuations in the wake of the difficult months on the stock market.

The authors of the report emphasize that the US and European biotech sectors began 2022 in a bear market as the pandemic bubble burst and investors looked for Covid-19 recovery stories in other sectors. The highs of the pandemic era could never be maintained, and many consider the current retrenchment part of the cycle.

Although the Covid 19 party appears to be over for shareholders, there is much to look forward to in terms of new products, candidates and sales in 2022—and beyond.

Thorsten Schüller, CHEManager

Pharmaceutical Global Entity Portfolio Management

Creating and Maintaining Pharmaceutical Entities or Subsidiaries

In March 2022, Mercator by Citco published a report that provides direct insights into the practice and dynamics of Global Entity Portfolio Management (GEPM) within the pharmaceuticals sector — based on real-life data — when these businesses have been at the epicenter of one of the most significant global disrupters in modern times.

For the past two years, the Covid-19 pandemic has accelerated the way that pharmaceutical companies streamline their operations—from the supply chain stage through to sales and distribution. As companies sought to navigate the disruption and maximize efficiencies in order to meet demand, the need for a strong structure around GEPM became all the more important. At the same time, the robustness by which their global entities were established and managed was tested, as well as their knowledge of local regulatory changes brought in during the pandemic. In numerous instances, particularly those that involved licensing through local entities, a reliable GEPM framework acted as a vital support system for business-critical initiatives.

The analysis of this report focuses on three data points: regional and jurisdictional distribution of activities; duration for completing activities; and related cost.

This data is drawn directly from Mercator's GEPM technology platform —Entica —which individually records all the activities undertaken for clients. The data from the pharmaceutical sector represents over $600 billion in market capital, with entities spread across 70 jurisdictions worldwide.

Global Centers of Pharma Entities

Mercator's data shows that there exists a correlation between the duration of activities and pricing thereof per region. Generally, those that have the shortest duration would have more optimized cost levels.

Europe remains the hub for a significant portion of pharma clients outside of North America, which is reflected in the relatively high volume of activities in that region. APAC, on the other hand, has traditionally been used as a location for business support and marketing services.

Most pharmaceutical companies are organizationally agile, with robust business continuity plans in place. In relation to the ability to implement changes in the structure of entities, the challenge was in the availability of resources to implement local requirements on schedule. Corporate services providers also had to deal with a changing regulatory landscape. Changes to global entities usually need to run in a synchronous manner, and local resources must be able to work through their backlog well.

A good portion of the projects it has accommodated for its pharma clients during the pandemic, says Mercator, are related to high-value, high-impact corporate initiatives intended to optimize their value-chain, minimizing the commercial impact of any disruptions of stakeholders. As such, there was a strong consideration for cost control. This itself was an area of challenge particularly in the first few months after the initial lockdown.

Cost and Duration Analysis

Based on Mercator's records of actual activity data as captured in the company's technology platform, when the cost and time of completing tasks is taken into consideration, the Netherlands comes out on top as the best jurisdiction to base entities: it is both one of the cheapest jurisdictions to operate, combined with some of the shortest timelines for completing corporate secretarial tasks—followed by Singapore and Belgium. All three jurisdictions have the ideal combination of cost levels and competitive duration. Further, all three are well regarded as global financial centers with a long-established history of managing international trade, and this translates into the ease with which multinationals can manage entities in these locations. Brazil was the most lowly ranked on cost and duration combined, followed by Republic of Korea and People's Republic of China; all have a combination of relatively higher cost levels, and less competitive duration.

Guidance for Pharmaceutical Multinationals

Mercator emphasizes that the purpose of its report is not to advise pharmaceutical companies on where to base entities or subsidiaries—as this is obviously dictated by necessity —but to set expectation and provide foresight on the relative cost and time it will take to manage entities in each jurisdiction.

Nevertheless, the results of the report can assist pharmaceutical multinationals by serving as a benchmark for their company secretarial expenditure and efficiency in operating globally. In addition, the data may serve as a useful practical guide when setting up new overseas entities in their structure. (rk)

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Expanding Into Oligonucleotides

Bachem Invests, Leverages Expertise and Equipment to Support the Development of Novel APIs

The global market for oligonucleotide therapeutics is expanding rapidly. Bachem, an innovation-driven company based in Bubendorf, Switzerland, has entered this competitive environment a few years ago and meanwhile has passed certain milestones on its way to become a preferred oligonucleotide manufacturing partner for pharmaceutical companies. Extending its focus from peptides to oligonucleotides will also lead to a transformation of Bachem's organization. Seamus White, business development manager at Bachem, provides an update on the company's strategy and progress in the field of oligonucleotide manufacturing.

CHEManager: Bachem's journey into oligonucleotides initially started in 2018. What led to the decision to enter this field?

Seamus White: The potential of oligonucleotide-based medicines is finally receiving the focus it deserves. Rare diseases, especially, are benefiting from these molecules. This demand will get even greater as oligonucleotide therapeutics move more into chronic diseases, too. However, there are significant unmet needs in the field—revolving around capacity, cost-effectiveness, and sustainability. Thus, we saw an opportunity to expand Bachem's customer base by leveraging existing expertise and equipment and to ultimately support the development of novel active pharmaceutical ingredients.

As the leading company in developing and manufacturing peptides and oligonucleotides and an API manufacturer, we are offering the best solutions for today and are developing tomorrow's innovations. We work with passion and dedication to support our customers in achieving breakthrough medical advances that will significantly transform patients' lives, and we will address larger-scale patient populations and indications by transforming the processes of how oligonucleotide therapeutics are supplied.

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Seamus White, Bachem

What are Bachem's achievements in oligonucleotides so far?

S. White: We started by purchasing and installing off-the-shelf synthesizer and invested considerable resources in the design of a custom-built cleavage and deprotection system. This set-up is used for complex siRNAs synthesis in multi-hundred-gram quantities. A first GMP batch for clinical investigations was released in 2019.

In 2021, we completed the qualification of the pilot plant dedicated to the downstream processing of oligonucleotides. This will allow us to efficiently process material under GMP conditions in the single-digit-kg range. Recently, we completed the installation of our first large-scale equipment train for oligonucleotides. The line has been designed for the processing of multi-kg batches, and we have already started using it in collaborations with some pharma and biotech companies.

© Bachem

What differentiates Bachem from other CMOs in the oligonucleotide market?

S. White: With 50 years' experience in the development and manufacturing of innovative medications, with customer-centric excellence, we have proven to be a trusted and reliable partner for pharmaceutical and biotech companies. With our tailored approach, we are committed to serving customer's needs and ultimately always have patients in mind. Because of this, we keep innovating and developing new technologies! We want to transform the oligo field by bringing solutions to our partners for scalabil-

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ity, cost-effectiveness and sustainability. We will bring innovation to every piece of equipment and processes—from solid-phase synthesis to downstream processes.

Can you share some information on process innovations used for your oligonucleotide manufacturing?

S. White: At Bachem, we have mastered the art of large-scale solid-phase synthesis, chromatographic purification and lyophilization with tailor-made engineering solutions over decades. We now find that some of these solutions can be adapted for oligonucleotides. An example is the MCSGP technology for the purification of crude materials in a continuous chromatography mode. MCSGP is short for multi-column countercurrent solvent gradient purification, which is a chromatography method that is used to separate or purify biomolecules. We have introduced this technology for peptide APIs and meanwhile demonstrated feasibility for oligonucleotides as well. We are convinced that MCSGP technology will be cost effective and reduce waste substantially.

> *"The potential of oligonucleotide-based medicines is finally receiving the focus it deserves."*

We are also working on multi-faceted solutions to make the oligonucleotide synthesis process more scalable and more sustainable. Here, we are trying to leverage our scientists' experience in protecting-group chemistry and in solid-phase synthesis.

What lies ahead for the oligonucleotide market?

S. White: With 14 oligonucleotide medicines already approved by the FDA and the EMA, these products are now delivering on their promise of curing rare diseases. Furthermore, we see that the pace keeps increasing with about 200 clinical trials and more than 600 preclinical trials for oligo-based products. The market keeps growing as well as the demand, so we want to keep pace with these changes and truly help our pharma and biotech partners develop and manufacture their oligo-based therapeutics that will transform patients' lives.

How will Bachem respond to the increasing market demand?

S. White: Simply put, we keep investing in our manufacturing capabilities and capacities for peptides and oligonucleotides. Worldwide, we will invest in the next few years about $500 million in new equipment and production facilities. At the Bubendorf site specifically, we started the construction of a brand-new Tides manufacturing building which will house additional equipment trains for the production of oligonucleotide-based APIs at commercial scale.

