CHEManager INTERNATIONAL 3/2021

Markets & Economy

New Business Models and Strategies for Chemical Companies, Digital Data Exchange Platforms, Processes4Planet: Transforming the EU Process Industry

Pharma & Biotech

Pharma 4.0: Digitalization in the Pharmaceutical Industry, Smart Biopharma Production Facility, Manufacturing Supply Chain for Antibody-Drug Conjugates

Innovation

New Ecoplastics from Biobased Building Blocks, Toll Production to Scale up Biobased Molecules Production, New Drug Design with Artificial Intelligence

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Markets & Economy

Feature: Pharma 4.0

Digitalization

Pharma & Biotech

Innovation

Processes4Planet: EU Cross-Sectorial R&I

Ten Sectors of the European Process Industry Deliver Innovation for Society and the Planet

The European process industry is engaged in a deep transformation to deliver the green industrial revolution. With climate change pushing the investment agenda, the urgency to drastically reduce CO_2 emissions will drive process industry decisions in the years ahead. How can the process industry contribute to the very ambitious targets set by the European Green Deal and the Paris Agreement?

Climate change is visible in every inhabited region in the world and the sense of urgency must permeate the actions of the entire socio-economic system, according to the Sixth Assessment Report 2021 of the Intergovernmental Panel on Climate Change (IPCC). Despite the need for wide and deep action in the next two decades, according to Jeffrey Sachs, the financial system and larger countries have so far failed to capitalize the hundreds of billions of dollars needed annually. On June 2021, at the Tri Hita Karana (THK) Climate Forum, Sachs pointed out that we need a second Bretton Woods and he called for the G20 Bali Summit 2022 to be such a historic breakthrough for humanity: the "Bali One" that can trigger a real global green economy.

Besides climate change, feedstock dependency and resilience will also dominate our future economic system. Given the limited timeframe (only about two investment cycles are left until 2050), for the ten sectors engaged in the Association SPIRE (A.SPIRE), there is only one way: work together to find joint cross-sectorial solutions to common problems.

Process Industry: Highly Ambitious R&I Agenda

A.SPIRE, representing the EU Process Industry, is the private partner of Processes4Planet (P4Planet) R&I Partnership formalized through a Memorandum of Understanding (MoU) with the European Commission. The MoU constitutes an agreement to undertake all efforts necessary to jointly develop and finally deliver the required solutions on climate neutrality, circularity and competitiveness identified in the P4Planet Strategic Research and Innovation Agenda 2050 (SRIA), developed by the A.SPIRE community.

"No single technology can reach 100% greenhouse gases (GHG) emissions reduction on its own."

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The process industry is key to achieving this transition. Reaching a net-zero scenario by 2050 and holding the increase of the earth's temperature well below 2°C will require the delivery of climate neutral and circular solutions at an unprecedented scale and pace. Improvements in emissions reduction at materials processing plants has a multiplying effect across different value chains (automotive, construction, digital devices et al.). The energy-intensive industries also have the capacity to reintroduce bulk amounts of waste transformed into new secondary resources to feed industrial processes, avoiding landfilling or incineration. The challenge for this recycling is to do it with fewer emissions and less cost compared to the use of virgin materials to remain globally competitive.

P4Planet's Strategic Research and Innovation Agenda (SRIA) sets three high ambitions for 2050: 1) net-zero greenhouse gas emissions; 2) near

Tab. 1: Processes4Planet innovation areas

Innovation areas
Renewable energy integration
Heat reuse
Electrification of thermal processes
Electrically driven processes
Hydrogen integration
CO_2 capture for utilization
CO_2 & CO utilization in minerals
CO_2 & CO utilization in chemicals and fuels
Energy and resource efficiency
Circularity of materials
Industrial-Urban symbiosis
Circular regions
Digitalization
Non-technological aspects

zero landfilling and near zero water discharge; and 3) a thriving EU process industry with gross value added (GVA) growing quicker than EU gross domestic product (GDP). The SRIA identifies 14 Innovation Areas and 36 Innovation Programs to develop the required solutions (see tab. 1).

