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Markets & Economy

Key Challenges for Europe's Chemical Industry; Megatrends Affecting the Surfactants Industry's Value Chain; Sustainable Surfactant Solutions

Pharma & Biotech

The Evolution of the CDMO Sector; The Biologics and Advanced Therapies CDMO Landscape; Increasing Popularity of Biosimilars

Innovation

Graphene-Based Additives for Coatings, Plastics and Composites; Turning Plant Leftovers into Plastic-Free Biomaterials

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European Chemicals Pulse Check

Chemical Value Chains at Risk of Shifting to Non-European Countries

Representatives of the European chemical industry expect a shift away from Europe, especially for energy-intensive production steps. The biggest beneficiary of this change is the USA, as Deloitte's latest European Chemicals Pulse Check shows.

For their report, Deloitte surveyed 66 senior executives from the European chemical industry and sector associations in April 2023. The survey participants represent different branches of the sector, such as base chemicals, specialty chemicals and plastics & materials. 41% of respondents work in companies with revenue of more than €10 billion. 30% represent companies with revenue between €2 billion and €10 billion.

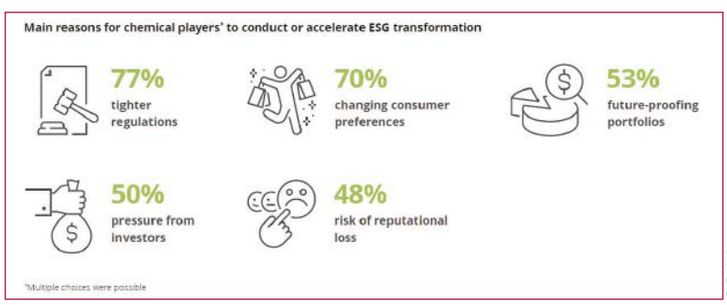
"2023 and 2024 will be key years for the chemicals industry in Europe."

81% of respondents expect that parts of the chemicals industry value chain will move out of Europe. They named high energy prices, strict ESG requirements, attractive conditions outside of Europe, and geopolitical developments as causes. More than two thirds of respondents (68%) also see an increasing risk of demand destruction in the chemical sector in Europe.

Responses to the question about the effect of EU regulations such as the EU Emissions Trading Scheme and the EU Carbon Border Adjustment Mechanism were mixed. For example, 63% of survey participants fear that regulations will jeopardize the export capabilities of companies in the sector. At the same time, 70% see an opportunity here to accelerate investments and innovations in sustainability and new business models.

"In view of the geopolitical tensions, European chemicals manufacturers are reviewing their investment strategies overall."

It is high time to set the course for sustainable growth. On the one hand, higher energy costs burden the competitiveness of chemical companies in Europe. On the other, the uncertain regulatory environment makes it difficult to plan for the long term. Chem-



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icals manufacturers are well-advised to continuously assess regulatory and geopolitical developments and integrate them in their strategies. Scenario thinking is becoming enormously important.

Marked Skepticism towards China

Investments are already shifting to the USA, report 58% of respondents, while 71% are considering their first or further steps in this direction. Expectations are clear: 87% anticipate that the USA will maintain its cost advantage in energy and raw materials over Europe until at least 2030.

Meanwhile, the survey respondents are more skeptical towards China. For example, 51% report that they are reassessing their future investments in China. In addition, 71% now want to manage their digital and physical assets in China more independently from the rest of their global business.

"Chemicals manufacturers are well-advised to continuously assess regulatory and geopolitical developments and integrate them in their strategies."

In view of the geopolitical tensions, European chemicals manufacturers are reviewing their investment strategies overall. Companies are regionalizing their supplier networks and production capacities and using investment incentives to position themselves more resiliently.

Green Transformation Drivers

Two out of three respondents (66%) view the ESG transformation as a reason to rethink their business model. However, ongoing regulatory developments are creating insecurity about investment decisions, which is causing delays for planning and implementing investments, say 58% of respondents. Also, 56% are afraid that the energy and competitiveness challenges in Europe could slow down the ESG transformation.

As a central driver of the transformation, respondents mention tighter regulations (77%) and changing consumer preferences (70%). Other causes named are future-proofing portfolios (53%), pressure from investors (50%), and risk of reputational loss (48%).

2023 and 2024 will be key years for the chemicals industry in Europe. Companies will need to make long-term investment decisions. Their focus should now be on Net Zero targets, the circular economy, and the energy transition, as well as turning these into concrete action plans. Their business models urgently need further development. This is the only way in which we will ensure a successful and prospering chemicals industry in Europe in the coming decades.

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Rethinking Carbon

How Europe's Chemical Companies Can Win their Commercial Future

The European Chemical industry is facing a triple threat: Inflation, recession, and energy crisis. As a consequence, chemical companies are beginning to shift production and investments to North America or China. How can this be reconciled with the goal of maintaining production and jobs in Europe in the long term?

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According to a recent Simon-Kucher panel study, environmental sustainability is now the priority for executives in the European chemical industry. How a company makes the transition from fossil fuels and feedstocks to alternative sources will determine its financial viability, competitive advantages, and ability to back up its sustainability claims with tangible improvements.

Rethinking carbon is not only an innovation challenge, but also a marketing challenge. Innovation will require time, engineering capacity, and top talent to shift companies away from an asset base that consumes too much expensive energy and emits too much carbon. Successful marketing will require strong value propositions anchored in quantifiable claims rather than high-level promises.

Four Actions that Leaders Need to Take

Leaders in the chemical industry should initiate these four actions as they rethink the role of carbon in their business.

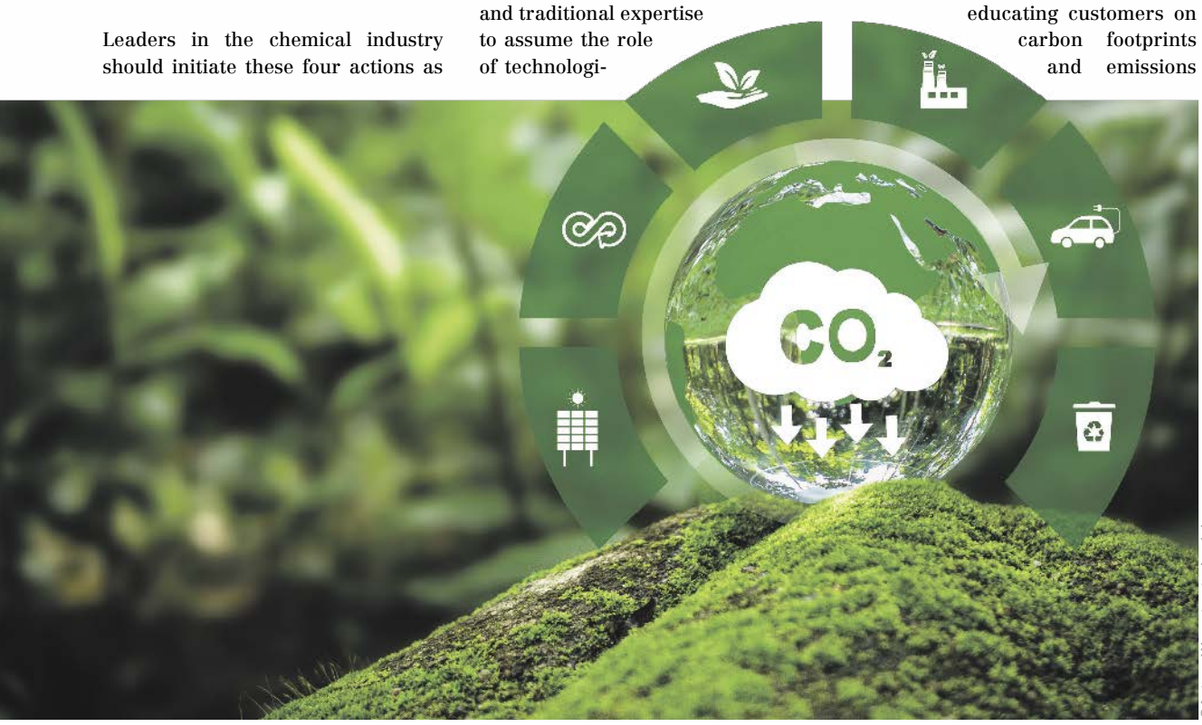
1. Pursue the green price premium as long as it exists

High premiums still exist for first movers to capitalize on in sustainable growth markets, as shown in fig. 1. Our experience determines that a premium of 20% is a reasonable target; up to 30% is also feasible in urgent situations.

The opportunity of achieving these premiums to diminish rapidly after the early maturity stage, as green becomes the new standard.

However, the positive effects of moving first extend beyond the purely financial advantages and flows toward innovation. The faster and better the upstream companies can innovate, the more opportunities their customers will have to innovate as well. This creates a vast opportunity for companies with the talent, infrastructure, and traditional expertise to assume the role of technological leadership. Germany, for example, has advantages in human capital that can outweigh current disadvantages such as access to reliable clean energy.

Energy-intensive production of fossil-based chemical commodities may continue to move to North America, the Middle East, or Asia. But European companies can still maintain their advantages in the development and production of innovative chemicals and materials.



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2. Translate engineering performance into superior perceived value for customers

Enhancing lifecycle value propositions is a top priority requiring concrete and ambitious targets for physical emission reductions (Scope 1,2,3) and beyond.

Top managers plan to allocate around 20% of their time to drive R&D and investments. In contrast, they are spending less than 15% of their time on pure brand marketing campaigns. This reflects the idea that customers and consumers want actions with quantifiable impact rather than high-level messages that raise the risk of greenwashing. So, having a strong value proposition is more essential than ever, but it should be anchored in quantifiable claims rather than bold, high-level promises. This means educating customers on carbon footprints and emissions savings rather than making general claims.

A leading aluminum producer wanted to strengthen its value proposition and asked customers which dimensions of sustainability were important and which were hygiene factors.

Certifications, claims of social responsibility, and geographical proximity of suppliers play a less important role for customers than information on how much renewable energy and how much recycled aluminum the company uses.

Managers also expect to spend about a third of their time on establishing a transparent, trustworthy chain of custody of material and reduce their own Scope 3 emissions through alternative, low-carbon feedstocks. Beyond increasing operational flexibility, they will focus over 40% of their time on value chain reconfiguration and feedstock transformation.

3. Capitalize on the synergies from sustainability and digitalization

Digitalization has always had the immense potential to enable cost savings and drive revenue growth. Sustainability will not supersede digitalization. In fact, digitalization will play an essential role in helping companies communicate transparently on emissions and collaborate with customers and suppliers on sustainability objectives.

Let's look at two examples of the synergies of sustainability and digitalization:

- Enabling cost savings: Several German automakers have formed a new cloud-based platform called Catena-X to help reduce CO_2 emissions and make resource consumption more efficient. The platform will use a digital supply chain to deter-

Success factor #5: Use the first mover price advantage to support coverage of your investment costs

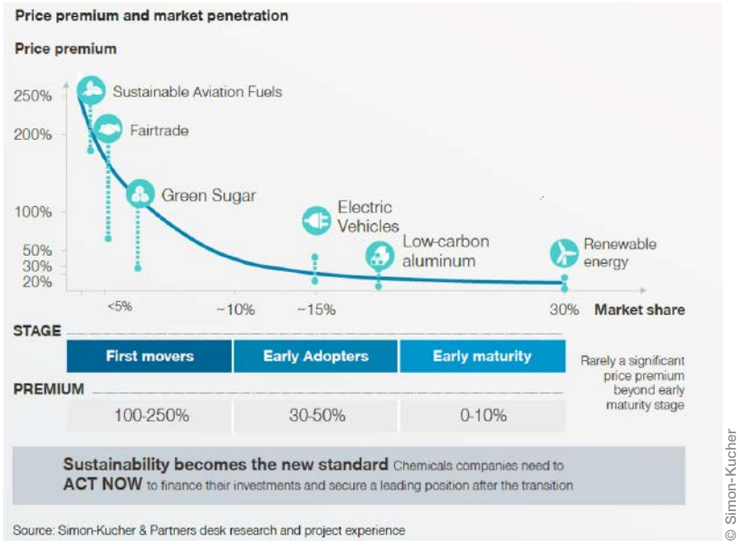

Fig. 1: Price premiums create a strong incentive for chemical companies to act now.

Success factor #1: Drive for a common definition in your value chain to build credibility in competing for the sustainable customer

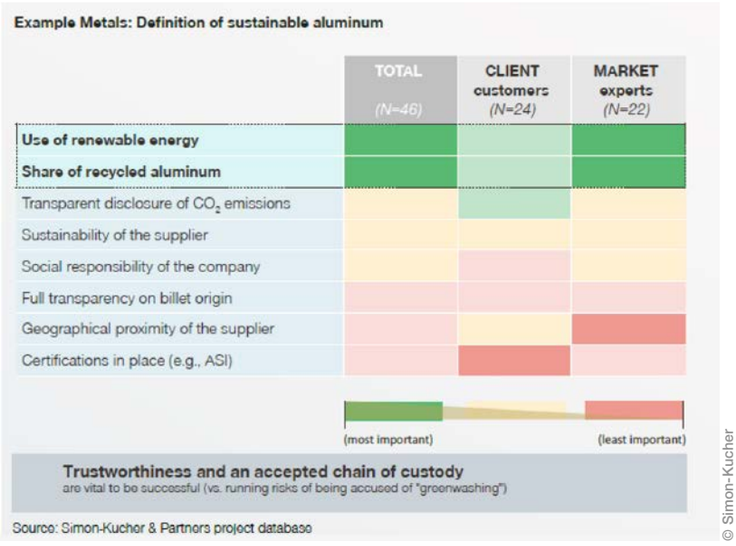

Fig. 2: Fact-based value propositions build trust.

mine the CO_2 emissions in the production of a vehicle.