What do you foresee for oligonucleotide therapeutics and where will Bachem position itself in this field?

S. White: With the increasing use of oligonucleotide therapeutics, advances in scalability and sustainability of oligo manufacturing are key for the coming years. As a matter of fact, we have launched an internal innovation program to address these challenges. In addition to large-scale and sustainable manufacturing, we see a steady evolution in medicinal chemistry and oligonucleotide conjugation. The molecules tend to become more and more complex featuring various backbone modifications and new conjugation moieties to address pharmaceutical targets located also outside of the liver.

> *"Advances in scalability and sustainability of oligo manufacturing are key for the coming years."*

We are in a great position to support this trend with relevant experience in conjugation chemistries for peptides, lipids, PEGs et cetera, and expert analytical capabilities. We will help enabling the benefits of oligonucleotide treatments to expand from rare to chronic diseases—and into more therapeutic indications. Ultimately, we want to use our proven innovation to transform lives—the lives of everyone we work and partner with—and ultimately of course, the lives of patients.

■ www.bachem.com

Ramping Up Biomanufacturing Capacity

Capital Investments in Biomanufacturing Continues to Be an Active Area for CDMOs/CMOs

Biomanufacturing for both traditional biologics and new modalities, such as cell and gene therapies, continues to be an active area of investment for CDMOs/CMOS. Some of the major investments by the larger CMDOs/CMOs are outlined below.

Fujifilm Diosynth Biotechnologies

In October 2021, Fujifilm Diosynth Biotechnologies broke ground on a new, $2-billion, large-scale cell-culture biomanufacturing facility in Holly Springs, North Carolina. The company had announced the investment in January 2021. The facility is expected to be operational by the spring of 2025.

The new facility is one of several biomanufacturing investments announced or proceeding by Fujifilm Diosynth. In December 2021, the company announced plans to invest £400 million ($533 million) to expand its site in Billingham, Teesside, UK, with the addition of a viral gene-therapy facility and a mammalian cell-culture facility. The new facilities are expected to be operational by late 2023. The investment is part of a 90 billion Yen ($797 million) global capital investment package initially outlined by the company in June 2021. In addition to the gene-therapy and cell-culture manufacturing expansion in the UK, the investment includes doubling cell-culture production for recombinant vaccines in the US and doubling microbial fermentation capacity at an existing UK facility.

In addition, the company is investing 100 billion Yen ($928 million) at its site in Hillerød, Denmark, near Copenhagen, to double drug-substance biomanufacturing capacity, expand its capabilities to include fill–finish, and enhance its current assembly, labeling, and packaging services. Fujifilm Diosynth acquired the facility from Biogen in 2019 for approximately $890 million. The investment will expand production lines for bulk drug substances with the addition of six mammalian-cell bioreactors, which would bring the total capacity to 12 x 20,000-liter bioreactors by the fall of 2023.

The company is investing to expand its advanced therapy manufacturing capabilities. Earlier this year (2022), Fujifilm Diosynth announced a $300-million expansion of its single-use manufacturing campus in College Station, Texas, through the addition of a new production facility that will double the company's advanced therapy and vaccine manufacturing capacity in the US. The investment is part of the company's previously announced global capital investment package initially outlined by Fujifilm in June 2021. This new facility, expected to be operational by 2024, will add approximately 138,000 sq. ft. to the existing campus and grow the site to 300,000 sq. ft.

Also, earlier this year (2022), Fujifilm agreed to acquire a cell-therapy manufacturing facility in Thousand Oaks, California, from Atara Biotherapeutics, a South San Francisco, California-based biopharmaceutical company, for $100 million. The facility can produce both clinical and commercial cell therapies, including allogeneic T-cell and CAR T immunotherapies. The acquisition is expected to be completed in April 2022. Fujifilm Diosynth is also expanding its viral vector and gene therapy offerings in Darlington, UK, with process development laboratories and manufacturing capabilities for early-stage gene therapies. The process development laboratories are operational with manufacturing services starting in the spring of 2022.

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Patricia Van Arnum, DCAT

Samsung Biologics

One of the largest expansions announced or ongoing expansions by CDMOs/CMOs is Samsung Biologics' KWR 2-trillion ($1.7-billion) investment for a new biomanufacturing plant, the company's fourth, in Incheon, South Korea, and for a second bio complex. The company broke ground on the new facility in November 2020, which, upon completion, will provide 256,000 liters in total biomanufacturing capacity. The plant will have a modular design that will allow flexibility for certain parts of the plant to begin manufacturing activities by the end of 2022, with the goal to commence full operations in 2023.

In January 2022, Samsung Biologics, announced plans to start construction of a new manufacturing facility for multi-modal products, including cell and gene therapies and vaccines using mRNA, pDNA, and viral vectors, all at a single site. This facility will be in addition to the mRNA vaccine drug-substance manufacturing suite the company is adding to its existing facility in Songdo, South Korea.

The company says it is also venturing into securing additional sites within Songdo for the construction of a sixth manufacturing facility and innovation center, and also overseas in multiple locations to maximize its manufacturing capacity to produce large-scale biologics.

Lonza

Lonza is proceeding with expansions in the US, Europe, and Asia. In 2021, Lonza announced plans to invest approximately CHF 850 million ($935 million) to add two mammalian drug-substance manufacturing facilities at its sites in Visp, Switzerland, and Portsmouth, New Hampshire. The expansion in Visp will add a new 27,500-

m² large-scale mammalian drug-substance manufacturing facility. The facility is expected to be completed in 2024 with an investment of approximately CHF 650 million ($715 million).

In Portsmouth, New Hampshire, the company is adding a new biomanufacturing facility for small-to-mid-volume production. The CHF 200-million ($220-million) facility will add capacity for up to eight 2,000-L single-use bioreactors to support Phase III clinical and commercial small- to mid-volume products. The facility is expected to be completed in 2023. In addition, Lonza began operations in 2021 at its new 17,000-m² mammalian-cell biomanufacturing facility in Guangzhou, China.

Lonza is continuing to support its collaboration with Moderna for mRNA vaccine manufacture with a new mRNA line in Geleen, the Netherlands, as well as three new mRNA lines in Visp, making a total of eight mRNA commercial-scale lines the company has across Europe.

In addition, in November 2021, Lonza announced an investment to expand microbial development capacity at its facility in Visp, and in October 2021 announced plans to expand its biologics development services at its site in Tuas, Singapore.

Boehringer Ingelheim

In October (October 2021), Boehringer Ingelheim (BI) inaugurated a new €700-million ($780 million) large-scale, cell-culture biomanufacturing facility in Vienna, Austria. The facility has up to 150,000-liter manufacturing capacity for BI products and contract manufacturing activities. The company broke ground on the facility in 2017, and the facility adds to the company's biomanufacturing network in Biberach, Germany; Vienna, Austria; Fremont, California; and Shanghai, China.

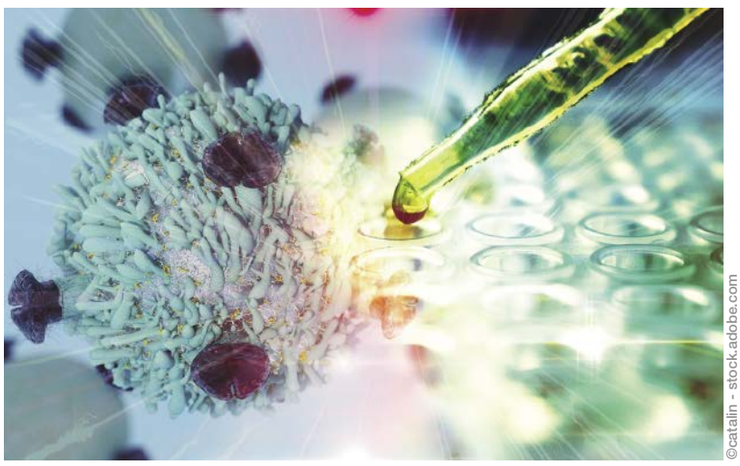
Thermo Fisher Scientific

Thermo Fisher made several moves to expand both cell- and gene-therapy manufacturing and traditional biomanufacturing. In 2021, the company added to its contract viral vector manufacturing services with the acquisition of Henogen, Novasep's viral vector manufacturing business, for approximately $875 million.