To achieve net-zero emissions, P4Planet's SRIA includes solutions to move from fossil fuel emissions to the electrification of the process industry through an increased use of renewable energy and the valorization of process emissions. This will involve adapting processes to cope with alternative resources, reducing energy needs and other disruptive innovations. To achieve the circularity ambition, we need to move from waste to resources at scale, by keeping resources with the right quality in the industrial loop as opposed to landfilling or incineration. The eco-design of materials that are free of toxic elements is important so that, soon, nearly 100% of waste can be upcycled.

"Improvements in emissions reduction at materials processing plants has a multiplying effect across different value chains."

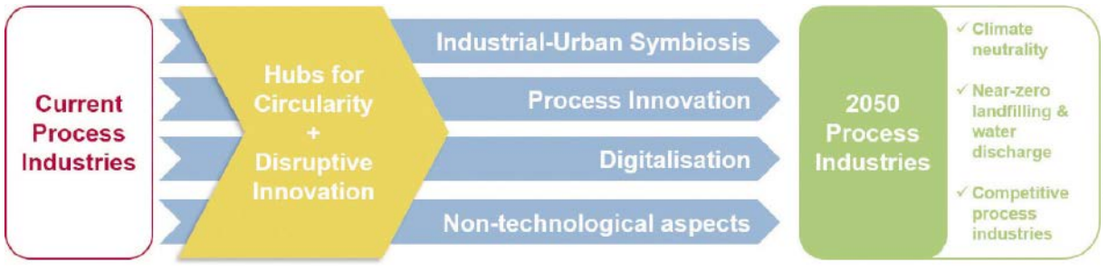

Fig. 1: Processes4Planet transformation levers towards the ambitions

Since competitiveness is at stake, non-technological aspects are equally relevant. Identifying and raising awareness of the public sector on the framework conditions for market uptake will be key to creating a market for climate neutral and circular solutions. Manufacturing industry, under pressure from consumers, will increasingly ask for materials that are safe, high-performance and with lower carbon footprint. And competitiveness can only be achieved by having the right talent at all levels of an enterprise (from the operational sites in the plants to the blue-collar jobs etc.). The learnings from P4Planet's projects on these aspects will be key to raising the voice of A.SPIRE members in discussions with the European Commission, the European Parliament and EU Member States.

Sustainable Investments for Impact

The transition to climate neutrality and a new paradigm of green

Continued Page 6 ▶

and circular economy will only be reached when these solutions are rolled out. This is when impact happens. Two key initiatives are included in P4Planet's SRIA to reach this impact phase. No single technology can reach 100% greenhouse gases (GHG) emissions reduction on its own. They need to be integrated in First-of-a-Kind (FOAK) processing plants, and FOAK units within existing plants, that can completely transform the industrial processes. Such integration

"Digitalization will accelerate faster development of novel solutions by the process industry."

can deliver the next generation of the energy intensive industries with a drastic reduction of GHG emissions. Hubs for Circularity (H4Cs) are the second initiative focusing on the generation of impact in specific industrial sites or regions. The H4Cs aim to scale up a new model of circular economy, enabled by the process industry (closing the circle), that makes the best use of all the resource streams (energy, materials, data etc.) from industry and from municipal waste.

The EU process industry estimates at least €34.5 billion are needed to develop the required innovations up to 2050; of which at least €19.8 billion need to be invested within the next decade to reach the EU Green Deal Targets. The P4Planet Partnership will play a key role in providing funding and financing support to de-risk the required innovations to transform the process industry. Following the MoU with A.SPIRE, the European Commission has allocated a €1.3 billion funding envelope within Horizon Europe (2021—2027), the current EU R&I program, to support projects that will address the ambitions of the partnership. Horizon Europe supports innovations at pre-competitive level. Further support to the FOAKs and H4Cs at scale will also be regularly discussed with institutional funding and financing bodies to reach the deployment (impact) phase. The estimates for investment for roll-out point to the need for hundreds of billions or even trillions of euros. A high sustainable private leverage will be key to achieving the level of investment required.