- Driving revenue growth: Some 88% of participants believe that transforming to a more data-driven business will enable their company to capture revenue growth opportunities. One example is metals company Klöckner's ability to precisely calculate product carbon footprint and document tangible CO_2 reductions. Customers can incorporate the emissions data and comply with regulatory requirements, measuring their own sustainability targets.

The rationale is that increased visibility and communication make it easier for chemical companies to do business with their customers. Around 74% of the respondents observe that customers are increasingly expecting a more digital and more seamless buying experience.

4. Achieve energy security and diversity

Electricity prices have remained persistently high in Germany throughout spring 2023. While many companies can tolerate prices that are higher than historical average, these increased prices may do much more than suppress short-term profits. They can also act as a brake on the long-term investments the chemical sector in Germany and other European countries urgently need.

In a press release in May, Lanxess CEO Matthias Zachert stressed the importance of "competitive energy prices" as well as faster approval procedures, better infrastructure, and an industry-friendly attitude. Emphasizing the prevailing conditions in Germany, Zachert added that "[if] we want our home country to be able to compete internationally in the future, we have to act now. Create the right framework conditions now. Only then can we as an industry also make a powerful contribution to maintaining our nation's prosperity."

Sufficient, reliable, affordable, and stable supplies of electricity and hydrogen from renewable sources will underpin the economic transition to new carbon platforms. Energy security and diversity are ways for European suppliers to increase resilience and to confidently make the first moves to finance their green transition and meet customer demands.

Volatile supply dynamics are expected to accelerate the push to diversify energy sources—and toward renewables in particular—faster than regulatory frameworks will require. In other words, the accelerated shift becomes a source of competitive advantage and not merely a compliance obligation.

The Time to Act Is Now

There's never been a more apt time to act than now when the chemical industry is reeling under the triple threat of inflation, recession, and energy crisis. Executives recognize that accelerating the green transition can become a "win-win-win" opportunity to meet new demand, increase resilience, and improve margins. It is about accelerating growth and mitigating cost risks at the same time.In other words, waiting is not an option.

As BASF CEO Martin Brudermüller said in an interview with the German newspaper Handelsblatt, "Protecting the environment affects each and every one of us. It is clear what is happening and there is not much time left. And that is a huge opportunity."

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The Evolution of CDMOs

From the Birth of an Industry to Its Present Significance, and the Challenges It Is Facing

CDMOs (contract development and manufacturing organizations) are a crucial part of the life sciences industry. Some companies and organizations simply don't have the internal resources or expertise to manufacture certain products. So, they turn to CDMOs to produce their latest developments.

Strangely, despite its current prominence, the CDMO industry is a relatively young one. There have been significant developments over its short lifespan, and it is likely that we see even more growth in the years to come. However, as for most industries, there are both opportunities and challenges in paving the way forward.

A Brief History of CDMOs

Although CDMOs have been around for a while, they've only become critical to bio and pharma organizations within the last 20 years. In fact, before 1996, dedicated contract drug-product manufacturers were quite rare. Instead, it was common for major bio & pharma companies to manufacture products for similar businesses — especially if it didn't enable competition. A key turning point was in 1996, when Patheon began purchasing various facilities, while Lonza secured Celltech and cemented its position in contract biologics.

With these acquisitions, Patheon and Lonza alerted other organizations to the opportunity that outsourcing product development and manufacture could provide. In turn, individual CDMOs began popping up and sparked the development of the industry. This was the birth of the CDMO industry as we recognize it today.

A decade later, the financial crisis had mixed effects on the CDMO industry. Several organizations were forced out of business, while some others benefited from investments from private-equity firms. The low-interest investments and long-term prospects were very persuasive in attracting investment, and many were able to purchase production facilities being offloaded by pharmaceutical companies.

Typically, these facilities were obtained for very reasonable prices, and in exchange, exclusive contracts were signed that provided the pharma companies with cheaper production methods.

The Industry Right Now

Currently, the CDMO industry is in a "melting pot" of change. Recent events like the Covid-19 pandemic and the talent crunch have plunged the industry into another period of change. In response, some organizations feel the need to expand and diversify offerings in order to maintain their market presence.

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The Covid pandemic provided a massive boost to the CDMO industry. While biopharma and biologics businesses developed Covid vaccines, there simply wasn't enough internal production capacity available to produce the quantities needed.

CDMOs filled this gap in supply and worked to meet the global demand. If not for the role contract organizations played, the effects of Covid could've been far more severe. In response, the contract industry has cemented itself as a crucial part of the life sciences industry.

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What the Future Holds

With the industry still so young, it's difficult to know exactly how it will change and grow over the coming years. But by analyzing previous trends and how previous global events have impacted the industry, certain developments can be predicted with some accuracy.

CDMOs Becoming PDMOs

Some CDMOs are expanding their services and swapping their "contracts" for "partnerships", evolving the term "CDMO" into "PDMO". By getting closer to their partners, CDMOs can move past some of the pressure, and instead, offer consultative support or innovation to develop products in new ways.

The outsourcing industry has always been quite fast-paced. Moving to this new model allows businesses

to be more efficient in bringing new life-saving advanced therapies and drugs to the market.

Private Equity Investment and Development

There is a huge strain on manufacturing capacity and supply to help take some of the new technologies, like cell therapies, to market. Now is a prime time for private equity firms to invest in CDMOs. With pharma organizations selling off facilities and outsourcing production instead, CDMOs with sufficient investment have a prime opportunity to scale up at an exponential rate.

If enough CDMOs manage to source this investment, we will likely see massive growth in the industry over the next several years. We saw something similar happen after the financial crisis of 2008. While some individual companies may not survive, the industry as a whole is likely to expand drastically. In fact, with the CDMO space expected to achieve 10.0% CAGR between 2020–2027 and grow to a nearly $300 billion industry in the next five years, the future is bright.

Pharma Selling Off

Pharma companies continue to sell off their development and manufacturing sites. Producing drugs, medicines, and other medical equipment themselves remains expensive — especially when you consider the cost of running and maintaining the facilities and their staff.

By selling their facilities to CDMOs, Big Pharma is saving money and reinvesting back into the R&D of new products and modalities. Allowing them to maintain a more constant revenue stream and have multiple active projects at any one time.

Meanwhile, the CDMOs can focus their attention on improving their value chain and meeting demand with greater efficiency. The more facilities contract organizations can gain ownership of, the fewer shortages we'll see.

The Talent Crunch

Something else that is influencing the development of the CDMO industry is the talent crunch. With the lessons learned from the pandemic and its effects on the global supply chain, we have seen over $150 billion of investment from private equity and the National Institutes of Health across North America alone — the fastest growth rate for the life sciences industry.

Naturally, with this level of investment comes growth. Growth in client demand, the requirement for resources, materials and, of course, talent. Over the next five years, 98% of life science organizations have set plans to increase their headcount, meaning that talent demand is higher than ever.

The main challenges during the talent crunch will be the attraction and retention of highly qualified employees. It's becoming obvious that to remain competitive amidst the talent crunch, life science businesses will have to keep investing in their team.

For CDMOs, there are a couple of challenges being faced, some old and some new:

- The industry has been known for having tighter budgets for salaries. This is due to the nature of the business being services-driven; however, over recent years, outsourcing businesses have become more competitive in line with large pharma & biotech organizations.
- The CDMO market is exciting but highly fast-paced; contract organizations are managing multiple partnerships simultaneously and having to deliver to a high standard of quality every time.
- With inflation rising in the US and across the globe, companies that are too rigid to adapt quickly to market conditions are struggling to keep up with the pace.

Outsourcing businesses' greatest strengths are also their greatest weakness in talent retention. It comes down to the fact that CDMO employees make very marketable candidates within other industries. They are candidates who are good at working under pressure, are comfortable with being client-facing, and topping it all off, they are usually outstanding, affordable profiles for local large-scale pharma & biotech businesses.

Therefore, given the sheer scale of hiring that has taken place across the market in the last 2-3 years, talent retention has become one of the most complex challenges leaders will face in the coming months.

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Competition Is Working

Biosimilars Are Becoming Increasingly Popular but Pharma Associations Warn Against Price Wars

The development of biosimilars is one of the more recent success stories in the pharmaceutical industry. Since these drugs first appeared on the European market in 2006, they have increasingly replaced original biopharmaceuticals whose patents are expiring. In the process, they often achieve high market shares from a standing start. However, with their triumphant advance, biosimilars are also setting in motion the usual market mechanisms. Biopharma interest groups warn against the automatic substitution of originator drugs and argue that price wars could lead to the relocation of production.

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At the end of January 2023, the best-selling Humira was also lost in the USA: The biotech group Amgen launched Amjevita, the first biosimilar to AbbVie's number one sales driver. This also heralded the end of Humira's 20-year dominance in the world's largest pharmaceutical market as the biologic with the highest annual sales of all time, at more than $21 billion.

Humira, which contains the active ingredient adalimumab, is used primarily to treat severe inflammatory diseases such as rheumatoid arthritis. For almost seven years, Abbvie had tried to fend off the threat to its blockbuster therapeutic from adalimumab biosimilars in the United States by means of patent and legal disputes. While this succeeded for a long time on the other side of the Atlantic, also thanks to several settlements, Abbvie was less able to fend off the troublesome competition in Europe. The first Humira biosimilars came onto the market here four years earlier, and as of June 2023 there were already ten.

This example is representative of the rise of this still comparatively young generation of drugs. The basis for the emergence of biosimilars is original biopharmaceutical drugs, which usually have a complex molecular structure. According to the Pro Generika association, these are becoming increasingly important for our drug supply — biopharmaceuticals account for almost one-third of the German pharmaceutical market. In addition to insulins, these include corona vaccines and novel immunotherapies for the treatment of cancer for example. When the patents on these products expire after 20 years, the time has come for biosimilars. Although these successor products are just as complex in structure as the originals and also require considerable development effort, they are generally significantly less expensive than the reference product and thus help to relieve the financial burden on healthcare providers.

76 Biosimilar Approvals in the EU

According to figures from the European Union, 76 biosimilars are currently approved centrally by the European Medicines Agency (EMA). In addition to biosimilars for the arthritis product Humira, these include follow-on products for monoclonal cancer antibodies, the ophthalmic drug ranibizumab, the anemia product epoetin alfa, the rheumatism drug etanercept, the autoimmune drug infliximab, the diabetes drug insulin aspart, or the immunostimulator pegfilgrastim.

Biosimilars usually show a steep growth curve with their market launch. In Germany, for example, they achieve market shares of up to 80% in the first year. According to figures from the Boston Consulting Group (BCG) and VFA bio, the biotechnology interest group in the German Association of Research-Based Pharmaceutical Companies (VFA), their share of sales in 2022 averaged 64%, while total sales in the German market rose by 7% year-on-year to €2.3 billion in 2022. The authors also determined that biosimilars achieved a sales share of 92% in the pharmacy market at the end of 2021 in the case of the active ingredient rituximab, 90% for bevacizumab, 89% for infliximab and 85% for trastuzumab. In addition, on average three biosimilars competed with the original.

The numbers show: Competition with biosimilars is working, both in terms of the pace of market penetration and the share of prescriptions. These products are also helping to improve patient care, according to biopharma associations.

However, the success of downstream products depends on a number of factors. A decisive one, in addition to the number of biosimilar products available, is the price difference compared to the originator product. Only if this is large enough physicians will feel an incentive to prescribe the biosimilar to their patients, which in case of doubt is less well known than the original. One example: the cost of Humira biosimilars in Denmark fell by 82% from September 2018 to December 2018. In addition to price, education plays an important role. Experience shows that biosimilars only gain acceptance if physicians and patients feel they are informed in a factual and up-to-date manner.

Different Speeds

However, market penetration in Europe and the USA is proceeding at different speeds. While the United States is often ahead in innovation, the opposite is true for biosimilars, where Europe is much faster. The main reasons for this are patent disputes, which numerous pharmaceutical companies in the USA are pursuing with all their might against their competitors—as in the case of Humira.

Although the main patent for Humira's active ingredient expired back in 2016, AbbVie was able to maintain its market exclusivity for many more years through more than 100 additional Humira patents. This resulted in patent infringement proceedings, but also in financial settlements that AbbVie reached with competitors. These included, for example, biosimilar manufacturers taking their time with market entry and paying AbbVie a royalty upon market launch.

Restraint in the USA

In addition, it is possible that the availability of biosimilars in the USA could be deliberately restricted. For example, the powerful pharmacy benefit managers can influence whether and how many Humira biosimilar options are offered in their drug lists. Many experts fear that ultimately only a few Humira biosimilars will have access to the US market and many will not even be listed. In addition, health insurers' contracting practices could help preserve sales of more expensive brand-name drugs.

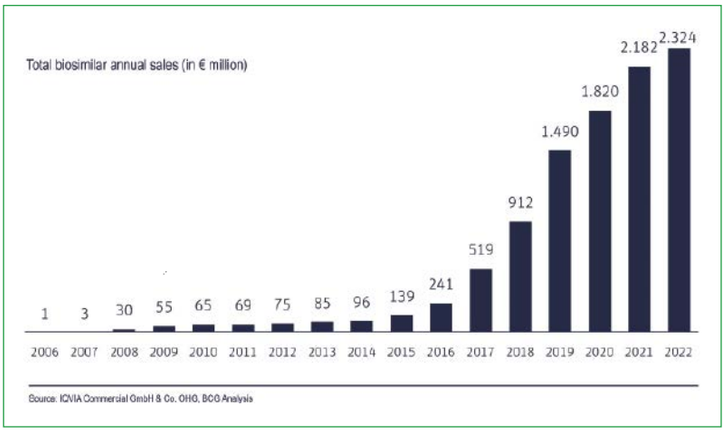
This development is also reflected at the financial level; price reductions following the market launch of biosim-

ilars in Europe and the USA diverge significantly. Experts therefore expect that Humira biosimilars will not lead to cost savings in the USA as quickly or as significantly as in Europe.