Also in 2021, Thermo Fisher Scientific opened a new pDNA manufacturing facility in Carlsbad, California.

Additionally, this year (2022), the company will launch mRNA synthesis capabilities at its site in Monza, Italy, to produce drug substance for vaccines and therapies.

The company is also moving forward with its partnership with the University of California, San Francisco (UCSF) for development and manufacturing of cell-based therapies. A new 44,000-sq-ft. cell-therapy development and cGMP manufacturing center at UCSF's Mission Bay campus is slated to open later this year (2022).



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These expansions build on the company's continued investment in cell- and gene-therapy manufacturing facilities, including: (1) viral vector facilities in Cambridge, Lexington, and Plainville, Massachusetts, and Alachua, Florida; (2) a new cell-therapy manufacturing facility in Princeton, New Jersey; and, (3) a new dedicated cryocenter in Weil am Rhein, Germany, to provide specialized cryogenic and cold-chain supply-chain services to support clinical trials across Europe and globally. The new commercial manufacturing site in Plainville, Massachusetts for viral vector capacity for gene therapies and vaccines is slated to be completed later this year (2022).

Also, later this year (2022), Thermo Fisher will begin operations at a new biologics manufacturing site in Lengnau, Switzerland. The company had earlier formed a strategic partnership with CSL Limited, a Melbourne, Australia-based biopharmaceutical company, to operate the site, for both CSL and other customer projects. Thermo Fisher is also expanding operations at its biologic drug-substance manufacturing facility in St. Louis, Missouri, and is expanding in Asia-Pacific with an integrated biologics drug-substance and sterile drug-product manufacturing facility in Hangzhou, China.

Catalent

Catalent is investing to increase biologics drug-substance manufacturing and cell- and gene-therapy manufacturing. In July 2021, Catalent announced that it will begin the first phase of a planned $100-million expansion at its facility in Anagni, Italy, to add biologics drug-substance manufacturing. The initial expansion is expected to be commissioned and operational for customer projects in April 2023. Catalent's Anagni site now provides aseptic filling, secondary packaging, and oral dose manufacturing for late-stage and commercial product launches. Since Catalent acquired the facility in January 2020, it has become a European hub for Covid-19 vaccine manufacturing as well.

Also, on the biologics drug-substance side, in 2021, Catalent completed the expansion of two new suites at its biologics drug-substance development and manufacturing facility in Madison, Wisconsin. The expansion increased the number of manufacturing suites at the site to five, which more than doubled its overall cGMP-scale capacity.

In cell and gene therapies, in 2021, Catalent acquired RheinCell Therapeutics, a Langenfeld, Germany-based developer and manufacturer of human induced pluripotent stem cells, which became part of Catalent's Cell & Gene Therapy business. In May 2021, Catalent acquired Promethera Biosciences' cell-therapy manufacturing subsidiary, Hepatic Cell Therapy Support SA (HCTS), including its 32,400-square-foot facility in Gosselies, Belgium. The facility will accommodate Catalent's commercial-scale pDNA manufacturing and is located on Catalent's existing campus in Gosselies, adjacent to the Delphi Genetics building. Catalent announced the acquisition of Delphi Genetics in 2021, a spinoff from the Université libre de Bruxelles and a bioproduction CDMO with capabilities in pDNA development and cGMP manufacturing. Catalent gained its facilities in Gosselies, Belgium, with its $315-million acquisition of MaSTherCell, a provider of cell- and gene-therapy development and manufacturing services in 2020.

In addition, in October 2021, Catalent announced a $230-million expansion project to add three commercial-scale viral-vector manufacturing suites and associated support facilities and services at its gene-therapy campus in Harmans, Maryland, which brings its total investment at the site to $360 million. A second facility is under construction following an initial $130-million to add five new manufacturing suites. When completed at the end of 2022, the campus will house a total of 18 viral-vector manufacturing suites.

WuXi Biologics

Last November (November 2021), WuXi Biologics completed the first GMP production of a new 24,000-L line of its drug-substance facility (MFG) in WuXi, China. This followed the initial GMP operations of the 36,000-L biomanufacturing line at the facility earlier in 2021. The facility has a total of 60,000 L of biomanufacturing capacity to support late-phase and commercial projects across multiple modalities, such as monoclonal antibodies, bispecifics, and fusion proteins, providing the company with total biomanufacturing capacity of approximately 150,000 L.

Also, in 2021, the company completed three acquisitions to increase its production capacity: a drug-substance facility in Wuppertal, Germany, from Bayer; drug-substance/drug-product facilities in Hangzhou, China, from Pfizer; and the Chinese CDMO CMAB Biopharma.

Note: Currency conversions at time of announced investments.

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Micro- and Millireactors on the Upswing

Flow Chemistry: Well Proven, but not yet Implemented. What are the Reasons?

Flow chemistry, and in particular microreaction technology (MRT), is no longer a pure academic or R&D field — it is proven to run in production scale, even in world-scale tonnage. This means, micro- and millireactors have entered the final stage of establishing themselves in world-scale dimensions globally.

The main advantages of continuous operation in micro- and millireactors are ultra-fast mixing, highly efficient heat transfer, simple process control due to low system volume and high operational safety due to minimum hold-up. These properties of continuous flow reactors are particularly advantageous for fast, highly exothermic reactions with explosive or toxic substances; due to the safety risk, these processes are often difficult or impossible to handle in batch reactors.

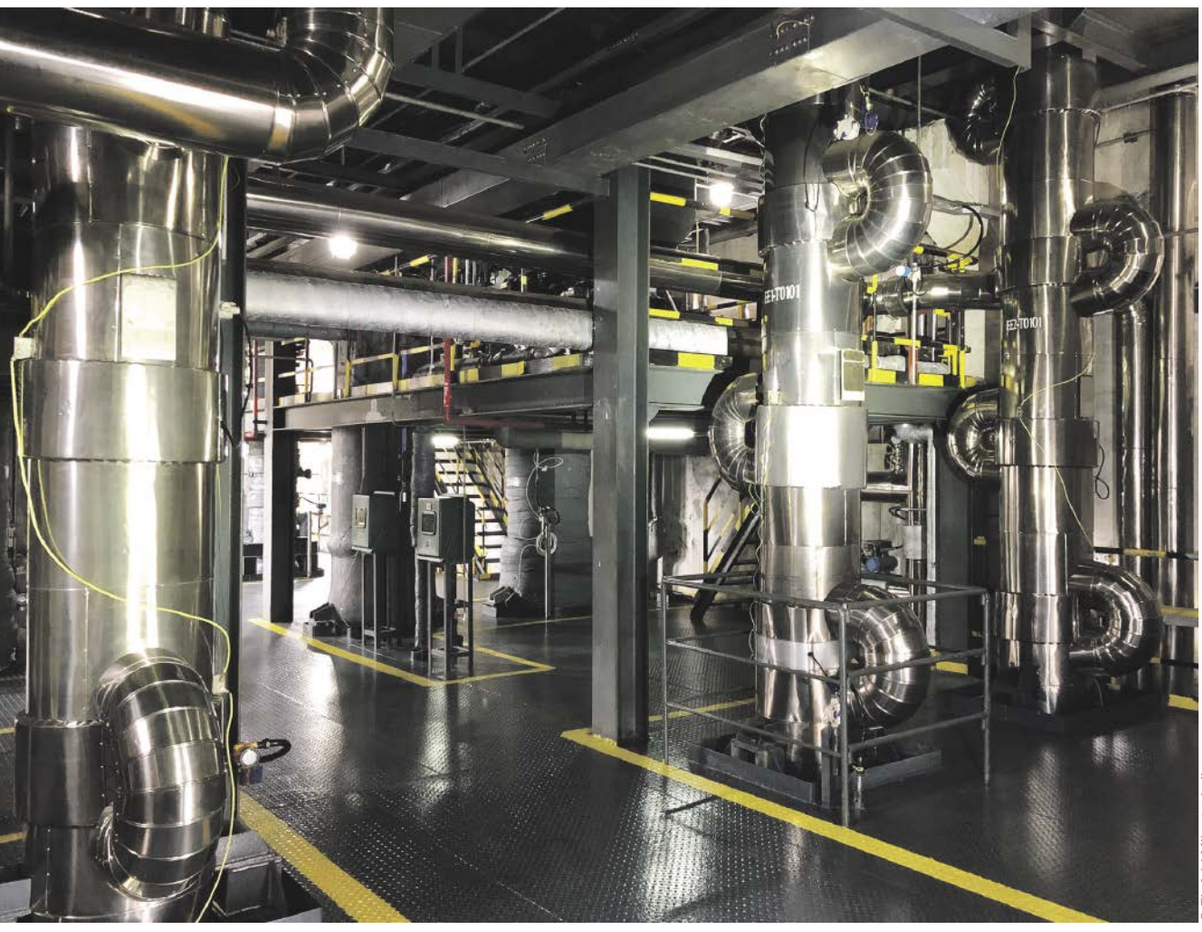
The economic benefits resulting from the technology are mainly due to the high yield and the low proportion of by-products, but also to the sustainable plant safety, lower energy consumption and a smaller carbon footprint.