The Case of the Chemical industry

The chemical industry is one of the largest sectors of the process industries and one of the higher contributors to greenhouse gas emissions. The chemical sector's involvement in P4Planet through A.SPIRE is strongly based on the cross-sectorial approach. Indeed, by developing together with other sectors, new technologies, expertise and assets can be combined to reach a faster transition in, e.g., the electrification of crackers, furnaces, kilns etc. (all high energy systems, currently fossil-fueled). Together with the refining industry and the pulp and paper industry, the chemical sector can develop new value chains based on renewable or sustainable resources by using waste, residues, and biomass as feedstock to produce new molecules and materials in the future. Industrial symbiosis will combine sectors to use, for example, CO_2 emissions from steel as chemical building blocks in the chemical industry. This can only be realized via the establishment of H4Cs based on proximity and so reducing the costs of logistics and assets. The chemical and refining industries will also play a crucial role in industrial-urban symbiosis transforming domestic waste (and also wastewater) into feedstock for new materials via chemical and thermal recycling processes. To make the energy switch, strong interaction with renewable energy providers and green hydrogen producers (via, for example, hydrogen valleys) is required to reach the CO_2 emission goals in time.

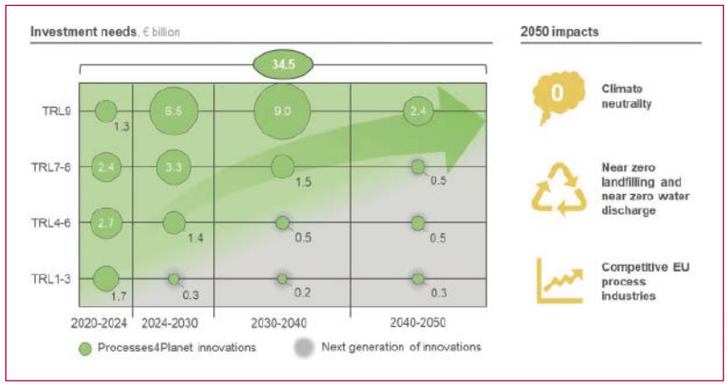

Fig. 2: Investment needs for P4Planet's innovation pipeline. TLR=technology readiness level

Enabling the Transition to a Green Economy

Electrifying the process industry through renewable energy and green hydrogen can enable the drastic abatement of industrial CO_2 emissions provided there is enough clean energy available at an affordable price. The success of the energy sector can enable the process industry to achieve its climate ambition. In turn, electrification of the industrial plants will imply a higher electricity demand. This high demand from the process industry can enable a competitive clean energy transition. Energy efficiency is also at stake. The process industry will play a key role in testing how to use the mix of renewable energies more efficiently and flexibly, enabling such practices along the whole value chain.

Digitalization will accelerate faster development of novel solutions by the process industry. A holistic approach is needed for a more intelligent operation of installations and all business and industrial processes. It is important for the process industries to collaborate with key digital companies that can target digital innovations (artificial intelligence, smart data, cybersecurity, digital twins, etc.) to the specific needs of process operations and the various value chains (including the full recycling, tracking, and tracing). It is also important to attract digital talent to the process industries to help them accelerate their transformation. A systemic perspective will enable the achievement of a real circular economy paradigm and will require the involvement of the full value chain.

"The EU process industry estimates at least €34.5 billion are needed to develop the required innovations up to 2050."

Conclusion

The energy intensive industries are highly engaged to pledge for climate action. The challenges they face are cross-sectorial and some solutions are sector specific. Processes4Planet is an essential tool for A.SPIRE's ten process industry sectors to maintain a cross-sectorial dialogue and jointly develop R&I solutions that can be transferred from sector to sector to meet these pledges. The process industry, united, is stronger and can deliver higher targets.

References for this article can be requested from the authors.

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A Roadmap for Pharma 4.0

ISPE Accelerates Digital Transformation with Pharma 4.0 Initiative

Despite the transformational potential of digitalization, the pharmaceutical industry has historically been slower than other sectors in adopting digital tools and in making associated changes in strategic priorities and workplace culture. Now, however, the Covid-19 pandemic may be accelerating the pace of change. The International Society for Pharmaceutical Engineering (ISPE) and its members are developing the roadmap to introduce Industry 4.0 at the pharmaceutical industry. Pharma 4.0 is defined as an operating model based on the Industry 4.0 elements, resources, information systems, organization/processes and culture. The pharma-specific enablers "digital maturity" and "data integrity by design" are added. Michael Reubold and Ralf Kempf asked industry experts Thomas Zimmer, Wolfgang Winter, Christian Woelbeling and Josef Trapl — all members of ISPE's Pharma 4.0 group — about the idea behind this initiative and the challenges on the way to realize the digital transformation of the pharmaceutical industry.