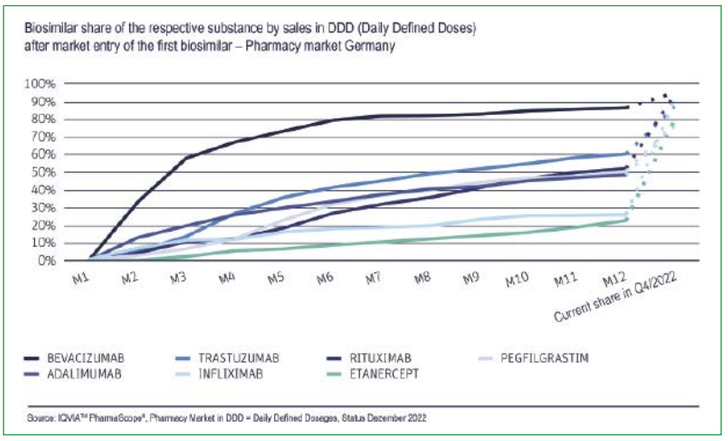
Resistance to Automatic Substitution

But the German biosimilar market is not all sunshine either. The European Medicines Agency (EMA) and the heads of national medicines agencies (HMAs) argue that biosimilars approved in the European Union (EU) are scientifically interchangeable with originator products in pharmacies. The German Federal Institute for Drugs and Medical Devices (BfArM) supports this position. The substitution would automatically make the most favorable biosimilar subject to prescription. Originally, biotechnologically manufactured drugs were to be automatically substituted for each other in pharmacies starting in August 2022. Shortly before, this date was postponed by one year, but has since been decided by the Federal Joint Committee (G-BA), albeit with the possibility of exceptions.

However, the pharmaceutical associations and biopharma interest groups BAH, BPI, AG Pro Biosimilars and VFA are vehemently opposed to the automatic substitution of original biopharmaceuticals by biosimilars. They argue that there is no reason for automatic substitution in view of the stable financing of the statutory health insurance funds: The biosimilar market is functioning and competition is in full swing. With instructions on the prescription of biopharmaceuticals for physicians anchored in law in 2021, sufficient care has already been taken to ensure that biopharmaceuticals are prescribed economically and used safely.



Biosimilars in Germany with continuous sales growth.



Competition works: Biosimilars in Germany with rapid uptake and high prescription shares.

This group considers automatic substitution of biopharmaceuticals to be simply "dangerous." The lobbyists refer to a regulation anchored in the SHI Financial Stabilization Act and "warn of the negative consequences for Europe, which is currently still a robust biotech production location, and for supply security." Politicians must not make the same mistake as with generics and endanger the competitiveness of European manufacturers through unrestrained cost containment in the SHI system, they say.

In this context, Pro Generika points out that two thirds of generic active ingredients are now produced in Asia, especially in China and India. In biosimilar production, however, the situation is still different: More than 50% of the biosimilar active ingredients intended for the European market are still produced in Europe, 30% of them in Germany.

However, Europe's lead in global location competition is melting, and global competition in the biosimilar market is becoming increasingly intense. Asian manufacturers in particular are expanding their expertise in biotechnological production and development: China and India have risen to become the world's leading nations in biotech research and manufacturing in recent years, he said. The first biosimilar active ingredients are already being manufactured exclusively in China.

The argument of the opponents of substitution is that once pharmaceutical production has migrated, it is difficult to bring it back. From the point of view of the resilience of the healthcare system, the slogan is therefore clear: "If you want reshoring, you have to avoid offshoring."

But perhaps the concern behind this outcry is that it could be made too easy for biosimilar manufacturers to replace the often financially very lucrative original products at the stroke of a pen. Who likes to give up lucrative sales? Ultimately, however, this discussion shows that biosimilars have arrived at the center of the pharmaceutical market and patient care.

Thorsten Schüller, CHEManager

New Biologics and Advanced Therapies

Opportunities and Challenges in the Therapeutic and CDMO Markets

The pharmaceutical market is undergoing a profound transformation, driven by innovation among biologics and advanced therapies (ATs). This shift is not only redefining the treatment landscape but also presenting new opportunities and challenges related to the drug development and manufacturing value chain.

With this backdrop, contract development and manufacturing organizations (CDMOs) play a pivotal role in enabling sponsor companies to bring groundbreaking therapies to patients.

The Dynamic Growth of Biologics and ATs Market

In recent years, the biologics and ATs market has experienced substantial growth, driven by intensive R&D efforts and breakthroughs in expression systems and manufacturing techniques. Challenges remain, especially the need to scale production to meet the large commercial opportunity. Forecasts suggest the biologics and ATs market will exceed the market for small molecules by $201 billion by 2027, supported by a projected 10.5% compound annual growth rate (CAGR) from 2022 to 2027. Note that all data are from Alira Health's "2023 Biologics & Advanced Therapies Contract Manufacturing Report."

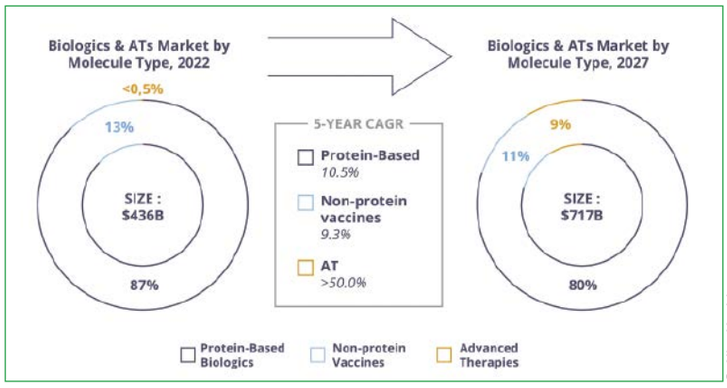


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Fig. 1: ATs will contribute to about 10% of the market by 2027, up from a mere 0.5% today.

Unveiling Market Dynamics: Trends by Therapeutic Class

As of 2022, protein-based biologics made up the majority of commercial biologics and ATs, comprising 87% of the market ($376 billion), followed by non-protein vaccines at $58 billion and ATs at $2 billion.

The rapid development and market release of Covid-19 vaccines has been a transformative force in the biologics and ATs landscape, driving momentum for the regulatory approval of non-Covid-19-related innovative therapies. Despite pandemic-related challenges, the United States (US) and the European Union (EU) maintained or increased annual approval rates for biopharmaceuticals in 2020 and 2021, showcasing industry resilience. The effectiveness of biologics and ATs against Covid-19 has continued to drive investments in R&D. This trajectory is projected to drive a substantial $281 billion growth in the biologics and ATs market over the five years from 2022 to 2027. Looking ahead to 2027, protein-based biologics are likely to maintain dominance with 80% of the market, while ATs are expected to grow to 9%. A notable trend is the rising demand for viral vector manufacturing, prompting considerable investments by CDMOs and transformative acquisitions.

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The Evolving Landscape of Research and Development

The innovation pipeline for biologics and ATs is deep, with 23,718 therapies in development. Early developmental assets, including both discovery and pre-clinical stage, make up 67.1% of this array 15,924 products. Notably, antibodies and cell and gene therapy products take the lead as extensively developed therapies,

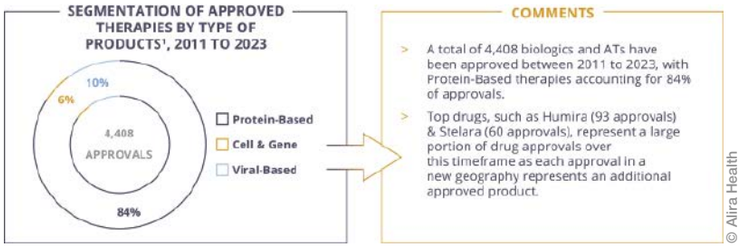

Fig. 2: Most approved products fall in the protein-based category, still accounting for 84% of total approvals during the period.

contributing to over half of pipeline products across various stages, signifying their role in advancing medical treatments.

Oncology emerges as the dominant clinical indication, boasting an impressive 9,000 pipeline products dedicated to various facets of this crucial therapeutic area. From 2011 to 2023, a notable 4,408 biologics and ATs secured regulatory approval worldwide, with protein-based therapies comprising 84% of these approvals. Blockbuster monoclonal antibodies like Humira, with 93 approvals, and Stelara, with 60 approvals, significantly shape the landscape, with each approval in a new geographical region amplifying their significance and expanding the range of approved products.

Considering key geographical regions in which biologics and ATs are developed, North America leads at 14%, followed closely by China at 10%. The EU+UK regions follow at 9%, with India at 8% and Japan at 4%. Collectively, these five regions contribute to a significant 45% share of the entire biologics and ATs market as of 2023.

CDMOs: Opportunities & Challenges

The increased funding in R&D activities and the growth outlook for the demand of biologics and ATs are formidable drivers for the CDMO industry.

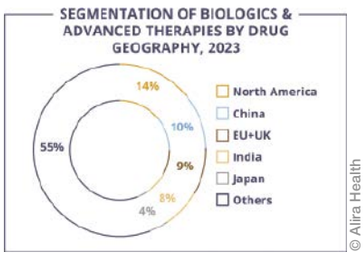

Fig. 3: North America commands the highest number of candidates and commercial stage molecules, followed by China and the EU+UK region.

As of 2022, the estimated value of the biologics and ATs CDMO market is $18.6 billion. This value is anticipated to grow at a remarkable CAGR of 14.1%, reaching $36 billion by 2027. The surge is driven by increasing demand in all three segments (biologics, non-protein vaccines, and ATs). Specifically, the last two segments combined are on track to constitute 32% of the total market by 2027, up from 23% today.

The protein-based segment, holding the highest market share, is anticipated to grow at an 11.5% CAGR from 2022 to 2027, while the bulk of the expected market growth is propelled by non-protein vaccines and ATs, projected to grow at impressive rates of 24.6% and 18.3%, respectively.

As a result of this impressive market growth, CDMOs aspiring to lead in biologics and ATs manufacturing are venturing into the integration of technologies capable of addressing the evolving landscape.

The landscape is rich in opportunities and challenges. For example, one of the critical drivers of the demand for contract services is the patent expiration of many biologics and ATs and the rise of biosimilars. Biosimilars enjoy global policy support in response to escalating healthcare costs, exemplified by the EU's biosimilar approval pathway. As intellectual property protection for originator biologics and ATs diminishes, biosimilar manufacturers are enabled by the support of CDMOs, which can provide a rapid turnaround and lower manufacturing costs while ensuring supply chain flexibility.

The vibrant growth of the ATs sector, including cell and gene therapy products, is another major boost to CDMOs. ATs sponsors hold the potential to address previously untreatable diseases, drawing substantial research and investment focus. However, challenges persist, with burgeoning demand outstripping manufacturing capacities. Ensuring product stability and quality introduces complexity, raising concerns over automation and scalability. CDMOs provide ATs sponsors with the critical capacity and quality necessary to make them successful.

Finally, the complexity of manufacturing cell therapy products creates major opportunities for CDMOs. Sponsors may lack the internal capabilities to efficiently identify, validate, and deploy processes, particularly for autologous cell therapies. Scaling these operations requires deep expertise and robust process development capabilities, which CDMOs can supply to the industry.

In summary, sponsors of biologics and ATs products will increasingly seek CDMOs as external manufacturing partners to enhance production, optimize capacity, reduce costs, and create a secure supply chain. CDMOs must navigate the opportunities and challenges driving the biologics and ATs field, while supporting the entire spectrum of development, manufacturing, and therapy delivery.

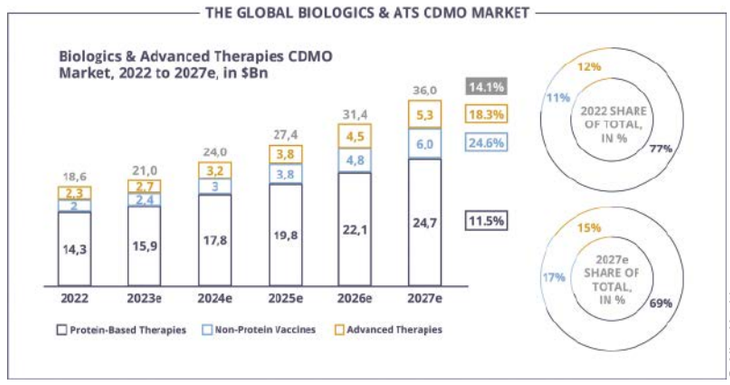

Fig. 4: The overall biologics and ATs CDMO market is expected to outpace the commercial market growth driven by strong demand for services.

The Biologics and ATs CDMO Landscape

Large CDMOs currently command the majority share at 65.2% of the global market, but the rise of small and micro competitors is set to fuel innovation and consolidation within the sector. The competitive landscape is primarily shaped by eight large players, each generating revenues of $1 billion or more, who together constitute 65% of total revenue for the CDMO market. Medium players contribute an additional $6.5 billion, so that large and medium players combined represent nearly 90% of the total revenue.