And yet, due to various reasons, MRT has not achieved the status of implementation, for instance, in fine chemicals and active ingredients production that one might expect — at least not in Central Europe.

At an online roundtable event hosted by CHEManager, a group of industry experts with a diverse range of professional backgrounds, thus bringing technologic as well as economic expertise to the virtual table, discussed those reasons and various business and production aspects of MRT.

Microreaction Technology

MRT replaces the discontinuous batch process with a continuous process in which reactions take place in structures with a reduced size. The main components are mixers with excellent mixing speed and heat exchangers with high heat-transfer capacities. This results in improved process conditions and significant miniaturization of reactive volumes. The excellent mixing and temperature control with hardly measurable temperature gradients over the whole reaction volume cannot be achieved in a classical batch reactor. Due to the exact controllability of the reaction process, the reaction parameters can be better adjusted, resulting in higher product quality and better yields.



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Drawbacks and Hurdles

Why are many chemicals manufacturers still foot-dragging when it comes to investing in and implementing MRT? Five topics emerged from the expert discussion: In addition to technology, the cost side plays a decisive role, and regulatory aspects, mindset as well as know-how in the chemicals companies need to be improved.

In addition to the technical imperative to support the continuous improvement process through technical progress, there is always the economic imperative in business practice: costs and benefits must be in balance. However, there are examples that prove the technology to be economical, for instance in China.

The MRT Lighthouse Project

Shaoxing Eastlake High-Tech, an established Chinese agrochemical ingredients producer located near Shanghai, invested heavily in the technology. In 2016, the company, founded in 1990, commissioned a millireactor which was designed, manufactured and supplied by Ehrfeld Mikrotechnik. The German company develops micro- and millireactors from laboratory up to production scale. The continuously operated Miprowa production reactor at Shaoxing Eastlake with a capacity of up to 10,000 t/a is using milli structures on a production scale and was designed for a highly exothermic alkoxylation reaction. It replaced more than 20 batch reactors while doubling the original capacity. This millireactor was the first visible lighthouse project for the use of MRT on an industrial scale.

According to Jessen Gu, Board Member of Shaoxing Eastlake High-Tech, the entire process — from the first trials to the commissioning of the production plant — took the company less than four years. Since then, the processes have been running continuously and the company has accumulated a lot of knowledge about the technology/process. And Ji Sheng, General Manager of Shaoxing Eastlake Hi-Tech, confirmed that MRT is a safe, sustainable and efficient large-scale production technology.

In November 2018, Shaoxing Eastlake implemented two additional millireactors of the same size, thus tripling their production capacity at its Shaoxing site to 30,000 t/a. The company recovered its first investment in MRT within almost one year.

Joachim Heck, Managing Director of Ehrfeld Mikrotechnik, explained that one important advantage of MRT is the yield increase, which means the generation of fewer by-products and less waste within the production processes, thus reducing the efforts and costs for downstream processing. This can also lead to a significant contribution to climate protection and reduced energy demand for chemical and pharmaceutical processes overall. As energy costs for separation of by-products during downstream processing can make up between 40% and up to 80% of total cost, this can make a significant difference.

Heck explained that millireactors in production are forecast to be reaching a throughput capacity of more than 100,000 t/a. "With the achievement of this capacity, the proof of concept for establishing micro-/millireactors as process technology will be fulfilled," said Heck.

Ehrfeld's next two reference reactor are scheduled to be commissioned in 2023: these consist of six modular stages with a volume of 80 l each and will have a throughput of 20,000 t/a. But despite the existence of such lighthouse projects, the use of MRT varies widely across the globe. In Ehrfeld's experience, the establishment of MRT in Europe and the USA is still progressing slowly. In contrast, MRT is advancing much faster in China, as evidenced by the strong growth of Ehrfeld's subsidiary in Shanghai.

One reason may be that new industrial parks for greenfield chemical plants are currently being established in China and that the use of the latest innovative technology is mandatory.

Shizhe (Steven) Tian, Chief Scientist at Shaoxing Eastlake, said that some months ago, the Chinese government issued a catalogue in which they encouraged 32 technologies—and MRT was on number one.

Regulatory Environment

Claudia Barkowsky, representative of the German Mechanical Engineering Industry Association (VDMA) in Beijing, China, explained that the Chinese government is doing a lot to promote especially technologies that are not yet available in China, or even future technologies that are not yet fully developed.

Regulations such as the „Foreign Investment Catalogue" list industries and technologies that are explicitly encouraged in the Chinese market and those that are more restricted. The „Catalogue for Industrial Restructuring Guidelines", revised two years ago, specifies which industries and technologies should be promoted and which should be phased out. MRT is one of the technologies that is promoted, although not on a large scale.

> *"Shaoxing Eastlake recovered its first investment in MRT within almost one year."*
>
> Jessen Gu, Board Member, Shaoxing Eastlake High-Tech

"Promoted technologies can be introduced and established by companies—including foreign ones—with lower regulatory and tax costs and simplified approval procedures," Barkowsky said. This is an important reason why both the chemical and pharmaceutical industries are growing at a rapid pace in China.

Also, in a highly regulated environment like the manufacture of medicines and their active ingredients the introduction and qualification of novel synthesis technologies takes time and is costly. Therefore, many manufacturers refrain from changing their established and audited production methods and stay with their batch reactors for the synthesis of new molecules—at least in Europe and the US.

Heck explained: "MRT is not suitable for multi-purpose production as it is a dedicated reactor. Nevertheless, you could set up a production process installing multiple—smaller—MRT units in parallel, that could be used, for example, for the custom synthesis of complex molecules. But there are also projects in an early phase with specific reactors that use continuous processes with multiple synthesis steps. In general, we see that the use of flow chemistry is picking up in custom manufacturing, even for pharma customers."

Mindset

In addition, especially in China more and more conferences are addressing MRT, and both regulators and industry associations are becoming increasingly aware of the technology. Quan Liu, General Manager of Ehrfeld Process Technology in Shanghai, added that in China flow chemistry is mentioned as one of the most important technologies for the coming years, especially for hazardous reactions like nitration.

Compared to Europe and the US, it seems that China is more open-minded, motivated and willing to adopt new, innovative technologies, Heck said. In his opinion, China is a leader in the introduction of new technologies. "Another aspect is that in the last decade, the market leaders, especially in Europe, were waiting until start-ups or SMEs had established new technologies on the market and only then adopted them. China handles this differently," he added. "According to my experience, the most decisive point for entering MRT is that top-down decisions of the management are necessary to embrace this technology and to build it up from lab to production scale. A bottom-up decision for this technology normally doesn't work," Heck explained.

That's why lighthouse projects as the one at Shaoxing Eastlake and other successful implementations of MRT need to get as much visible in the industry as possible. And they probably will.

"As China—compared to Europe and the US—is not attached to established technologies it is more flexible in the adoption of new ones," Barkowsky said. "There is no need for a change of mindset in China."

Based on the experiences with the lighthouse project at Eastlake, Gu said, the company believes that the continuity of the manufacturing process and the environment-friendly production technology together with the high efficiency of engineering equipment will be the three key factors for the manufacture of high-quality chemical products in the future.

He strongly believes that MRT is the most effective technology to enter new or more applications in the coming years. In China, there are already companies using MRT to produce difficult intermediates, replacing other technologies.

These products can then be used, for example, in lithium batteries or other energy sources. With the use of MRT, the chemical industry is not only consuming energy, but can support—at least to some extent—the generation of new energy.

Ralf Kempf and Michael Reubold, CHEManager

Making Plastics Circular

Mitsubishi Chemical Europe Pilots GreenToken to Make its Recycled Plastics Supply Chain Transparent

Take, make, dispose. For decades, this has been the standard approach of production and consumption. Products were used until they were finally disposed of as waste. And this amount of waste grew bigger each year. Only 12% of plastic waste is currently reused or recycled, according to a McKinsey study. The great majority of used plastics end up in incineration, landfills, or dumps, which means losing the material as a resource forever.