Thomas Zimmer is ISPE Vice President, European Operations. He previously was Senior Vice President of the Corporate Division Safety, Quality & Environmental Protection at Boehringer Ingelheim, where he worked from 1981 to 2013 and held several positions in pharmaceutical development and manufacturing as well as in management operations. Zimmer was also chair or member of several industry associations and scientific institutes. He studied pharmacy at the Goethe University in Frankfurt/Main, Germany, and holds a PhD in pharmaceutical technology.

Wolfgang Winter is OpenLab Platform R&D Director in the Software & Informatics Division at Agilent, based out of Waldbronn, Germany. His primary focus is on re-usable components, connectivity and data standards to enable the digital lab. He joined the industry in 1989 as a software engineer with a Master's degree in Electrical Engineering / Biomedical Devices. Winter joined ISPE in 2003 and currently co-leads the Pharma 4.0 Plug and Produce workgroup. Since 2021, he is also a chair-member of the Pharma 4.0 group.

Christian Woelbeling is Executive Industry Advisor & Senior Strategic Account Manager at Körber Pharma Software in Lüneburg, Germany. He holds a Master's degree in mechanical engineering. Working in life sciences manufacturing IT for 30 years, Woelbeling has great experience in all GMP related processes. He is Founder & Chairman of ISPE's Special Interest Group "Pharma 4.0", ISPE "GAMP MES Special Interest Group" Co-Chair, ISPE GAMP Member at large of the European Steering Committee, and "PAT & Lifecycle Control Strategy" CoP Steering Member.

Josef Trapl is Global Head of MSci Innovation within the Global Manufacturing Supply Organization (GMS) at Takeda Pharmaceuticals in Zürich, Switzerland. He joined Takeda in 2015 and, in his current role, supports the Takeda network with innovation in manufacturing. Trapl is a chartered chemical engineer (MChE) and has an MBA degree from Mannheim Business School, Germany. Since 2010, he is an active ISPE member and currently co-leads the Pharma 4.0 Plug and Produce team and is a chair-member of the Pharma 4.0 group.

CHEManager: Why is the digital transformation in the pharmaceutical industry happening slower compared to other industries?

Thomas Zimmer: Historically, the uptake of innovation in the pharmaceutical industry takes longer than in other industries. It is often explained with high regulation and long-lasting subsequent change management processes in this sector. This is only part of the explanation. Many pharma companies started very small with low margins. There was no environment to engage in technological innovation on an industrial scale. Products had very long lifecycles, some over decades, there was no pressure to change them, thus, pharma companies are lacking this sort of change culture. In contrast, this situation created a certain culture of hesitance to go new ways. In addition, generic pharmaceutical products have low margins, which do not support investment in innovation. Use cases sometimes miss to provide — or prove — convincing business targets or company strategies.

> *"Change management is seen as a burden and not as an opportunity."*
> Josef Trapl

Wolfgang Winter: Sometimes, low-margin products such as generics may not be candidates for innovation at first sight, but they can be candidates for other process improvements that improve efficiency and decrease cost or risk, e.g. faster QC methods that are more robust based on better product understanding. This eliminates technical failures that may have previously been out of trend or potentially out of specification and required lengthy investigations and regulatory scrutiny.

The intention of ISPE's initiative Pharma 4.0 is to transform industry-generic 4.0 models for pharma operations. What is the concept behind Pharma 4.0?

Christian Woelbeling: The key concept behind the ISPE Pharma 4.0 Operating Model is to combine operational excellence with the requirements which are specific to the pharmaceutical industry, for example regulatory and validation requirements. From the beginning, the goal was not to reinvent the wheel, but to use and apply best practices for the manufacture of pharmaceutical drug products to the benefit of the patients.

The Operating Model is a holistic approach to each, the pharmaceutical development and pharmaceutical delivery supply chain — end to end — from the raw materials or patient cells up to the final drug and along the ICH Q10 pharmaceutical lifecycle from development via tech transfer to commercial manufacturing. We call this the holistic control strategy approach, as the ICH Control Strategy plays a key role in the lifecycle of a drug.