Despite the prominence of small and micro manufacturers on the global biologics & ATs outsourcing scene, they together represent a modest 10% of total CDMO revenue due to capacity constraints. This fragmentation offers several attractive opportunities for industry consolidation in the coming years.

Pivotal Role for CDMOs in an Evolving Landscape

In conclusion, the evolving landscape of biologics and ATs is reshaping the treatment paradigm while introducing a spectrum of opportunities and challenges. Companies with novel therapies will increasingly look to CDMOs to bridge the gap between innovation and patient access. CDMOs must balance growth with adequately addressing the challenges posed by complex manufacturing processes. As the biotech sector propels forward, CDMOs will continue to play a pivotal role in enabling the realization of groundbreaking treatments.

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Creating Sustainable Concepts

Intelligent Engineering for Optimized Pharmaceutical Manufacturing Processes

ACG, founded as Associated Capsules Group in 1961, today serves pharmaceutical and nutraceutical companies all over the world. As a supplier of integrated manufacturing solutions to these industries, the India-based group offers a complete range of solutions: beginning with empty capsules; granulation and coating; capsule filling; tableting; packaging films and packing, as well as end-of-line solutions with almost 24,000 machine installations worldwide. In March 2023, ACG announced that Richard Stedman will be re-joining the group as the CEO of its Engineering division, a position he had held from 2017 to 2021. CHEManager asked him to analyze current market trends and present his strategy to further develop and grow the engineering business.

CHEManager: How has the pandemic and its repercussions changed the industry and the markets? Which challenges are ACG's customers currently facing?

Richard Stedman: I'd argue that one of the biggest challenges the pharma industry is currently facing is that of supply chain disruption. This started in 2020 during the Covid pandemic and has intensified over the last couple of years. At ACG, we have had to be agile in our response to the situation to continue to deliver on our promise to 'make it better' for our clients and end-users. We're now learning how we are going to live with and manage the disruptions that will undoubtedly continue to prevail—creating significant delays and issues for our sector. The industry has had to adapt accordingly in order to continue successfully delivering services to end users.

Talent shortages are also creating difficulties for the industry—finding qualified associates and professionals has become a difficult task. The sector needs people with an understanding of the pharma manufacturing processes to be able to help solve the growing challenges the industry is facing. One example is the issue of how to collect, manage and analyze data, whilst providing security and encryption assurances.

What are the lessons learned from the global supply chain disruptions caused by the pandemic? Have your customers changed their approach to safeguarding the supply of critical components?

R. Stedman: Shortages of raw materials are continuing to yield severe pharmaceutical manufacturing supply line disruptions. In some cases, European manufacturers are experiencing a doubling of supplier lead times, uncertain and fluctuating prices, and orders that are often subject to delays. Numerous additional sector threats including soaring inflation and global talent shortages have left many manufacturers with plants not operating to full capacity—compounded by increases to overall running costs.

As our head of global supply chains, Nikunj Desai, commented: "Looking to Darwin's philosophical reasoning: 'It is not the most intellectual of the species that survives; it is not the strongest that survives, but the species that survives is the one that is able best to adapt and adjust to the changing environment in which it finds itself'." In an article published at the end of last year, Desai advised that: "Now, during one of the greatest manufacturing crises on record, is a time to consider doing things differently rather than accepting the scarcity of multiple resources and running a leaner operation to match."

To ensure they are able to weather this current—and future—crises, customers are having to strengthen their processes when it comes to a number of factors.

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Can you explain some of these factors in more detail?

R. Stedman: These factors include the following:

More resilient supply chains—built on strong foundations with robust processes and systems that enable their stakeholders to have full visibility and subsequent control.

Managing risk—anticipating potential disruptions and building resilience to adapt to unforeseen events.

Track and trace—being able to identify products' whereabouts in the supply chain is also key—from production through to delivery.

Process automation—reducing errors and increasing accuracy and precision.

To better understand how ACG is positioned to support their customers in managing these challenges, please give us a quick overview of ACG Engineering's core competences and capabilities.

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Richard Stedman, CEO, ACG Engineering

R. Stedman: For more than 60 years, ACG has been committed to 'making the world better' by providing materials, equipment and technology to the pharma industry, helping its customers to provide products to the end user, so they can have a better life.

ACG is the world's only integrated pharma manufacturing solutions company, with products ranging from capsules to films & foils, to engineering equipment and inspection systems—all that meet international regulatory requirements. For ACG, it's always about finding innovative solutions to the world's greatest health challenges, together.

ACG's Engineering provides end-to-end pharmaceutical engineering solutions, manufacturing tablet press, capsules filling and packaging machines.

The company also continues to grow its packaging solutions across the global customer base. Customers are able to leverage the synergy across the ACG Engineering business or combination supply arrangements, leveraging both engineering solutions combined with the supply of ACG Capsules and/or Films and Foils. ACG has a unique unmatched consumables and machine supply value proposition—One ACG.

So, how can ACG Engineering help customers to strengthen their processes and drive pharmaceutical innovation while at the same time meet regulatory as well as qual-

ity, anti-counterfeiting, and cost efficiency requirements?

R. Stedman: ACG machines and processing technology are prepared and equipped for the future of pharma. Our focus is centered around optimizing processes and working to reduce downtime.

Regulatory compliance will continue to be a top priority in pharmaceutical machine manufacturing. Stringent regulations governing the production of pharmaceuticals, including tablets and capsules, will drive the development of machines that ensure compliance with good manufacturing practices—GMP—, international standards, and regulatory guidelines. This will involve robust documentation, validation and qualification processes to ensure the safety, efficacy and quality of pharmaceutical products.

Developments in pharmaceutical machines, including automation, advanced sensors and monitoring systems, material handling and feeding systems and improved machine design have resulted in increased efficiency, precision and quality in manufacturing processes. As a result, this has hugely benefitted the pharmaceutical industry and—ultimately—the patients who rely on these medications for their health and wellbeing.

ACG has redesigned and realigned its entire documentation suite to meet international compliance requirements.

We are also changing how we optimize our equipment. For example, we are looking at digital twins during design and maintenance, and how we replicate in order to increase output and the lifetime of the machine.

Digitalization has umpteen of faces; how will digital solutions transform drug formulation and pharmaceutical manufacturing?

R. Stedman: Pharma 4.0, digitization and automation are game changers and will lead to exciting changes and developments in the next generation of machines. We will witness the integration of cutting-edge technologies, such as artificial intelligence—AI—, machine learning—ML—, and the Industrial Internet of Things—IIoT—, into pharmaceutical machines to enhance their efficiency and precision. This will result in increased productivity, reduced downtime and improved quality control, leading to higher yields and cost savings for pharmaceutical manufacturers and lowering the total cost of ownership.

There are also massive amounts of data being created in the industry, and how we use this moving forward is hugely exciting. Utilizing smart connected machines and IIOT helps our customers to combine reality with the digital environment.

ACG Engineering has had success in working with customers partnering in developing systems to monitor stoppages/downtime and improve productivity. ACG has the advantage of developing these digital proof of concept models in its own manufacturing facilities and applying the learnings very successfully to customer solutions.

Sustainability is today's buzz word, and manufacturers constantly look to optimize their equipment's energy and performance efficiency. How can ACG Engineering support them?

R. Stedman: There will be a growing emphasis on sustainability and environmental consciousness over the next decade. Pharmaceutical machine manufacturers will continue to focus on developing eco-friendly machines that minimize waste, reduce energy consumption and comply with stringent environmental regulations. This will involve the use of renewable energy sources, the implementation of green manufacturing practices, and the adoption of recyclable and biodegradable materials across machine components.

Sustainability is a driving force in ACG's initiatives. This includes changes to the raw materials that are being used and how we can reuse, recycle and reduce to create sustainable concepts in the design of the machine for a healthier future.

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ADVERTORIAL

BioLizard: Providing Solutions by Making the Most of Biomedical Data

Many life science companies generate large swathes of data. Perhaps the greatest example of data in biotech is DNA sequencing, but as more companies generate more data, questions — and challenges — arise. How can we deal with increased amounts of data? What can we learn from more data? And how can tools like AI help?

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Liesbeth Ceelen, CEO, BioLizard

According to an IDC white paper published in 2017, by 2025 there will be 163 zettabytes of data. We've become used to megabytes, but now we tend to talk in gigabytes. A phone, for example, may have 512 GB of memory. To put it into perspective, a zettabyte is a trillion gigabytes.

Fortunately, as more data are generated, methods of storing and analysing data have evolved, too. Hardly a day goes by without a news headline related to artificial intelligence (AI). However, for many biotech companies, AI and big data means big questions.

With more and more companies entering the field, knowing where to turn can also be an issue. One company standing out from the crowd is BioLizard, which is headquartered in Ghent, Belgium. It's perhaps an unusual name, but there's a reason. Lizards are agile creatures that can adapt to new environments. And when it comes to partnering with biotech companies to help them navigate data, being agile and adaptable are very useful traits. Indeed, companies differ in what they need, so tailoring solutions based on those requirements isn't just handy, it's essential. This agility is why BioLizard's experts call themselves Lizards.

BioLizard, which has clients in Europe and America, offers services and has experience in bespoke software development, data governance and architecture, and bioinformatics and advanced data analytics including single-cell and multi-omics analytics. The company supports biotech, pharmaceutical and diagnostic companies, and research institutions of all sizes to enable data-driven discovery and preclinical, translational and clinical R&D processes.

Liesbeth Ceelen, CEO of BioLizard, and her colleagues acknowledge how big data, AI and the underlying IT infrastructure can pose major challenges to life sciences companies. While they are well aware that smart integration of AI and maximized use of data are key to staying competitive in the drug and biomarker market, many struggle to acquire the necessary expertise to stay on top of developments in data science.

So, how does BioLizard approach making sense of data, and bringing it all into focus?

Liesbeth Ceelen: Biological data are diverse and come from a huge variety of sources. Often, companies find their data are all over the place, and that interpretation is difficult. It can be a real challenge to realise the full potential of data.

When you work with BioLizard, we go beyond just tweaking an existing approach. We first figure out what's really needed, and then create a plan of action. We are not just a technology provider but more of a partner in innovation, offering personalized solutions and support to accelerate your scientific discovery. Data analysis can be daunting, but we break it down into steps, and we have several teams to help along the way.

Could you give us some examples of how your teams work on a project?

L. Ceelen: First, we understand your challenges and translate your research problem into an IT problem to be solved. Adhering to your system's requirements, we set up a hard- and software blueprint to produce the required output, cost-efficiently and quickly. We break down the project into smaller tasks, and we have expert teams that take care of these. When these individual solutions are put together, these form a complete answer to the client's request.

We work on a wide range of projects, and that involves everything from setting up new systems to interpret and manage data efficiently, such as developing a software application to interpret complex biological data or designing of a new system for *in silico* operations. We also consult on implementing best practices for coding and advise on cloud infrastructure. An example of this would be creating web platforms that manage the processing of wet lab samples.

In summary, we aim to make your data easier to manage, share, analyze, and report on.

Could you go into a little more detail on your teams?

L. Ceelen: Sure. Data management has recently gained increased importance in life sciences. Today, researchers generate 10,000 times more data per experiment than they did a decade ago, but spend 30% to 40% of their time searching for, aggregating, and cleaning data.

Our data and infrastructure management team ensures that all organizational data are findable, accessible, interoperable, and reusable —FAIR. Effective data management is also essential for generating the best and most accurate scientific insights, because it enables a less biased approach for data collection and analysis, and it means that no data will be left behind or forgotten. Reliable data management and data governance structures are necessary to apply advanced analytics tools like AI or ML.

The AI and analytics team works on projects ranging from single cell data analytics and multi-omics, all the way to protein engineering and design.

The core activities of our bioinformatics team are focused on the processing and analysis of sequencing-re-

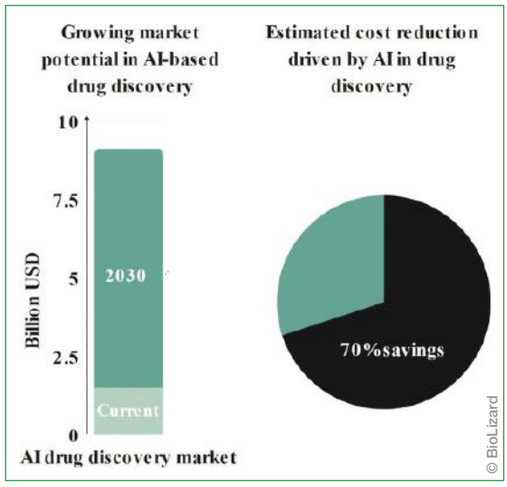
Personal Profile

Liesbeth Ceelen is CEO of BioLizard and has been with the company for more than 4 years. As an experienced leader with a track record in roles ranging from operational, quality, and project management to scientific leadership, sales, and business development, she brings both the scientific background and profound management skills to make BioLizard the go-to bioinformatics consultancy company across Europe and the US.

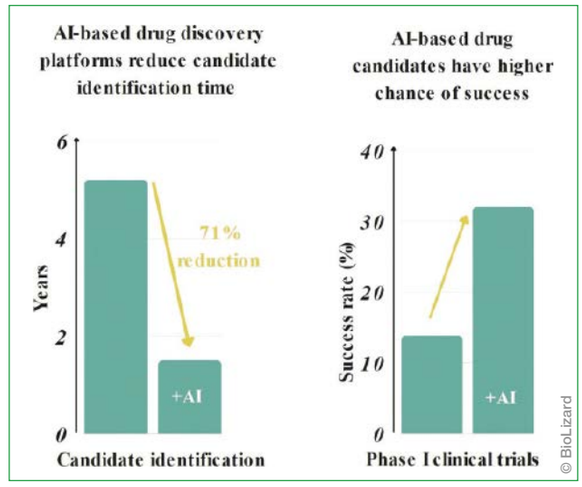
lated data and its visualization. This includes all kinds of omics-related data, from proteomics to whole-genome sequencing. The range of projects includes things such as examining differential protein expression and post-translational modifications; cell type deconvolution; transcriptomics, proteomics, and whole genome sequencing for biomarker and drug discovery.