As regulators move forward with bans and taxations and consumers shift their buying preferences towards greener products, businesses are under increasing pressure to become more sustainable and adopt a circular economy approach. The global resource demand and its resulting waste have led to a push for action that will profoundly disrupt all industries over the next decade. A report by the Ellen McArthur Foundation shows that by 2040, a circular economy has the potential to reduce the annual volume of plastics entering our oceans by 80%.

From Plastic Waste to Products

Enabling a circular economy of plastic waste into raw materials is top of mind for Mitsubishi Chemical Europe. By using different recycling technologies, resources can be saved, and the environmental footprint reduced. The company offers and sells highly developed chemical-based products, including high-performance engineering plastic, polymer films, and semiconductor solutions, and is the world's largest producer of methyl methacrylate (MMA).

> *"More transparency is needed along the value chain to substantiate environmental, health and safety claims."*
>
> Nicole Kambeck, Circular Economy Director, Mitsubishi Chemical Europe

"Customer demand for sustainable products has been growing in recent years", says Nicole Kambeck, Circular Economy Director at Mitsubishi Chemical Europe. "In the future, it will no longer be enough to just offer a product that contributes to a circular economy and decarbonization. Additionally, more transparency is needed along the value chain to substantiate environmental, health and safety claims," she adds. "As a trusted manufacturer, we believe that blockchain technology can address this demand along the lifecycle."

Polymethyl methacrylate (PMMA) is one of the most versatile materials in the world, used in signage, protective Covid-19 screens, lighting, automotive fittings and many more applications. Mitsubishi Chemical aims to build and run a fully operational acrylic recycling plant to break down end-of-life PMMA into its original building block of MMA using a process called molecular recycling. This will then be used to produce 100% circular MMA and circular PMMA.

In today's global economy, supply chains typically involve multiple par-

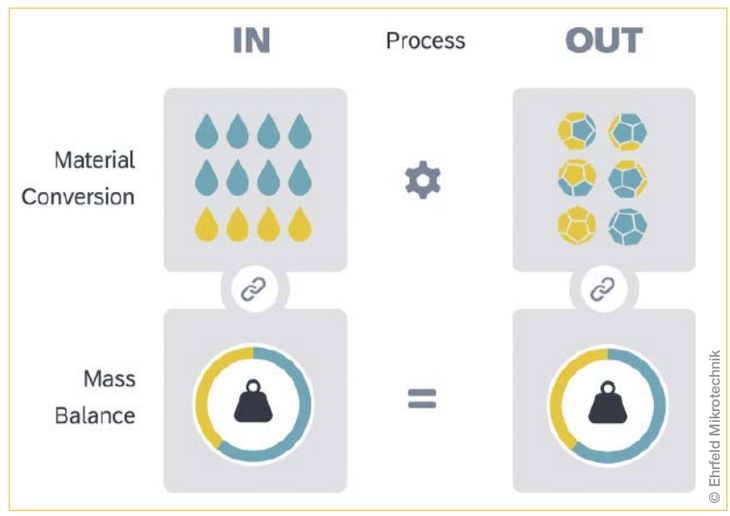


Fig. 1: A simplified mass balance overview.

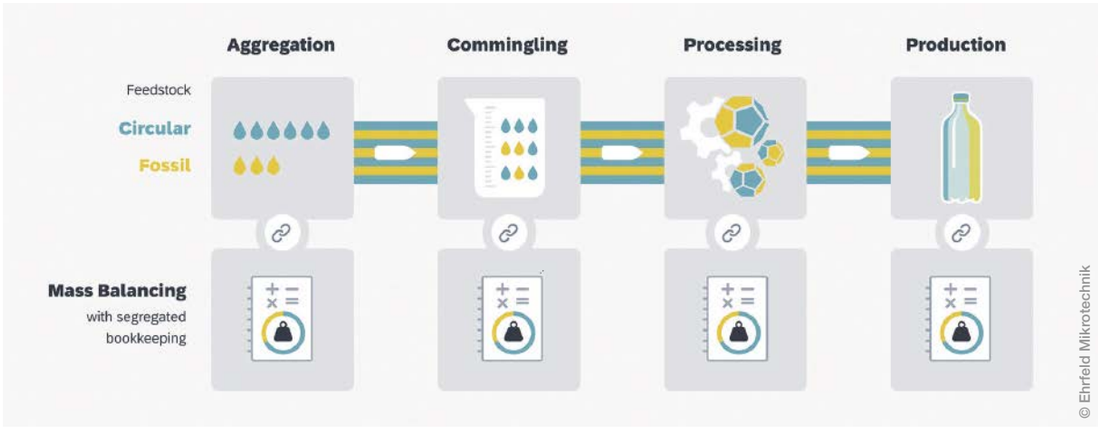


Fig. 2: Traceability of commingled materials with mass balance.

ties, and information about the origin of materials is difficult to track—but essential to promote a circular economy along the product lifecycle. To prove to its customers that the plastic they use contains certain amounts of chemical recycled content, Mitsubishi Chemical Europe piloted the GreenToken solution by SAP in their MMA supply chain.

Add Transparency to Opaque Supply Chains

Combining principles of mass balance accounting, tokenization and blockchain, GreenToken enables Mitsubishi Chemical Europe to trace commingled plastic raw material across the global supply chain, from the exact source of origin to the final product. "Usually, the raw material comes from both circular and conventional, non-circular sources. To give transparency to these opaque supply chains, we use tokens that represent the origins of a small, fixed amount of the raw material—100 kg of raw material could be represented by 100 tokens in our system," explains James Veale, co-founder of GreenToken by SAP. "We use different colored tokens to represent different raw material attributes, such as green tokens for circular recycled materials and red or no tokens for conventional," he adds.

Records of these tokens are stored on the underlying blockchain ledger. As the material moves along the supply chain, the GreenToken cloud system passes the equivalent number of tokens that represent the mass of material bought or sold. The tokens are moved from one supply chain actor's digital wallet to another's, creating a tracing history—an immutable chain of custody that adds complete auditable supply chain transparency and makes the data trustworthy. Comparing the ratio of green to red tokens instantly gives customers the circular content of their new polymer product.

"Rethinking how we design, make and use resources, requires granular, high-quality data," says Veale. "Based on the information provided by GreenToken about sustainable attributes of the raw material, such as the percentage of recycled content, Mitsubishi Chemical Europe can make informed decisions on how to meet their circular economy commitments."

Future Circular Business Models

The GreenToken solution serves as a seamless complement and accurate representation of the physical flow of materials through the built-in accounting, allocation, and transfer between various supply chain members. The application of this solution in different value chains can enable new business models in the respective industries, which are required for the transformation towards a circular economy. The abilities offered by tokenization of sustainability attributes will play a key role in the development of future circular business models.

Stefan Gürtzgen, CHEManger

An Innovative Wet Sulfuric Acid Process

Oxysulf Technology for the Recovery of Sulfuric Acid and Energy

In many industrial applications the wet sulfuric acid process is the most important technology for recovery of sulfuric acid and energy from sulfur bearing compounds. The Austrian engineering company Kanzler Verfahrenstechnik (KVT) has developed a proprietary process, Oxysulf, for which a thermal efficiency of >85% and a tail gas sulfur dioxide (SO_2) emission value of <5 ppm(v) have been demonstrated in a recently commissioned plant.