How can the digital maturity, id est, the level of digitization and digitalization at pharmaceutical companies, be assessed and compared?

T. Zimmer: There are a number of maturity models, e.g., from BioPhorum Group and also from the ISPE Pharma

4.0 working group "Impact and Maturity" which describe basically six levels of maturity: computerization, connectivity, visibility, transparency, predictability and adaptability. In addition, the Pharma 4.0 working group has described barriers, which work as an obstacle to achieve the next level of digital maturity: misalignment, distrust, weak business objectives, low respect and inflexibility. It is interesting that the hurdles are primarily not of technical nature but liaise with behavior and culture.

Where do you see the biggest areas for improvement or development?

T. Zimmer: One of the biggest development areas is quality management. It starts with the development of technical standards for electronic data. In parallel, regulatory standards for data integrity have to be implemented. The next step is to create a computerized systems landscape and architecture. Systems need to be connected to enable interoperability, and a harmonized and holistic view on all parameters is needed to make quality and compliance related decisions.

> *"Pharma 4.0 is not a one-size-fits-all approach."*
> Thomas Zimmer

On a managerial level and complementary to this, there is the need to define a holistic control strategy and to define digitalized setpoints for monitoring and control. The Pharma 4.0 oriented Holistic Control strategy has an extended scope to the full value network, from suppliers for starting materials to the patients and all stakeholders in pharmaceutical products on the market.

There are a number of conceptual questions to resolve, e.g. how to enable systems to make or prepare decisions, and the role of humans in such a process. How can regulators get a mechanistic understanding of a computer-driven decision in order to develop confidence with the new processes? Where is it wise to install computer-driven decisions? How do algorithms for predictability of results look like? What does validation 4.0 look like?

As shown in the Pharma 4.0 Operating Model, technology and IT are just one element among others like culture, behavior, readiness to leave traditional silo-thinking behind. Integration of all relevant functions including a good risk and issue management is key to success for smooth and reliable operations in future.

How can the pharmaceutical industry overcome the obstacles to digitalization?

C. Woelbeling: Pharma 4.0 needs a strategic approach. It is needed to gain insight to benefits of digitalized operations. Mechanistic understanding is needed for cause and effect chains: how does digitalization accelerate the implementation of regulation; how does it improve quality oversight and facilitates GMP inspections; how does it help to improve patient safety, how to improve productivity and optimize cost; how does it support drug availability in the market and help to avoid drug shortages; and last but not least, how does digitalization reduce time to market for new medications.

Just as an example: The conventional thinking of automation coming with the two-years ROI is not appropriate. Pharma 4.0 and digitalization are enabling new business models and business processes, for example, for integrating contract manufacturing organizations into the marketing authorization holder organization or for real-time release and continued process verification or demand planning based on direct patient feedback. Still far away from this broad usage, at least singular use cases are available for first exploration. Also, established change management practices require significant evaluation prior to implementation. While change management practices are necessary to maintain product quality, they are often seen as a burden instead of an opportunity.

Which industry 4.0 automation and digitalization technologies can be applied to pharmaceutical manufacturing and which challenges are companies facing?

Josef Trapl: In the current world of digitalization, Industry 4.0 means automation and data exchange in pharma manufacturing. A smart pharma factory in the framework of Industry 4.0 is the new wave of digital transformation driven by recent technical development in cloud computing, AI, analytics, IoT, and application programming interface (API) technologies, which are needed when data must be exchanged between software applications and no defined interfaces are available. There is yet good progress in the adoption of modern operation and information technologies toward intelligent and connected machinery, automated processes and the use of predictive analysis. The three main challenges are well known from our legacy production sites:

- isolated and monolithic systems,
- interoperability and adaptability between machinery and systems,
- lack of harmonized standards and complexity of technical integration.

> *"Pharma 4.0 is a philosophy of driving a data-driven business model!"*
> Christian Woelbeling

In our Pharma 4.0 journey, the intention is to help to overcome these barriers by enabling a seamless flow of information with the use of APIs that secure integration between systems and devices in a standardized way. The use of APIs allows to develop a microservice-based architecture, which can be combined with other systems as a component without impacting the backend, enabling the reuse of components and delivering new features and applications.