And then there's the software and IT architecture team. They apply modern software and IT tools to biological projects, in order to improve their efficiency and scalability. Like our other teams, they also function as 'translators' between different stakeholders in life science companies, bridging the gap between IT professionals, biologists and data scientists.

Of course, there is extensive collaboration between the teams to, for example, perform a differential expression analysis on an RNA-sequencing data set, where the client would also like to build a predictive model on the same data and perhaps an interactive dashboard to further explore the data and results.



AI is revolutionizing methods for drug discovery and enables massive cost savings by moving research from in vitro to in silico.[1]



Improved chances for success and time savings by AI-based drug discovery.[2]

Could you tell us about your platform?

L. Ceelen: BioLizard's proprietary platform is an extension of our software development solutions. We have designed this platform to empower clients to turn data into clear, interpretable, and actionable insights. The platform ensures data stay safe and secure in a closed cloud environment, and we provide user-friendly front-end interfaces with easy export of results and reports.

What can BioLizard help with?

L. Ceelen: BioLizard can support you at every step from disease modelling through to drug development.

At the strategic phase of your projects, we use our life science and data science expertise to determine the most efficient and effective course of action to leverage your data and achieve your goals. A solid strategic plan ensures efficient use of resources, realistic expectations, and optimal value generation. We tailor our strategies to align with your specific goals and requirements and make the process of complex data analysis more manageable and outcome-oriented.

We enable consistent and scientifically rigorous interpretation of biomedical data by employing a combination of advanced tools and methods (for example bioinformatics, AI and ML) and user-friendly, interactive interfaces that allow you to deeply engage with your data, to support you in discovery and validation of drugs or biomarkers, extracting insights from existing datasets, and replicating or validating previous publications.

Could you give us an example of this?

L. Ceelen: Yes, on behalf of a client, we have created a software tool for microbiome analysis for modelling causal relationships between microbial community composition or dynamics and their outcomes. This lets us identify modifiable risk factors for the purpose of drug development or find novel biomarkers for microbiome-associated diseases.

For drug discovery & development, we are able to optimize the selection of promising drug candidates to save time in the wet lab. By implementing high throughput *in silico* workflows to screen potential therapies, we enhance the efficiency, quality, and probability of success of drug discovery pipelines — helping to de-risk and speed up the therapeutics development process. For instance, for our client Madam Therapeutics we mined public data for antimicrobial peptide sequences and predicted activity and toxicity to determine suitable drug candidates.

We can also build *in silico* libraries for specific use cases. For example, for another client, we set up a drug candidate library and prepared a tailored graphical software to enable researchers to predict whether candidate compounds could be purified via a protein A column. We also supported Calypso biotech with screening for drug repurposing potential by mining data to screen for target compound activity in various disease contexts, to determine new indications for the clients' proprietary antibody.

What about clinical trials, how can you help there?

L. Ceelen: Well, by combining data on disease pathology and the drug mechanism of action—MoA—, data science can be applied to gain insights into side effects and statistically-effective subject identification and stratification for clinical trials. BioLizard can support you in achieving enhanced understanding of MoAs by integrating multiple layers of data, consolidating in-house data together with publicly available data, and analysing and interpreting complex datasets. Following this approach, we supported a client with AI-based biomarker development to predict clinical outcomes for kidney transplant patients by determining risks for transplant rejection.

As AI seemingly takes over the news headlines, there are many companies emerging to take advantage. So, what sets BioLizard apart?

L. Ceelen: Well, I have to say, we are avantgarde service providers who stay engaged with frontline scientific developments in biology and data science. We bring together almost 50 experts from different scientific fields such as bioengineering, mathematics, computer science and biology. This combined knowledge allows us to truly understand biomedical data challenges as well as software/IT requirements our clients face, and to provide tailor-made solutions suited to their needs. We work in a highly complementary and collaborative manner, meaning that you don't have to look beyond BioLizard to address all of your data needs.

We are trusted by key players in the pharma and biotech industry, and also have robust experience working in the animal health field as well as in supporting food and agriculture R&D. Next to this, we have established partnerships with producers of cutting-edge technologies like Illumina Connected Analytics Implementation, Parean Biotechnologies, and Tercen that recognize and support us as a skilled and competent biomedical data services partner.

Ultimately, it's all about helping clients achieve biologically and clinically relevant, actionable insights that advance their research in a data-driven way.

We also always comply with security and privacy guidelines, and fully explain our data science approach to solving your biological challenges — there's no black box when you work with BioLizard.

Our ability to 'speak the language' of both biology and data science means that we can perfectly fit the needs of our clients every step of the way.

Literature

[1] bit.ly/3ORpDBF; bit.ly/47HVFbV
[2] bit.ly/3YPyWGJ; bit.ly/45IMOom; bit.ly/45nPYy3; bit.ly/3Eb1TDA; bit.ly/3YLsosP

■ https://lizard.bio

Building Quality into Biopharmaceutical Processes

The Impact of GMP Annex 1 Revisions on Sterile Biologics Manufacturing

The biopharmaceutical industry is experiencing a drive towards biologic products due to their promise as treatments for chronic diseases. This is reflected in the biologics market, which was valued at $382 billion in 2022 and is expected to grow rapidly with a compound annual growth rate (CAGR) of 9.1% to reach $893 billion by 2032.

Due to their sensitivity, biologic products can degrade or lose their activity when passing through the harsh conditions of the gastrointestinal system if administered orally. As such, most biologics are formulated to be administered by direct injection into the body. To ensure safety and quality, biologics must therefore be sterile.

Good manufacturing practice (GMP) regulations define product standards through strict regulations, which become even more stringent when dealing with sterile materials. Biologic products must be formed aseptically or terminally sterilized for quality and safety purposes. The GMP guidelines set out strict rules spanning all components of production, from materials and equipment used, to cleaning techniques and validation. Recently, as a result of the advances in technology used for aseptic processing, Annex 1 of the GMP guidelines has been revised, re-evaluating how the biopharma industry approaches sterile manufacture. The modifications brought about by Annex 1 revisions aim to guarantee that product quality is built into the production process while ensuring staff safety through efficient training, risk assessments and procedures.

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Overcoming Quality and Safety Challenges

Biologic manufacturing is complex, comprising several different processes and transfers throughout production. Incorporating sterility into manufacture adds further complication, with additional considerations required to protect the material from potential contamination. The presence of any contaminants in a sample—from environmental particulates to bioburden—poses a significant risk to the recipient. A significant risk occurs when transferring a product between subsequent stages of production, with exposure to the outside environment much more likely. Cross-contamination risk can still be present despite the use of validated cleaning procedures.

Numerous stringent regulatory requirements must be adhered to when producing a drug for human use as defined by the GMP guidelines. These regulations ensure that all products meet the required quality and safety standards, and that manufacturing remains consistent between batches. Revision of GMP guidelines assures that the highest possible standards are maintained, as is the case for the newly modified Annex 1.

Annex 1 Dictates Quality and Safety

Quality risk management (QRM) is embedded throughout Annex 1 to significantly reduce the risk of microbial and particulate contamination in the final product. Enforced from August 2023, changes to Annex 1 demand a manufacturer's pharmaceutical quality system (PQS) to be integrated into production, outlining effective risk management strategy steps—to reduce contamination risks to personnel—as well as equipment and procedure training to build quality into the process.

In addition, a contamination control strategy (CCS) must be introduced for every sterile processing line. This living document should be continuously revised to identify any potential vulnerabilities throughout manufacture where containment breaches may occur. The risk will then be minimized through the introduction of preventative measures.

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Revision of Annex 1 aims to decrease microbial and particulate contamination risks within a batch. Single-use technology (SUT) is one strategy to reduce exposure and contamination risks. Although associated risks to integrity of products such as extractables and leachables must be addressed as part of the CCS, using SUT can be an effective way of instilling sterility.

Leveraging SUT for Quality and Safety

With the largest risk to sterility in aseptic processing occurring during product transfer between processing lines or equipment, the biopharmaceutical industry is harnessing SUT such as split butterfly valves (SBVs) and chargebags. SUT forms a barrier between the product and the outside environment and can be used to store, transfer and handle products without exposure, significantly reducing the risk of contamination.

SBVs are used to seamlessly transfer powdered materials throughout the production line. Resulting in a closed filling line, SBVs significantly reduce the risk of exposure during product transfer. When they are harnessed in combination with chargebags, the product can be stored or packaged in the container until it is needed for subsequent processing steps.

These SUTs can be integrated into current operations and help manufacturers meet the sterility requirements defined by Annex 1, significantly minimizing exposure and contamination risks to meet safety regulations. Quality assurance is also built into the process, removing the need for cleaning methods or validation when using SUTs. Each piece is replaced after use, which significantly reduces the risk

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of cross-contamination or bioburden within a drug compound.

As demand for biologics continues to increase, changes in manufacturing capacity will follow. Traditionally used for small batch manufacturing, SUT will continue to evolve, increasing its ability to handle larger drug product capacities. Customer-driven innovation in the SUT space is transforming the sector. By harnessing SUTs' flexibility, tailored solutions can be formed, meeting the needs of the customer and addressing changing demands in the biopharmaceutical industry.

Biomanufacturing Needs Quality by Design

Manufacturing drug products that meet defined safety and quality standards is essential. As the industry adapts to the revised GMP Annex 1, a quality-by-design methodology for sterile products is being built into aseptic processing.

To further mitigate contamination and exposure risks, the industry is moving towards SUT. These flexible systems protect drug products from the outside environment, allowing for effective product storage and transfer between processing lines, and integrating sterility into manufacture.

A specialist supplier that has expertise in providing high-performance SUTs can aid in navigating the changing regulatory landscape, tailoring single-use systems to meet manufacturing and customer needs.

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References to this article can be requested from the authors.

ADVERTORIAL

Innovation is Key

How CDMOs Can Contribute to Pharma Supply even Better

The demand for medicines is increasing rapidly and R&D pipelines have doubled over the last decade. According to current market analyses, global spending on pharmaceuticals is expected to reach around $1,742 billion in 2025, while spending on Covid-19 vaccines and therapeutics could reach around 53 billion US dollars worldwide in the same year.

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End-to-end development services at Aenova

Two main trends can currently be identified in the pharmaceutical market: innovative drugs, which offer significant therapeutic benefits, are strongly on the rise, and the oral solid dosage form will continue to be the preferred dosage form on the global market.

Challenges in Overcoming Poor Bioavailability

On the one hand, innovative active pharmaceutical ingredients are designed to be highly specific to their biomedical targets, which enables therapeutic breakthrough and lowered side effects. On the other hand, these substances have specific challenges, especially when formulation as oral solid dosage form is targeted. Such challenges are poor solubility and oral bioavailability, as well as the highly potent nature of active ingredients (up to OEB 5).

Consequently, to meet the global demand for these drugs, contract developers and manufacturers must be able to offer their pharmaceutical customers innovative technologies to provide patients worldwide with the urgently needed medicines. This applies not only to commercial manufacturing, but already to formulation development to better meet market challenges. As a result, developers and manufacturers must use innovative technologies and offer solutions for handling highly potent active ingredients.

An example from the field of oncology can demonstrate this more clearly.

Specific Requirements for High-potent Active Pharmaceutical Ingredients

Oncology and immunomodulating therapy have become increasingly important in the past decade, as innovation in drug research allowed to develop more and more target specific substances. These active substances exhibit an improved risk-benefit profile. Consequently, high potent active pharmaceutical ingredients (HPAPIs) are on the rise and will play an important role in drug therapy in the future.

Market demand for cancer therapies in particular is growing rapidly. At the same time, the targeted patient group is becoming smaller, as are the SKUs (Stock Keeping Units) produced. However, the development and production of drugs with highly potent active pharmaceutical ingredients in the field of oncology is highly complex and often must be achieved under time pressure, as many of these new molecular entities (NMEs) are approved as "breakthrough therapy" in a fast-track process to quickly meet the high medical demand.

This makes it more important to have a competent CDMO partner who can facilitate a rapid time-to-market from development to commercial production. This includes not only innovative development know-how or experts for technical transfers, but also the right equipment for development scale-up and later high-volume production. It also requires the right concepts for handling highly potent active ingredients. These should be holistic and comprise production, processes and people as offered by Aenova at its Münster and Regensburg sites.

If development and manufacturing are then provided by the same CDMO partner, customers benefit from smooth and seamless transitions from development to production. This makes it much easier to bring new products to market quickly: in a short timeline, with low risk and cost efficiency.

Commercial manufacturing of high-potent medicines

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About Aenova Group

The Aenova Group is a leading global contract manufacturer and development service provider for the pharmaceutical and healthcare industry. As a one-stop store, Aenova develops, produces and packages all common dosage forms, product groups and active ingredient classes from pharmaceuticals to dietary supplements for human and animal health: solid, semi-solid and liquid, sterile and non-sterile, high and low dose, OEB 1 to 5 (Occupational Exposure Band). Approximately 4,000 employees at 14 sites in Europe and the U.S. contribute to the company's success. **www.aenova-group.com**

CHEManager INTERNATIONAL

INNOVATION PITCH

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Advanced Materials
Graphene-Based Additives for Coatings, Plastics and Composites

Renewable Materials
Plastics Alternative Derived from Natural Biopolymers

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Graphene for Sustainable Development

Reducing the Environmental Impact of Coatings, Plastics, and Composites

The French start-up Carbon Waters, based in Pessac near Bordeaux, specializes in the development and production of high-performance advanced materials. Founded in 2017, the company offers a line of ready-to-use, graphene-based additives for the industry. At the heart of Carbon Waters' breakthrough innovation is its unique dispersed graphene production process, for which the company already holds six family patents. Alban Chesneau, co-founder and CEO of Carbon Waters and Nicolas Castet, COO, share insights on the company's technology and its future development plans.