KVT has been active in the field of environmental technologies for more the 30 years, with experience in supply of turnkey off-gas treatment plants worldwide. The Oxysulf technology can handle sulfuric compounds such as SO_2, H_2S, COS or CS_2 in wide range of concentration. Plant sizes up to 200.000 Nm³/h and concentrations of sulfur bearing compounds from 2–200 g/Nm³ can be managed. Treated off-gas streams come from various sources, for example:

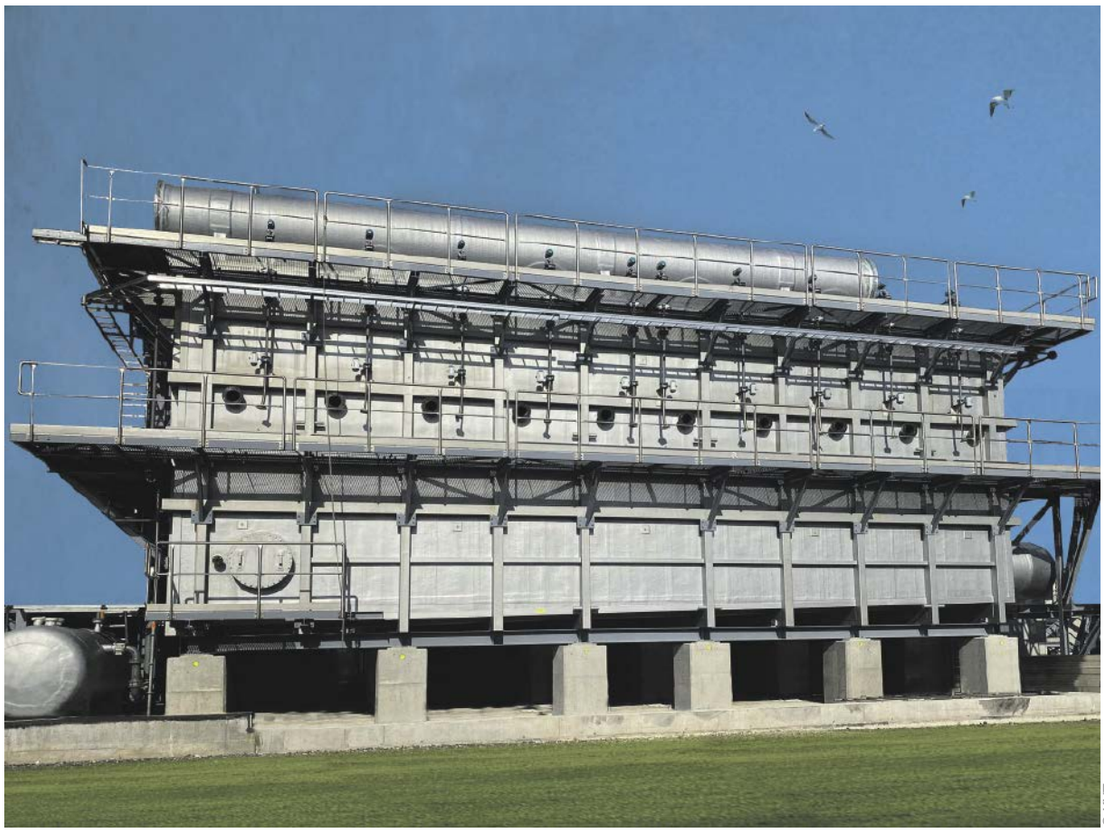
- Natural gas refining
- Furnace waste gases
- Metal smelter
- Viscose fiber industry
- Spent acid regeneration
- Oleum production

The process is based on thermal and/or catalytic oxidation of Sulfur-bearing compounds, by forming sulfuric acid.

The off-gas passes a pre-treatment system; depending on the application, this is a combination of a pre-filter, a scrubber, a DRY-FIL-hot gas filter, or a preheating. The pre-treatment is followed by the catalytic oxidation or thermal and catalytic oxidation, depending on concentration and kind of pollutant. In all applications the off gas is routed over a multi bed catalytic converter, followed by a concentration column and a tail gas treatment.

The catalytic oxidation of the sulfur-bearing compounds is exothermic, operating within the range of 360–550 °C, the resulting heat is typically recovered by a steam system. After the reactor, the process gas is passed through a concentration column where sulfuric acid is condensed and concentrated up to 98w%. The remaining sulfuric acid aerosols contained in the gas are precipitated in the wet electrostatic precipitator (WESP). To achieve lowest SO_2 emissions, further tail gas treatment is generally required.

The governmental regulations for SO_2/SO_3 emissions are becoming more and more stringent. Up to now the existing solutions to reduce the emission in the wet sulfuric acid process were limited:



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Exterior view of KVT's Oxysulf reactor.

Walter Kanzler, Kanzler Verfahrenstechnik

- Exceeding the oxidation rate of 99% in a single step wet oxidation process is impossible due to the reaction equilibrium.
- Adding of second catalytic stage, as in the dry process, results in an enormous increase of the investment and operational costs.
- Adding a scrubber system with hydrogen peroxide or caustic soda has a considerable influence on the operational and disposal costs.

For reaching a sulfur recovery rate of >99,9% and lowest SO_2 emission of <5 ppm(v), KVT has developed its own technology: the Oxytail reactor. Instead of an additional conventional high temperature process step, the company's Oxytail offers the possibility of SO_2 reduction with low investment and low operational costs.

In the Oyxtail reactor the remaining SO_2 contained in the gas is converted, washed out with demineralized water, and recycled to the process as weak sulfuric acid, without any extra utilities and avoiding any disposal costs.

KVT´s recently installed plant is treating 50,000 Nm³/h of high loaded gas up to 130 g/Nm³ of SO_2 at inlet of the main catalyst bed. While the inlet concentration to the KVT Oxytail reactor is within the range of 2 g/Nm³, SO_2 in the outlet of the reactor it is reduced to the value of 2–3 ppm(v).

With the new Oxytail unit KVT is setting a new standard for SO_2 emission control and makes the sulfuric acid recovery process more cost-effective.

Walter Kanzler, CEO,
Kanzler Verfahrenstechnik,
Graz, Austria

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- http://kvt.technology

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INNOVATION PITCH

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Chemical Value Chains
Blockchain for Information Tracking and Eco Footprint Analysis

Computational Toxicology
Molecular Signature Derived from Quantum Chemical Calculations

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Blockchain in Chemical Value Chains

Tracking Complex Information and Enabling Real-time Eco Footprint Analysis

ReCarbonX, a smart tracking system for manufacturing developed by the eponymous Swiss start-up, creates a digital twin of production, collecting data from materials supplies, logistics and every step in production processes along complex value chains. It works alongside and integrates with existing company ERP systems (even multiple partners' systems), process control systems and sensors, enabling real-time proof of quality compliance, track-and-trace and life-cycle analysis (LCA). All data is stored on a distributed digital ledger with smart contracts, for proof of origin and authenticity of the data, and for security and transparency as needed. Michael Reubold spoke with Jens Schmidt, co-founder, CEO and CTO of ReCarbonX, and an early adopter of blockchain-based systems.

© ReCarbonX

Jens Schmidt, ReCarbonX

Personal Profile

Jens Schmidt is an expert in chemical technologies, digitization, and sustainability, with deep international manufacturing experience. He studied Chemical Engineering at Hamburg University of Technology, Germany, where he received his PhD degree in 2002 and subsequently joined Dow Chemical as Lead Process Engineer. During his 19-plus-year tenure at Dow he held various positions and most recently was the highest-ranking Corporate Technology Fellow. A certified Six Sigma MAIC Black Belt and a seasoned entrepreneur, Schmidt is co-founder, CEO and CTO of ReCarbonX, founder and managing director at Trexcare, and currently also CTO at TES-H2, driving green energy transformation. He is a global industry advisor and IT/Tech architect with expertise in sensors, sensor control and process automation.

CHEManager: How did ReCarbonX get started and when was the idea born?

Jens Schmidt: Two years ago, I met my co-founder Oksana Pilatova who—at the time, like me—worked in the chemical industry. We went to Italy for a review of an innovative hydrogen start-up and during a lunch break talked about the upcoming need for sustainability and the associated complexity of tracking carbon footprints along value chains with multiple partners. That was when we developed the first high-level idea of ReCarbonX, using blockchain technology for value chain tracking.

How did you move from idea to starting a company?

J. Schmidt: At first, we defined and refined the concept and workflows, did a first minimum viable product—MVP—and a real blockchain implementation, and added back integration with IoT sensors and data gathering via mobile devices. Soon it became obvious that the solution could do much more than just eco footprint tracking in the chemical industry. Then, still in 2020, we brought our co-founders on board and established the company in Switzerland. We found an innovative food processing company in Bulgaria—our very first customer—and the installed system delivers excellent results.

How does ReCarbonX create value for its customers?

J. Schmidt: Sharing data across value chains with multiple partners is a necessity of today's business world, to ensure compliance and to understand material flows and product properties. At the same time, it's a cumbersome and resource-intensive process. ReCarbonX solves exactly these challenges. Essentially, it's all about providing manufacturers with security and control over the transparency of their own data, while giving them access to a tool that can not only improve the productivity and processes of production and reporting, but also calculate and showcase any product's real-time life-cycle analysis and full eco footprint. It is value made visible!

How has ReCarbonX been impacted by the pandemic and the war in Ukraine?