What is the best way to achieve the flexible and maintainable integration of IT systems for data-driven pharmaceutical manufacturing?

W. Winter: So far, our investigations and prototype developments clearly identified several key success factors for Plug & Produce, like a vendor-agnostic and machine-type-independent approach that is not locked into specific commercial platform products as well as an extensible, service-oriented architecture that enables transactions between systems — i.e., processes, machines, subsystems, components — with built-in mechanisms for security and data integrity.

In the earlier stages of the workgroup, we learned that the number, variability and complexity of use cases is growing faster than the implementations. This means that Plug & Produce needs an information metadata model that allows us to model the interactions that occur between level 2 and level 3 in the ISA-95 model. It also needs an abstract concept of services and transactions that are designed to transport any set of data, without defining the "what" by mandatory service or variable names or structures. This way, the Plug & Produce concept is not locked into specific use cases or machine types. And thirdly, we need to take provisions for

> *"Dinosaurs will be left behind, and we all know what happened to them."*
> Wolfgang Winter

The 12 Theses for Pharma 4.0

1. Pharma 4.0 extends/describes the Industry 4.0 Operating Model for medicinal products.
2. In difference to common Industry 4.0 approaches, Pharma 4.0 embeds health regulations best practices.
3. Pharma 4.0 breaks silos in organizations by building bridges between industry, regulators and healthcare and all other stakeholders.
4. For next generation medicinal products, Pharma 4.0 is THE enabler and business case.
5. For the established products, Pharma 4.0 offers new business cases.
6. Investment calculations for Pharma 4.0 require innovative approaches for business case calculations.
7. Prerequisite for Pharma 4.0 is an established PQS and controlled processes & products.
8. Pharma 4.0 is not an IT Project.
9. The Pharma 4.0 Operating Model incorporates next to IT also the organizational, cultural, processes & resources aspects.
10. The Pharma 4.0 Maturity Model allows aligning the organizations operating model for innovative and established industries, suppliers and contractors to an appropriate desired state.
11. Pharma 4.0 is not a must, but a competitive advantage. Missing Pharma 4.0 might be a business risk.
12. When moving from blockbusters to niche products and personalized medicines, Pharma 4.0 offers new ways to look at business cases.

GxP compliance and data integrity already in the design. For instance, we made sure that metadata is included in the design. This is necessary for the trustworthiness and reliability of critical data, e.g. through user IDs, timestamps or physical units of measure.

What is your strategy to achieve an accepted understanding of readiness and maturity in the industry?

W. Winter: We structured the Plug & Produce workgroup as a dialog platform where documents, guidelines, principles are collaboratively created and shared in knowledge exchange forums and conferences. During the pandemic crisis, we replaced face-to-face interactions with virtual events. Since 2019, we established a steering team and an advisory board and maintain a roadmap for Pharma 4.0. We deliver on the Pharma 4.0 roadmap with our ISPE Pharma 4.0 knowledge sharing calls, publication of peer-reviewed concept papers, articles, training sessions, virtual conferences, expert exchange webinars and networking events. All the deliverables are created by the volunteers in the Pharma 4.0 communities of practice and workgroups — all of whom are experts in their field. It is important to note that all our workstreams are cross-organizational and cross-functional by design, with experienced contributors from biotech/biopharma, automation, software, validation, consulting, academia, including ISPE Young Professionals, who helped "rock the boat" through their invaluable energy and fresh mindset demonstrated in various hackathons.

Pharma 4.0

ISPE and its members are developing the roadmap to introduce Industry 4.0, also called the Smart Factory, at the pharmaceutical industry as Pharma 4.0. The objective is to enable organizations involved in the product lifecycle to leverage the full potential of digitalization to provide faster innovations for the benefit of patients. Implementing new Industry 4.0-based manufacturing concepts in Pharma 4.0 requires alignment of expectations, interpretation, and definitions with the pharmaceutical regulations.

While Pharma 4.0 has been called a new industrial revolution, its implementation will more likely resemble an evolution in which digitalization and automation meet very complex product portfolios and lifecycles. It is therefore important to achieve an accepted understanding of readiness and maturity, starting with additional digital enablers and elements added to the ICH Q10: The Pharmaceutical Quality System along the product lifecycle.