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Alban Chesneau, CEO, Carbon Waters

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Nicolas Castet, COO, Carbon Waters

CHEManager: How did Carbon Waters come to be founded — and what does the company's name mean?

Alban Chesneau: Carbon Waters was created in 2017 following a meeting between a technology transfer expert in the chemical sciences, an industrial investor and two researchers from CNRS — the French National Centre for Scientific Research. The project emerged from 15 years of research on carbon nanomaterials at the CNRS, and then at Carbon Waters. Initial work focused on the first method of producing a carbon nanomaterial, graphene, of very high quality directly in "ready-to-use" and stable liquid form in water, hence the name Carbon Waters.

What is unique about your graphene production process and the product lines you offer?

Nicolas Castet: We have developed a patented and scalable technology to produce high quality graphene, a nanomaterial with multiple properties — the lightest, the strongest, the most impermeable material with excellent thermal and electrical conductivity performance — that will contribute to the environmental and energy transition of the industries.

Carbon Waters' graphene is produced in liquid dispersion — not in powder as usually available — for a safer and optimized utilization. Our graphene-based additives are pre-formulated and ready-to-use by industrials for better efficiency and competitivity.

In which major development areas are you currently active?

N. Castet: After five years of intensive R&D to develop technologies and products, we are in the process of transforming the company into an industrial player. The first production unit will be ready in 2024, while the commercialization of our graphene-based additives for coatings, composites and adhesives begins.

A. Chesneau: In parallel, we are completing our product portfolio by developing new additives for hydrogen storage and batteries applications. On the first topic, we have started multiple technical and industrial collaborations with chemical companies as end-users on graphene-enhanced epoxy and thermoplastics to enhance mechanical, thermal and barrier properties. On the second topic, we are developing new formulations with top academic laboratories to enhance energy density, charging time and fire protection of Li-Ion batteries.

What have been the most exciting projects so far?

N. Castet: Managing an industrial start-up is exciting in many ways! Specifically, receiving positive feedback from customers on new products that took several years of R&D to develop is one of the greatest satisfactions. We just had the case with our new additive for higher thermal stability of epoxy-based materials in composites and adhesives, which was very positively received by the market

Carbon Waters has been recognized as a decarbonization start-up in the materials category. What is the reason for this achievement?

A. Chesneau: Decarbonization is what drives us since the foundation of the company. The products will contribute to the decarbonization of the industry by substituting toxic additives in coatings (anticorrosion), by lowering the weight of transports' structure (thermal and mechanical reinforced polymers) and by improving lifespan and performance of batteries and fuel cells.

What's more, our production process is designed to minimize the environmental footprint. Finally, we are strongly involved in the circular economy as we are testing new raw materials from the production with green hydrogen as well as graphite from old battery electrodes for the production of our additives.

What will be the next key steps in the development of the company?

N. Castet: As mentioned earlier, we are taking the company to the industrial scale, with a first production unit that will start up in 2024. Our goal is to increase production capacity more than tenfold to meet customer demand and be cost competitive.

Then, we are working on our commercial development, with orders and contracts that will be signed in the coming months for the first products of our portfolio. These include anticorrosion additives for waterborne and solvent-based coatings — either to boost anticorrosion performance or to substitute existing toxic products — and thermal stability additives, to improve glass transition temperature of epoxy-based material in composites & adhesives.

Personal Profiles

Alban Chesneau, co-founder and CEO of Carbon Waters, holds a PhD in Biochemistry and a master's degree in business administration. He is a specialist in technology marketing and strategy with experience accompanying highly innovative businesses. He worked for seven years in innovation and R&D consulting for the chemical and life sciences industries. After meeting two CNRS researchers in 2015, Alban decided to launch Carbon Waters.

Nicolas Castet, COO of Carbon Waters, graduated in economics & finance at the Université of Bordeaux Montesquieu. He joined Carbon Waters in May 2022 after more than 20 years of experience in the chemical industries at multinationals such as Rhodia, Solvay, and Cerdia. He combines commercial & financial expertise in industrial and international environment.

Business Idea

Nanoscale Precision for Macroscale Impacts

The industry is changing, it requires new materials to address environmental & energy transitions by replacing toxic products, increasing lifespan of products and reducing environmental footprint.

Advanced materials are key to tackle these challenges, especially graphene that will play a major role thanks to multiple immense properties (the lightest, the strongest, the most impermeable, the best electrical and thermal conductive material). Carbon Waters has developed a unique technology to produce high quality graphene in a sustainable and scalable way, to offer ready-to-use products to support the on-going transitions in the industry.

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Carbon Waters
ENDLESS HORIZON OF MATERIALS

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Carbon Waters has developed a unique technology to produce high quality graphene in a sustainable and scalable way.

Elevator Pitch

Using Carbon to Decarbonize

Global industry is facing major challenges in terms of environmental transition, raw materials supply and REACh-type regulations. The use of disruptive innovations is essential to meet these multiple challenges.

This is the context in which Carbon Waters is positioning itself with the implementation of a very high value-added material, graphene, which they are pioneering as a turnkey solution for a wide range of industrial sectors.

Founded in 2017, Carbon Waters produces the next generation of ready-to-use graphene-based performance additives. The process makes it possible to exploit organic materials in a completely new way for use in cutting-edge industry, while reconciling biosourcing and recyclability.

Their team of 16 people works hand in hand with customers of all sizes from all around the world to meet their strategic challenges. The company has demonstrated the major impact of their products on the on-going environmental and energy transition.

Carbon Waters is now entering the industrialization phase, to meet growing commercial demand and plan to significantly increase production in the coming months/years.

Milestones

2008 – 2014
- Several patents filed on an innovative process for producing graphene-based nanomaterials

2015 – 2017
- project maturation phase
- Carbon Waters start-up founded at the end of 2017

2018
- first funds raised

2019
- Carbon Waters moves in a high-tech research center at the heart of the University of Bordeaux

2020
- Launch of a design office and development of the first prototypes

2022
- further fund-raising to build a pre-industrial site

Roadmap

2024
- First production unit to achieve a 3 tons capacity of additives (used at 0,1%)
- Customer qualification of water-borne and solventborne coating additives and first sales
- Launch of additive for Li-Ion cathodes enhancement project

2025
- Increase to 15 tons production capacity
- Customer qualification of thermosets additives

2026
- Increase to 50 tons production capacity
- International development
- Customer qualification of battery additives

© Carbon Waters

Graph'Up, Carbon Waters' graphene-based performance additives range.

Unlocking a Circular Future with Natural Polymers

Traceless, a Game-Changing Biomaterial

In this interview, Christene Smith from CHEManager talked with Anne Lamp, the CEO & Co-Founder of Traceless Materials, to delve into the groundbreaking world of natural biopolymer materials. Developed as a natural, plant-based plastic alternative, the Traceless material aims to tackle the environmental impact of plastics head-on. Join us as we explore the challenges faced in making industrial production fit for the future and uncover the potential of this pioneering biobased company.

> *"Although we are still in the scale-up phase and full market entry is still ahead of us, the reception of Traceless in the market has been overwhelmingly positive."*

© Traceless Materials

Anne Lamp, CEO & Co-Founder, Traceless Materials

Personal Profile

Anne Lamp is CEO and co-founder of the bioeconomy startup Traceless Materials from Hamburg. Holding a PhD in process engineering, she is the inventor of Traceless' technology. Describing herself as an environmental scientist by conviction and a tech enthusiast at heart, she is guided by circular economy principles from her voluntary work at the Cradle to Cradle NGO. Her work benefits from her extensive experience in biorefinery processes, commercial product development and her scientific expertise in environmental impact assessments.

CHEManager: What inspired you to start Traceless Materials, and what was the initial problem you aimed to address?

Anne Lamp: The inspiration behind the development of Traceless came from witnessing the alarming environmental impact of conventional plastics. Already during my studies as a process engineer, I was involved with the concept of circular economy, and volunteered with the "Cradle to Cradle" NGO. My initial goal was to create a material that is truly biocircular, one that is 100% plant-based, naturally compostable, and free of harmful substances. I aimed to provide a solution to the growing plastic waste problem and contribute to a cleaner, greener future.

Can you share a bit about your journey from the early experiments to the founding of the company?

A. Lamp: The idea for the technology arose during my PhD in process engineering in the field of biorefinery, which was focused on the valorization of biomass side streams. I discovered that residues of agricultural grain processing, like brewery or starch production side streams (which occur globally in high volumes), can be used to produce a plastic-like material. The first samples of Traceless materials were born. With a vision to bring this idea to scale, I filed a patent and founded the company together with my co-founder. We established a pilot plant, refined the production process, and started the development of product applications.

What were the key challenges you faced during the development of Traceless and the establishment of the company?

A. Lamp: Developing a new material and establishing a company around a novel technology came with several challenges. Scaling up the technology from lab scale to pilot scale and achieving price competitiveness with conventional plastics are significant hurdles. We are working relentlessly to optimize the production process and material properties, optimizing our materials for a wide range of processing technologies and product applications. Securing funding and building partnerships were also crucial steps.

How has Traceless been received in the market so far?

A. Lamp: Although we are still in the scale-up phase and full market entry is still ahead of us, the reception of Traceless in the market has been overwhelmingly positive. Collaborations with pioneering brand owners like Otto, Lufthansa and C&A allow us to showcase the potential of our product through pilot projects. We successfully launched our first in-store market pilot product with fashion retailer C&A: together, we developed an injection-molded hook made of Traceless material. Besides the brand owners, the interest from partners from the plastic converting industry has also been remarkable, and we are actively exploring partnerships to expand the applications of our material further.

Where do you see application potential for your material—can it replace all plastics?

A. Lamp: The plastics industry has played a crucial role in advancing high-performance applications for decades, and we recognize its continued significance in those areas. To now make these products truly circular, we must establish reuse, ecodesign, and closed material loops. For applications where reusable solutions are not sustainable and technical recycling is not feasible, we see biomaterials like Traceless offering a compelling alternative. We specifically focus on single-use packaging and products with low to medium requirements, as well as "hidden" plastics in adhesives and paper coatings, which can easily end up in the environment.

What are the next steps for your company? Are there any upcoming plans for scaling production or exploring new applications for the material?

A. Lamp: Our ambitious goal is to produce one million tons of Traceless material by 2030. To achieve this, we will first build a large-scale demonstration production plant with an output of several thousand tons of material per year, taking us one step closer to industrial-scale production. Recently, we received a €5 million grant for this step from the German Federal Ministry for the Environment. And of course, we're growing our team! Many passionate experts from process engineering, chemistry, plastics engineering, environmental and material sciences have joined our team already, and we're constantly looking for more talented people.

Business Idea

Biomaterial Revolution

Traceless Materials leads a biomaterial revolution with their material, a groundbreaking innovation. The female-founded circular bioeconomy startup envisions a future free of pollution and waste, where the materials we use impact positively on the planet. Their core idea centers around providing a natural and biocircular alternative to conventional plastics.

At the heart of Traceless lies a mission to combat global plastic pollution. By utilizing plant residues from the agricultural industry, the company has created a fully biobased thermoplastic granulate based on natural biopolymers. This material closely resembles plastics in appearance and functionality but is certified as plastic-free. The company produces their material in the form of pellets that can be further processed using many standard technologies of plastic processing like injection moulding, film extrusion or paper coating technologies.

Driven by a commitment to decarbonization and transitioning from fossil-based to renewable materials, Traceless achieves an outstanding ecological footprint. Carbon emissions are reduced by 91% and fossil energy demand by 89% compared to the production and disposal of virgin plastics. The patent-pending process is scalable, efficient, and environmentally friendly, positioning Traceless as a competitive alternative to plastics. While recognizing the indispensability of plastics in high-performance applications, Traceless Materials understands the urgency to address single-use products and applications with limited recycling potential. With Traceless, they offer a compostable and natural solution, ideal for applications like single-use packaging and products, paper coatings and adhesives.

The pioneering journey the team embarked on a few years ago, is founded on cooperation and collaboration. By bridging the gap between the agricultural industry and plastic processing, the company fosters a business model where multiple stakeholders' benefit.

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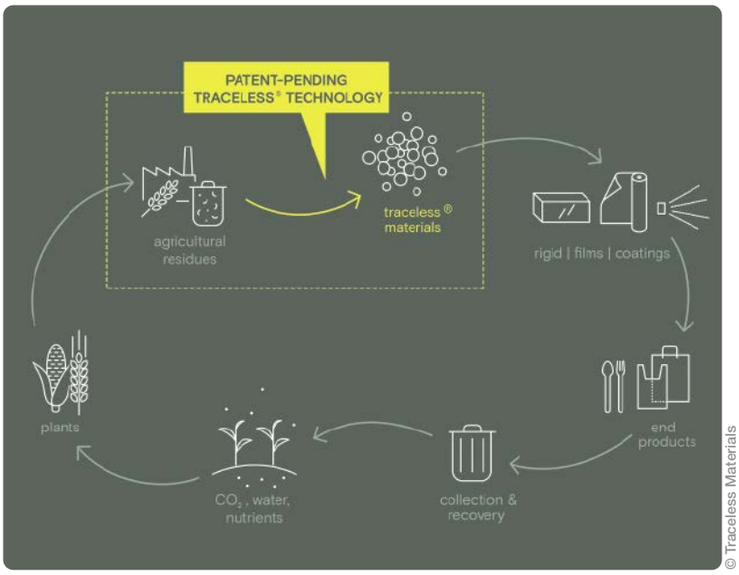

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Traceless provides a natural and biocircular alternative to conventional plastics.