J. Schmidt: It's a challenging time for start-ups. Oksana is Ukrainian, and we therefore as a team feel the impact of the crisis first-hand. We are all actively focused on using our skills to start and help volunteer initiatives that support people in need and those on the ground in Ukraine.

At the same time, we are working with people in companies who continue production despite the crisis in the region, and we can see that they and many others are suffering in at least two major ways: Firstly, with personnel challenges, the difficulty finding people to work in production—this is something that was also evident during the pandemic—and, secondly, with serious supply chain disruption leading to a lack of availability of raw materials and ingredients, with no way to reliably prove quality and provenance.

While we can see that many are floundering, we can also see that having the ReCarbonX system installed with a digital twin of production can bring reliability to workflows and proof of high-quality production when stress and systems chaos might otherwise lead to human errors and more distress for those involved. Our customer in Bulgaria found real benefits during the height of the pandemic, when the system allowed them to automatically capture, monitor and record compliance and quality documents and checks without the need for auditing personnel to be sent in person to the production plant. This continues to be a great time- and resource-saving benefit for them. Additionally, having the digital twin and defined workflows with hand-held tablets has meant that new personnel—even those previously untrained and under pressure to perform—are able to get up to speed with just one day of training, and carry out production steps like long-time employees.

What's next for ReCarbonX?

J. Schmidt: We've been doing pilots and showcasing various demos with our bespoke Sustainability Simulator for large chemical companies, oil & gas companies, and logistics majors. We have also been invited to present our unique solution to the EU commission on digital product passport in workshops of the German Chemical Industry Association and the Association of German Chemical Traders. We would like to use our links to organizations like DIN to continue to work on an open standard for data exchange between various systems along value chains, as we believe in open access and interoperability to reach the goal of truly transparent value chains.

Business Idea

Safe, Smart, Sustainable

Tracking and proving the authenticity of production data and being able to calculate the true eco footprint of products are huge challenges for manufacturers and producers in today's increasingly complex value chains.

ReCarbonX is an affordable and easily scalable "umbrella" system that works alongside, and integrates with, existing company ERP systems—even up- and downstream partner companies' systems.

The kinds of data collected include documents and reports, the type and origin of raw materials and percentage of recycled materials, waste, water use, the type of energy used during processing and for cooling chains, types of fuel used for transport and logistics, and distances traveled for delivery.

Especially unique is the ReCarbonX algorithm and Sustainability Simulator, which can calculate per-product eco footprints, and show the effect of relevant sustainability improvements in real time. The system provides on-demand CSR capability and verifiable data presented in easy-to-understand visualizations, as well as per-product industry comparisons.

Key features of the technology

- **Easily scalable** from small operations to large multinationals, starting in-house to seamlessly integrate partners up- and downstream, step by step as needed and value-adding.
- **Platform independent,** through the use of decentralizied solutions; adaptable to cloud-based or on-premises solutions, depending on customer needs.
- **Adaptable**. Designed as an open platform, easily adaptable to different industries and workflows, offering nondiscriminatory free interfaces for integration with other solutions.
- **Customizable** to specific needs from data gathering, processing, visualization of an individual production item or in ESG report for a production line, factory, entire region or company.

- ReCarbonX AG, Zurich, Switzerland
  http://recarbonx.com/

A digital twin of production processes is created with IoT sensors, ERP and manual inputs.

Elevator Pitch

Value Made Visible

ReCarbonX was founded in 2020 in response to key sustainability challenges faced by manufacturers who are under pressure to track, verify and report (or "make visible") their compliance, quality and sustainability improvements in increasingly complex and dynamic value chains.

ReCarbonX combines the benefit of distributed ledger technology (blockchain) and tailored interfaces with real-world IoT sensors, ERPs and manual entries in mobile devices to create a reliable and trustworthy digital twin of the entire value chain. The system is able to capture data for every logistics and production step, and each product and raw material along the chain.

The unique algorithm reliably calculates the true eco footprint of products in real time, and shows compliance, source and destination of goods and product streams, including the real percentages of recycled materials and waste. Up- and downstream partners can join at any stage, with full ownership and control of their own data and transparency.

Milestones

2018
- Idea

2019
- Founding team assembled

2020
- Develop minimum viable product (MVP)
- ReCarbonX AG founded in Switzerland

2021
- Implementation in food industry
- Presentation to multiple industry associations

Roadmap

2022
- Demonstration of portability of deployed solutions for new sectors such as textiles and wood industry
- Addition of individual product-based recycling tracking
- Support of the "Lieferkettengesetz" (Supply Chain Law) compliance

2023
- Expansion of deployed systems along the value chain by integrating multiple layers, and define open standards to allow data exchange and interaction with other solutions
- Addition of automatic reward systems for footprint reductions along value chains, allowing brand owners to automatically reward eco improvements early in the chain in a fair and data-based manner

2024
- Helping establish open standards as an industry norm
- Support EU product passport initiatives
- Meet standardized ESG reporting needs and global standards on product footprint reporting

ReCarbonX shows the impact of product sustainability improvements along complex value chains.

Quantum Computational Toxicology

A Paradigm Shift: When Computational Toxicology Intersects with Quantum Chemistry

Safety of chemicals (e.g., environmental pollutants and pharmaceuticals) is of paramount importance. FastCompChem is revolutionizing computational toxicology through a new concept of molecular signature derived explicitly from quantum chemical calculations. Unlike existing approaches, it is possible to cover large swaths of the chemical space since predictions are not tied to known motifs but to the effects on the electronic structure. Pedro Lopes, founder of FastCompChem, explains the company's technologies and describes the options and steps ahead.

Pedro Lopes, FastCompChem, UBIMedical

Personal Profile

Pedro Lopes is the founder of FastCompChem. He holds a chemical engineering degree from Instituto Superior Técnico (IST), Lisbon, Portugal, and a PhD in computational quantum chemistry. He held a faculty position at the University of Maryland, Baltimore, USA, where he developed CHARMM force fields and worked on drug discovery projects. As he became increasingly disillusioned with the current progress of computational tools, he addressed the bottlenecks of quantum methods. Starting with those core technologies, he founded FastCompChem to pursue technologies for quantum-based computer-aided drug design, with initial focus on toxicology.

CHEManager: What was your motivation to start FastCompChem?

Pedro Lopes: I decided to incorporate FastCompChem in 2019 to generalize quantum chemical methods in chemistry and biochemistry. Although I am a quantum chemist by training and vocation, I wanted to learn the art of parameterizing classical force fields. They are crude approximations of physical reality, but they became the de facto standard in molecular simulations. After working many years on CHARMM force fields, I became increasingly disillusioned since force fields have reached a dead end. Only quantum chemistry can sustain the progress of computational chemistry. I made two major contributions to generalize quantum methods. In 2017, I published a very fast approximation to electron repulsion integrals, and, in 2018, the results of an electronic structure optimization algorithm without formal diagonalization. Then FastCompChem was formed to develop solutions to drug discovery. Our current focus is computational toxicology.

Why do you focus on computational toxicology and not on other areas of computational drug discovery?

P. Lopes: Conceptually, it would be easier to develop technologies for virtual screening and molecular simulations. The underlying technologies are similar and much of the work would be replacing the classical with quantum calculations. The impact, however, would also be small since it's a crowded space and companies already have systems with similar functions. Computational toxicology is different. On one hand there is a strong push for new accurate methods. Safety concerns are a major issue in late-stage clinical trials and there is the need of alternatives to animal testing. An in silico solution that accurately predicts toxicity early will save the pharmaceutical industry millions of euros and for environmental effects it is a great way of evaluating chemicals. We have the necessary knowledge to develop the technology.

But there are currently methods for assessing the safety of chemicals, including using quantum descriptors. What differentiates FastCompChem?

P. Lopes: Quantum chemical descriptors are used, for example, in QSAR models, but our technology is radically different. Currently molecular descriptors are derived from molecular structures. Our concept is to develop new descriptors derived from the electronic structure instead. Besides physical observation only possible with quantum methods, the new technology covers the whole chemical space, when quantum calculations are feasible. We don't need to know the effect of each fragment or moiety but merely their combined effects. Although we are developing this technology for computational toxicology, the applications are much broader and can impact chemoinformatics.

What is required to develop the technology?