Elevator Pitch

Plastic Solution

The circular bioeconomy startup has developed the technology to turn agricultural industry residues into a novel, sustainable plastic alternative: Traceless material. Founded in 2020, the team plans to bring its innovation to market as quickly as possible. Collaborating with brand owners and converters on product applications, they launched a first market pilot in 2022.

With the aim of replacing plastics in large quantities soon, the company is scaling its technology from pilot scale to an initial large-scale implementation, which is planned for 2024. The continuously growing, interdisciplinary team consists of experts from various fields with a focus on technology and product development and is united by a strong mission: To offer a solution that tackles global plastic pollution as well as climate change, resource crisis and biodiversity loss, and be a change enabler for the green transformation of the industry.

Milestones

2019
- Technology development breakthrough at laboratory scale, at Technical University Hamburg

2020
- Foundation of Traceless Materials in Hamburg, Germany, by Anne Lamp & Johanna Baare, with a first voluntary team
- Winner of Advanced Materials Competition (AdMaCom) by INAM

2021
- Seed Investment closing with impact investor Planet A, High-Tech Gründerfonds and Biotechnology VC b.value
- Grant funding of 150k€ by IFB Hamburg
- Grant funding of €2.42 million from the European Innovation Council (EIC) under the Horizon Europe program
- Winner of Biopolymer Innovation Award, Science Breakthrough of the Year at Falling Walls Ventures, Top 50 German Startup Ranking Nr.1

2022
- Successful commissioning of Pilot plant near Hamburg, Germany
- Official announcement of cooporations with Sund, Das Futterhaus & Gala
- Launch of first in-store pilot product made of our material (fashion packaging/injection moulded hook) in collaboration with fashion retailer C&A (see below)
- Winner of German Founders Award, Next Economy Award (Deutscher Nachhaltigkeitspreis), German Startup Award (Female Newcomer of the Year for Johanna Baare) & Wissenschaftspreis

2023
- Grant funding of €5 million from the German Federal Ministry for the Environment (BMUV) for the demonstration plant
- Winner of Innovation Award Renewable Material of the Year 2023, Nomination for The Sustainability Awards by Packaging Europe
- Traceless featured in German Science-TV show Galileo

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Traceless provides a natural and biocircular alternative to conventional plastics.

Transforming Uncertainties into Opportunities

Exploring Megatrends and Value Chain Complexity in the Surfactant Markets

In the dynamic realm of the chemical industry, surfactants serve as indispensable components with versatile applications, particularly in the home and personal care sector. Companies are increasingly seeking innovative and sustainable solutions as the sector navigates the complexities of the value chain and responds to prevailing megatrends. With a legacy spanning almost 95 years, CEPSA has emerged as a global player in the energy and chemical sectors. Formerly known as Compañía Española de Petróleos, the chemicals branch of the company is now moving towards a more sustainable chemistry, not by ignoring its fossil-based roots but by adding raw materials of renewable and circular origin. Christene Smith sat down with Juliana Pantalena, Global Marketing Head for Surfactants at CEPSA Chemicals, to discuss the impact of megatrends and value chain challenges on the business and the company's sustainable product developments.

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Juliana Pantalena, Global Marketing Head for Surfactants, CEPSA Chemicals

CHEManager: What are the current megatrends in the surfactants industry, and how do they impact the global market?

Juliana Pantalena: Within the Home Care segment, manufacturers are seeking new formulations and more sustainable, effective, and suitable products. In Personal Care, consumers are changing behavior towards a more conscious consumption regarding environmental, ethical, and social impact. Various trends are driving the market:

- **Regional growth**: emerging countries, increasing population, income development, urbanization, and consumers´ rising sophistication are the main levers of this trend.
- **Convenience**: multipurpose detergents and changes in cleaning technology—fast wash cycles, autodosis washing machines, etc.—are factors shaping consumption.
- **Compact formats**: active reductions for the same performance at a smaller dose benefiting the environment due to the reduced CO_2 footprint, reduction of inner space, and saving in transport costs.
- **Hygiene**: increased hygiene concerns as consumers look to maintain a safe environment.
- **Regulatory trends**: regulatory agencies are reviewing and defining new parameters on the products that are used for home and personal care formulations.
- **Sustainability**: from raw materials to finished products, manufacturing, packaging, transportation, and usage by the final clients. The sustainability trend focuses on reducing packaging to reduce the amount of plastic and sustainable ingredients – plant-based products—targeting CO_2 reduction emissions to the atmosphere.
- **X-free**: informed consumers are forcing brands to use alternative ingredients to produce "chemical-free" products—sulfate-free, gluten-free, cruelty-free.

How does CEPSA stay ahead of evolving consumer preferences and requirements to deliver surfactant solutions that meet industry needs?

J. Pantalena: In the surfactant business, we are committed to research, development, and innovation to guarantee the sustainability of our industry and the quality of our products and providing technical services.

More than 175 detergent formulations were evaluated to improve the detergent's compaction and performance, and more than 500 assays were done and 3.000 hours per year were invested in adapting our products to the challenges of today´s detergent formulations. Our research center is equipped with the newest technologies, including analytical support and pilot plants, and is based on four main pillars. 1) Characterization and quality control to ensure full support to the technical and formulation requirements of the sector. 2) Evaluation and performance of surfactant´s properties and new products—foam, soil removal, rheology profiles, stability, etc.. 3) Technological radar to explore alternatives to offer more sustainable and innovative products, improving their performance and sustainability. 4) Customer support to develop and improve different types of home and personal care formulations.

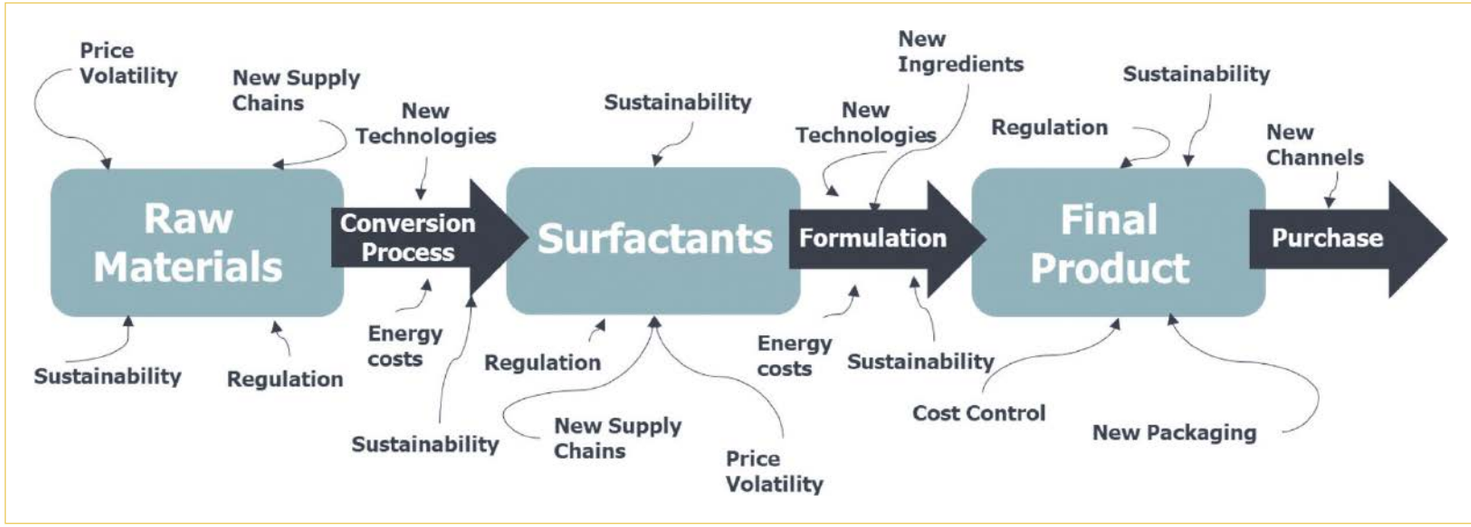

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Fig. 1: The surfactants value chain

How is the surfactants value chain evolving, and what specific complexities do you address in this regard?

J. Pantalena: The surfactants value chain is complex and affected by many trends and challenges. At CEPSA Chemicals, we are trying to transform all these uncertainties into opportunities. This is only possible by leading from the front. As market leaders in the linear alkylbenzene—LAB—business, we are actively partnering with customers and industry to shape the direction of the sustainability dialog within its core business segments.

We are involved in all steps of the value chain, from the definition and selection of raw materials to the surfactant production and understanding and support on the development of final formulations with our customers to the end user consumers. I believe that the surfactants industry is the link between nature and its offerings, by using sustainable chemistry, following all guidelines, bringing innovation, and meeting customers' demands to help create better products. That is not an easy task, there are many key impacts that the surfactant industry needs to be aware of and comply with. (Editor's note: cf. figure 1).

You mentioned the LAB business. How does this new sustainable linear alkylbenzene fit into CEPSA's sustainability roadmap?

J. Pantalena: LAB is an essential ingredient in the manufacture of biodegradable detergents. Now, with NextLab, we seek to maintain our leadership position in sustainable LAB. We are co-owners of the best manufacturing technology available on the market and are leaders in its industrial implementation with our Detal project at the Puente Mayorga chemical plant. We have completed the transformation of our chemical plant, which allows us to increase LAB production with a safer, more efficient, and sustainable process. NextLab will lead the industry's transformation and help customers achieve their sustainability goals and produce detergents with a reduced carbon footprint and based on alternative raw materials while keeping the exact specifications and performance.

How do you ensure regulatory compliance while maintaining product quality and competitiveness?

J. Pantalena: Our environmental management system allows us to progress in complying with applicable legislation and our environmental policies to transparently reduce the impact of our activities, aligning ourselves with our stakeholders' expectations. Collaborations are vital for adapting to this new regulatory environment. Thus, we work closely with clients, competitors, and associations like CESIO, CLER, etc.

CEPSA Chemicals's NextLab R product complies with the certification system ISCC PLUS. that covers all agricultural and forestry raw materials, waste and residues, non-bio renewables, and recycled carbon materials and fuels.

Recently we also obtained The Roundtable on Sustainable Palm Oil (RSPO) certificate. Technological innovation allows us to maintain product quality and competitiveness while ensuring regulatory compliance.

How do you assess the EU Green Deal and the EU's Chemicals Strategy for Sustainability? Do these programs set the right goals and sketch realistic pathways to reach them?

J. Pantalena: In CEPSA we are implementing a sustainability strategy for decarbonization and defossilization of our portfolio that aligns with the goal of EU´s Green Deal. Our approach comprises the entire supply chain, from sustainable sourcing to production processes. We prioritize the development and adoption of safer technologies while promoting the principles of the circular economy to minimize waste generation and resource consumption. The recent retrofitting of our factory at San Roque, Spain, from HF to Detal technology and the production of NextLab are proof of our commitment. Furthermore, our company is fully committed to carbon neutrality and has set ambitious targets to reduce the carbon footprint associated to our activities and products.

While we recognize the challenges ahead, our stakeholders share our vision and support our plan to not only drive positive environmental impact but also provide a more resilient and competitive future for our company and the industry as a whole.

With respect to the Chemical Strategy for Sustainability, the pathway must follow science-based methodologies and avoid overregulation.

How do you incorporate sustainability principles into surfactants production and value chain? With the rising demand for biobased and natural surfactants, how is CEPSA developing sustainable alternatives?

© CEPSA Chemicals

J. Pantalena: CEPSA is following the path set by the UN. Thus, we are committed to the sustainable development goals—SDGs. Regarding our product offering, we have a well-balanced portfolio of surfactants, such as SLES, SLS, and AE, and LAB/LABSA as intermediates to produce LAS. Now we are transforming the LAB business with our Next-Lab family of products, It has the same properties and outstanding performance as traditional linear alkylbenzene—excellent washing performance, flexibility, processability, and good compatibility with other ingredients—while having a reduced carbon footprint compared to its counterpart.

You said that collaborations are vital. Could you give an example?

J. Pantalena: Sinarmas CEPSA is such an example. It is a joint venture between CEPSA Chemicals and Golden Agri Resources—GAR. GAR offers an extensive portfolio of fatty acids, fatty alcohols, glycerin, and soap needles manufactured using stringent quality control processes. A global leader in palm oil production, GAR is producing more than 2.4 million tons of crude palm oil annually. It manages about 538,000 hectares of plantations, including smallholder farms across Indonesia and achieved 98% traceability to plantation of its palm supply chain at the end of 2022. As a result, Sinarmas CEPSA can offer a uniquely integrated business model in the oleochemical industry, which integrates activities "from tree to customer" with best industry practices and the most stringent sustainability policies.

Looking to the future, what opportunities and challenges do you foresee for the surfactants industry, and how are you preparing to capitalize on them while addressing associated challenges?

J. Pantalena: We are driving the shift towards sustainable chemistry. We are committed to climate change and support the transition to a circular economy that optimizes the use of resources to build a more sustainable, efficient, and fair world dedicated to supporting customers, partners, and associations.

CEPSA is working to stay ahead of industry challenges and consumer social and environmental awareness. Soapers are launching new plant-based products with alternative ingredients. Furthermore, alternative packaging with a reduced amount of plastic is being released by many companies, especially in developed regions. Convenience and sustainability are driving a shift in product formats with more concentrated formulas.

In terms of opportunities, a growing population in developing markets will help to increase the demand. The growth of the middle-class, hygiene consciousness, urbanization, and washing machine possession rates will also contribute to higher demand. CEPSA Chemicals is preparing to capitalize on them by focusing on innovation and sustainability. We have undertaken several innovation projects to develop new products, identifying biobased alternatives to fossil-based products and seeking more sustainable schemes.

■ www.chemicals.cepsa.com

Biosurfactants at Scale

Growth Success, Collaboration and the Future of Eco-friendly Surfactants

In response to the urgent need for sustainable solutions in the surfactants industry, companies like Locus Ingredients are developing environmentally friendly biosurfactants. The company is committed to revolutionizing the market by replacing traditional surfactants with sustainable alternatives. With a focus on superior performance and reduced environmental impact, it is driving the transformation towards a more eco-friendly future in the surfactants industry. And they are achieving success at a rapid rate. Christene Smith sat down with CEO Tim Staub to discuss their scale-up success, the importance of strong collaboration, and the focus on sustainability in the surfactants industry.

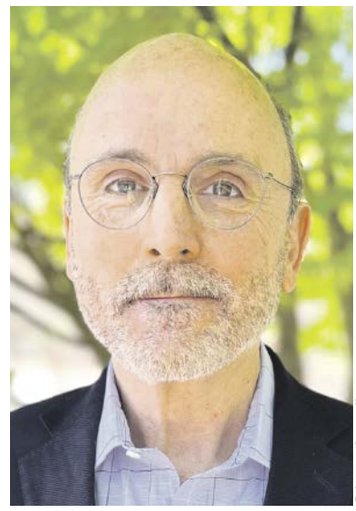
CHEManager: Your company has grown rapidly since its establishment in 2020. Can you tell us more about the factors that contributed to your successful scale-up and market penetration in such a short period of time?

Tim Staub: There are three key success factors:

- The first one is demand. The downstream markets that depend on innovation from the surfactants industry are hungry for new technologies that offer performance benefits while solving many pressing sustainability issues. Our biosurfactants are unique in that they are multifunctional and 100% bio-based with a low carbon footprint. The biosurfactants minimize skin irritation that may occur with traditional surfactants. They offer superior cleansing, degreasing and detergency. They can also be formulated easily as a co-surfactant with other bio-based surfactants such as APG's and amino-surfactants. They're great surfactants, with or without the 'bio.'
- The second factor is scalability. Fermentation-produced biosurfactants are not new. Glycolipids, and specifically sophorolipids, have been studied for decades. But they've been difficult to produce economically at any scale that makes sense.

Our ability to scale rapidly and cost-effectively in our patented modular fermentation platform has been important to our ability to move quickly for our customers and partners. We invested early and aggressively to build and scale our manufacturing capabilities to drive economies of scale. That has proven to be prescient.

- The third factor is our scientific expertise. We have world-class laboratories in both Solon, Ohio and in Richmond, Virginia. The work done by these highly skilled scientific teams has driven our ability to understand how our biosurfactants work, where they work and how they can be formulated to create a competitive advantage for our customers and partners.



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Tim Staub, CEO, Locus Ingredients

Collaboration appears to be a central driver of your success. How have partnerships and collaborations played a role in the growth and development of your business?

T. Staub: Our strategy is to drive market penetration and scale through collaborations. Your assessment is spot on—it is a central driver of our success. Our focus is to innovate, validate and collaborate throughout our commercialization process:

- **Innovate:** We innovate on our technology, how to produce it economically, how to build capacity cost effectively, how to build competitive advantage for our customers and partners, how to deliver that value, and how to protect that value in our intellectual property strategies.
- **Validate**: We validate by coming to the market directly to demonstrate our value proposition, and to understand the fundamental market drivers, including pricing, that drive our value proposition. Often, in the validation step, we recognize opportunities to refine the innovation step in a circular manner.
- **Collaborate**: While we are in the validation phase, we're assessing and talking to potential partners, and when the time is right, we select the best partner to move rapidly forward in a collaboration—resulting in demand volumes that drive the economies of scale necessary to grow a global surfactant business. Recent examples include our global distribution agreement with Dow to sell our biosurfactants in the personal care and home care markets; and our partnership with Veolia Water Technologies to develop new sustainable water and process treatment additives.

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Could you share some insights from your personal experience in the industry that have influenced your approach to sustainable biosurfactants and the overall vision of the company?

T. Staub: The biosurfactants business is both rewarding and challenging, but in many ways it's no different than any other surfactant or specialty chemical business. Locus Ingredients is driven by innovation, teamwork, relationships, competencies, and core values like integrity and trust. We're driven by customers, markets and applications. We're driven to create competitive advantages for our company, for our partners, and for our customers—but not necessarily in that order. It's important to remember that it's never about us. We exist only if we are creating value for our customers and partners. So, we focus our energy on understanding market and customer needs and aligning our team(s) to create an advantage—for us, but more importantly for the users of our biosurfactant ingredients.

The surfactant industry is experiencing a shift towards more sustainable products. In your opinion, what are the main drivers behind this trend, and how is Locus Ingredients positioned to capitalize on this market demand?

T. Staub: There are several drivers but ultimately, they culminate in the reality that climate change is real, and humanity is in a race to reduce environmental impact—minimize carbon, along with nitrous oxide and methane emissions. Consumers also want less hazardous chemicals in their products, less skin irritation, and less residual risk from compounds like 1,4-dioxane. Consumers care about deforestation and human rights, and they're reading labels to look for ingredients like palm oil. Investors are demanding change. Governments are demanding change. Boards are demanding change. All of this is rooted in the recognition of the negative impacts that chemical ingredients have on climate change, and the need for alternatives that are safer for both people and the planet.

We are well positioned to meet this market demand based on multiple key factors:

- **Company-wide decarbonization and biological focus**: The main mission of Locus Ingredients, our parent company (Locus Fermentation Solutions) and our sister business units is to develop high-performing biologicals as chemical alternatives that decarbonize the industries we serve—in agriculture, in energy, in water, in consumer products, in mining and in a myriad of other industries. We are a low carbon, non-GMO microbial discovery company. We have the scientific expertise, financing and production processes needed to make a global impact.
- **Proprietary fermentation with rapid scalability**: We have a core capability to rapidly build and scale fermentation production—anywhere in the world with access to water and electricity—in six to twelve months. We have some of the highest-performing and most sustainable biosurfactant solutions with rapid scalability to meet global demand. The process and applications are backed by thousands of patent filings. And our biosurfactant production facilities were just expanded by 100,000 square feet—with total future capacity to produce 2.5 million kilograms of biosurfactants annually.
- **Strategic collaborations**: We want to partner with the companies that are committed to the mission of a low-carbon future. These collaborations help accelerate commercialization and global availability of our sustainable biosurfactants.

The use of biosurfactants and bio-based surfactants is gaining attention in various industries. How would you describe the advantages of these types of surfactants compared to their conventional counterparts?

T. Staub: Many product formulations use chemical surfactants. In an effort to increase sustainability, many formulators are replacing surfactants made from petrochemical-based raw materials with surfactants made from bio-based, renewable feedstocks. These surfactants are known as bio-based surfactants.

However, it is important to note that "bio-based surfactants" and "biosurfactants" are not the same.

Both bio-based surfactants and biosurfactants are made from bio-based raw materials. However, bio-based surfactants can be chemically produced through traditional chemical synthesis and may not be 100% biobased. Biosurfactants are produced through fermentation with less energy and a lower carbon footprint. Locus' biosurfactants are also USDA certified as 100% biobased. Biosurfactants are a high-performance, low-carbon tool in the formulator's toolbox.

Can you elaborate on the specific benefits that Locus Ingredients' high-performance biosurfactants bring to the formulation of innovative products in the industrial and institutional (I&I) sector?

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Working in the lab

T. Staub: Our Amphi biosurfactants are multifunctional glycolipids that are great co-surfactants to improve wetting, emulsification, dispersal, cleaning, and degreasing. We have both lower HLB—Amphi CL, Amphi M—and higher HLB Amphi CH—biosurfactant choices. They are pH balanced for ease of blending and customization.

All of our biosurfactants are free of 1,4-dioxane and other toxic residuals such as formaldehyde or ethylene oxide. They meet regulatory compliance requirements such as REACh registration, and Amphi M has Toxic Substances Control Act—TSCA—and CleanGredients approval for use in Safer Choice-certified products, including for direct release to water applications.

The biosurfactants formulate easily with other ingredients, including surfactants and solvents. They're superb degreasers and cleaners, and while they're not known for foaming, they can be formulated with amino acid surfactants such as taurates and glutamates, to provide superior foaming in a formulation.

Our application lab in Richmond, Virginia has created a significant formulary library to provide formulation guidance to I&I customers in a range of applications. The clean-label formulations outperform the benchmark leading brands.

In addition to the advantages of your biosurfactants, what other sustainability initiatives or practices does Locus Ingredients embrace within its operations or supply chain?

T. Staub: Fermentation is, by design, a lower energy, lower carbon process. However, it does use some energy and requires raw materials. Decisions on the energy and raw materials used impact sustainability. Plant location decisions are important. Renewably sourced energy is important. Water usage and water recycling is important. Utilizing alternative raw materials derived from waste is important. Building right-sized facilities for available inputs is important. While these decisions are often invisible to the industry, Locus is optimizing all of these factors to ensure maximized sustainability in our processes.

Looking to the future, what are your aspirations and goals for Locus Ingredients in terms of further advancements in biosurfactant technology, market expansion, and sustainability?

T. Staub: We are actively working on expansions to our biosurfactant offerings and their applications. This includes the derivatization of our biosurfactants with partners like Veolia, the global leader in water technologies. We're working on collaborations in agriculture, in lubricants and metalworking, in paints and coatings and in other industrial markets.

We're also focusing on streamlining global availability of our biosurfactants. We secured our REACh registration in the EU, and DSL is in process in Canada. We are planning expansion to Latin America and Asia, in particular Japan, Korea and Oceania. Our parent company, Locus Fermentation Solutions, is leading the charge to decarbonize energy, mining and livestock industries, and in agriculture we are the market leader in monetizing carbon sequestration for farmers. Locus Ingredients is part of a much bigger decarbonization story with our parent company, and we're proud to make a contribution in the key surfactant markets we serve.

- https://locusingredients.com

CPhI Barcelona 2023

CPhI Worldwide, taking place in Barcelona, Spain, on October 24–26, 2023, is dedicated to pharmaceutical developments, trends, products and services. Exhibitors include providers of contract research and synthesis services, suppliers of APIs, excipients, ingredients, intermediates and finished dosage forms, as well as producers of pharma manufacturing and packaging equipment. The event offers additional online networking opportunities and content.

■ www.cphi.com

CIEX 2023

CIEX, the Chemical Innovation Conference, is once again taking place in Frankfurt am Main, Germany, on October 25–26, 2023. Created for C-level R&D and innovation experts from the consumer, industrial and specialty chemical sectors and brings together the right people to create synergies and actively network potential partners. Attendees will hear from and discuss with industry leaders, international experts and innovative thinkers from the world of specialty chemicals.

■ www.ciex-eu.org

Advanced Recycling Conference 2023

On November 28–29, 2023, the Advanced Recycling Conference (ARC) takes place in Cologne, Germany, focusing on the diversity of advanced recycling solutions and brings together stakeholders along the entire plastics value chain. The hybrid event targets technology providers, related industries, waste management companies, plastic manufacturers, and investors as well as policy makers and scientists active in the field of recycling.

■ www.advanced-recycling.eu

European Chemistry Partnering 2024

The 8th European Chemistry Partnering (ECP) congress, the business speed dating event for the chemical and biotech industry, will be held in two parts again in 2024: on February 6 as a live conference in Frankfurt am Main, Germany, and on February 20–21 as an online event. As the premier event of its kind in Europe, the ECP offers a unique platform for networking, knowledge-sharing and collaboration.

■ https://ecp.european-chemistry-partnering.com/8th-ecp

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Industrial Collaboration

Human plasma proteins – the natural excipient

For more than 10 years, we have been supporting industrial customers worldwide. We offer regulatory, technical, and quality assistance with pharmaceutical grade quality products. Our focus segments include gene and cell therapy, vaccines, in vitro fertilization, drug formulation and drug carriers.

Especially our Human Albumin is widely used as an excipient in drug formulation, as a component of cell culture media, for drug delivery, cryopreservation of cells, vaccine manufacturing, or coating of medical devices; ultimately making it a versatile agent in pharmaceutical and biotechnological products.

Human Serum Albumin (HSA)
HSA: 5 %, 10 %, 25 %

Virus Inactivated Plasma
Blood group: AB, A, B, 0

Human Fibrinogen Concentrate (FC)
FC: 1 g

Human Antithrombin III Concentrate (AT III)
AT III: 500 IU, 1000 IU

Human Prothrombin Complex Concentrate (PCC)
PCC: 500 IU, 1000 IU

Human Coagulation Factor VIII (FVIII)
FVIII: 250 IU, 500 IU, 1000 IU

Immunoglobulins (IG)
IVIG[1]: 5 %, 10 %
SCIG[2]: 1 g, 2 g, 4 g, 8 g

[1] IVIG = Intravenous Immunoglobulin
[2] SCIG = Subcutaneous Immunoglobulin

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