P. Lopes: Today, nothing is impossible to solve in computational chemistry if there is willingness and the right skills and collaborations. FastCompChem seeks a multidisciplinary approach, with the areas of quantum chemistry and computer science being very relevant. We also need extensive collaborations with the industry and academic groups. Those collaborations are essential to provide expertise in toxicology, to provide experimental data and general guidance to prioritize development. We have a collaboration with a leading quantum chemistry group at the University of Manchester. We are also establishing contacts with leading computer science research institutions. The ultimate goal is to form a large "coalition of the willing" of interested parties to develop the technology.

What is your business model? How do you plan to commercialize the solution?

P. Lopes: At this moment, I can say that it depends on the number of parties joining the project. With a large coalition of multidisciplinary collaborators, and considering the scope of computational toxicology, most likely a different entity will have to be established, for example a consortium. It will always be open to new credible and experienced partners, following a R&D operating model that encourages new partners to join, when needs are identified. Monetization can happen through licensing of the technology or through the execution of specific projects.

What do you expect FastCompChem to be in 10 years?

P. Lopes: Continuing with the best-case scenario I see FastCompChem diversifying into other areas, always with the goal of providing the most accurate solutions based on quantum chemistry. In drug discovery we want to offer complete solutions that also include virtual screening, molecular simulations, ligand-based strategies, etc. I also see great opportunities in other areas such as de novo design of enzymes and catalysis, to name a few.

Business Idea

Quantum Chemistry in Computational Toxicology

Computational methods for drug design are largely based on classical force fields and structure-based chemometrics. They have significant problems:

- The physical models are poor
- They are not easily generalizable to new systems and chemistries
- They cannot be significantly improved
- Only an infinitesimal part of the chemical space is covered

Progress in computational chemistry is possible with: (1) using much better physical models, and (2) reaching larger swaths of the chemical space. Quantum chemistry should underpin the next generation of computational tools as it is the most accurate theory to study matter and its interactions, while dispensing with specific parameterizations. FastCompChem developed very fast solutions that allow generalization of quantum methods: the fastest approximation to electron repulsion integrals and a very competitive electronic structure optimization algorithm. Diagonalization is an area of active research for other applications.

In terms of business development, FastCompChems's easiest move would be targeting technologies for virtual screening and molecular simulations. This is a crowded space and adoption of the new technology would face significant barriers. Computational toxicology offers greater opportunities and was chosen instead. Specific reasons for developing quantum-based computational tools for toxicology are:

- Reduction of time and costs of drug design processes by bringing safety testing earlier
- Provision of an effective alternative to animal models
- Extension of the same technology to chemoinformatics

Besides the significant impact of the quantum computational toxicology tools there are additional benefits. The technology will work as a Trojan Horse in driving acceptance of quantum technologies initially in drug discovery and in other areas of chemistry and biochemistry. The general adoption of quantal technologies by the industry is a crucial step in ensuring the continued development of computational chemistry and of its applications.

- FastCompChem, Covilhã, Portugal
www.fastcompchem.pt

Elevator Pitch

Changing Computational Chemistry

FastCompChem was founded to develop new quantum methods for drug discovery. Development is prioritized in terms of the perceived need and estimated impact. At FastCompChem computer science assumes an equal footing to quantum chemistry to allow fast prototyping of new concepts.

Milestones

2017

- Fastest approximation of electron-electron repulsion integrals (ERIs) is published. The proof of concept used 3-center integrals. The technology was subsequently extended to 4-center ERIs.

2018

- Results from a competitive alternative to formal diagonalization were published. It was based on an Extended Hückel Hamiltonian complemented with toy electron-electron repulsion functions. The future molecular dynamics software will likely be based on the tight-binding approximation.

2019

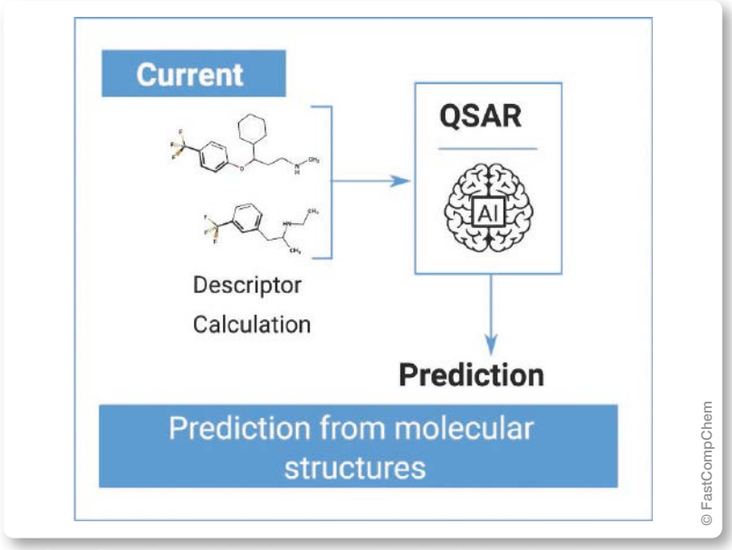
- Foundation of FastCompChem

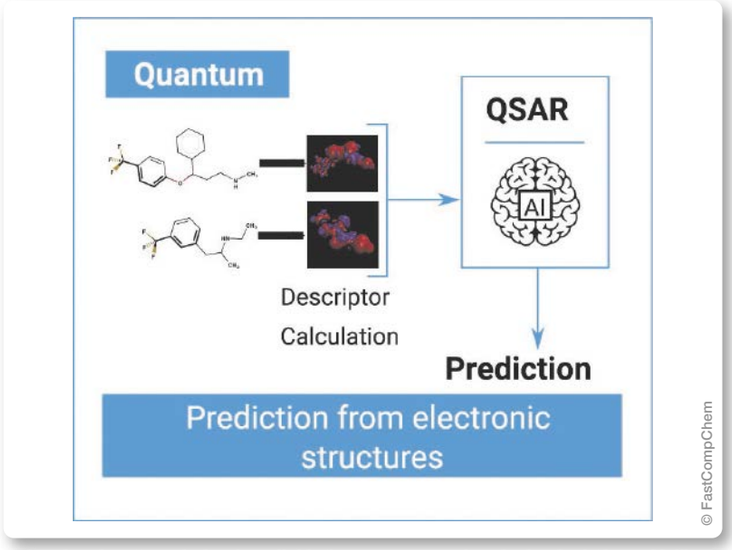
2020

- With the onset of the Covid-19 pandemic, FastCompChem was funded by the PT2020 program (€500,000) to develop novel diagnosis for the infection because of its expertise in AI, computer graphics/vision and scientific software development. Medical diagnosis became a totally separate R&D program of FastCompChem.
- FastCompChem received an investment from Portugal Ventures (€100,000). Work began on the concepts of the new quantum-based computational tools for toxicology.

Roadmap

FastCompChem is currently building collaborations. The development of new computational toxicology tools requires the active involvement of leading partners from the industry and academia. Development will be accelerated with the active participation of leading computer science institutions. FastCompChem already has a collaboration with the University of Manchester to advance the quantum chemical component.





FastCompChem is revolutionizing computational toxicology through a new concept of molecular signature derived explicitly from quantum chemical calculations. Unlike existing approaches, it is possible to cover large swaths of the chemical space since predictions are not tied to known motifs but to the effects on the electronic structure.

EuroChlor 2022

The 11th International Chlorine Technology Conference and Exhibition, EuroChlor 2022, will take place in Warsaw, Poland, from May 3 – 5, 2022. In addition tohealth, safety and environmental protection, this edition of EuroChlor will also focus more specifically on energy efficiency, how to become carbon neutral and how to contribute to the circular economy. In parallel with the conference, the exhibition area will give companies the possibility to showcase their expertise.

■ https://eurochlor2022.org

Interphex 2022

The International Pharmaceutical Expo (Interphex) will take place from May 24 – 26, 2022, in New York, NY, USA. The event is dedicated to pharmaceutical and biotechnological innovation from development to marketing. The annual trade show and technical conference brings together over 10,000 global industry professionals and 625+ leading suppliers through a combination of technical conference, exhibits, demonstrations, and networking events.

■ www.interphex.com

Chemspec Europe 2022

Chemspec Europe is to take place from May 31– June 1, 2022, in Frankfurt, Germany. 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

Achema 2022

Achema, to take place from August 22–26, 2022, in Frankfurt, Germany, is the world forum for chemical engineering, process engineering and biotechnology. Manufacturers and service providers from over 50 countries present their products for chemical, pharmaceutical and biotech research and manufacturing as well as energy and environmental services. The accompanying congress features scientific lectures and numerous guest and partner events.

■ www.achema.de/en

Index

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