Digitalization, an important component of Pharma 4.0, will connect everything, creating new levels of transparency and adaptivity for a digitalized plant floor.

ISPE is not alone trying to propagate the Pharma 4.0 concept in the industry. Wouldn't it be good to also harmonize the efforts of different organizations?

W. Winter: We realized quickly that we are working on solving a huge problem. Multiple initiatives and consortia operate in this space in parallel. Examples are Allotrope for scientific data exchange based on ontologies, NAMUR with Module Type Package (MTP), BioPhorum Group for single-use systems, Pistoia Alliance with the concept of e-methods, Spectaris with the coordination of a Lab Agnostic Device Standard (LADS), and OPC-UA, to name just a few.

The key take-away for all of us is: This is not a competition. The sum is more important than any individual piece. This only makes sense as a collaboration where each initiative covers a range of the spectrum. The trick is to put all the significant ones on the map and focus on how

we complement each other without reinventing the same wheel all the time.

As far as I can see, ISPE Pharma 4.0 is the only initiative with the explicit charter to cover the pharma- specific requirements, including the regulatory aspects, and "translates" them into the Industry 4.0 / Industrial Internet of Things (IIoT) context. If you asked me for a motto to achieve this standardization, maybe it should be "Reuse, Leverage, Augment".

Which expertise is required to implement Pharma 4.0?

J. Trapl: Successful implementation of Pharma 4.0 requires a lot of expertise from different functions. Teamwork and strong stakeholder engagement are key, with opportunities within the existing ISPE organization to utilize capabilities of established CoPs, workgroups including regulatory and GAMP community.

Does a pharmaceutical organization need external experts to implement Pharma 4.0?

J. Trapl: To drive Pharma 4.0, we understand that in addition to leveraging existing internal competencies, external collaboration is key. Pharma 4.0 provides the right forum to bring together the necessary stakeholders such as pharmaceutical companies, technology providers, consultants and regulators. In the dialogue with pharma companies, we define the business needs for Pharma 4.0 and discuss how the Workforce 4.0 should look like to support seamless end-to-end integration in the future.

Technology solution providers and consultants are playing an important role to consider upcoming technologies and ways to successfully apply them in the regulated environment. This gives us the opportunity to build the right capabilities to operate the manufacturing and to work on common harmonized standards.

How can all stakeholders be involved in either stage of the process?

T. Zimmer: It is essential for the success that experts from various functions collaborate in the same team. Also, regulators should be invited, some health agencies have offices for innovation. The ISPE Pharma 4.0 Special Interest Group founded several of these cross-functional teams.

When defining Pharma-4.0-related goals it is important to determine the strategic target. Pharma 4.0 is not a one-size-fits-all approach but has some common principles to apply, such as holistic view, digitalized data and a culture of trust and openness. In such a strategy the "what to do" and the "how to do" should be clearly explained, but most importantly, the „why" should be explained to get decision makers to buy in.

Such a profound industry transformation does not come at zero cost. What can companies do to keep the price tag of Pharma 4.0 as small as possible?

T. Zimmer: Companies should begin by defining an overall Pharma 4.0 strategy, i.e. the big picture, and the program elements that fit into the overall strategy including related business cases, benefits and financial returns. Successfully implementing pilots are key to building momentum and long term success of the overall strategy. Finally, an entrepreneurial spirit is needed to see advantages beyond business case return-on-investment calculations.

www.ispe.org

Please visit the CHEManager online portal (www.chemanager.com/en/tags/ISPE) for the complete interview incl. a publication list.

Transition to Digitalization

How to Effectively Digitalize the End-to-End Supply Chain in the Pharmaceutical Industry

ISPE and its members are developing the roadmap to introduce Industry 4.0, also called the Smart Factory, at the pharmaceutical industry as Pharma 4.0 — an operating model that is interconnected, meaning that the digital tools allow for a fully connected network to enable direct communication between all levels in an organization.

Despite the transformational potential of digitalization, the pharma industry has historically been slower than other sectors in adopting digital tools, such as cloud storage, artificial intelligence (AI), machine learning (ML), blockchain, and remote communication technologies, and in making associated changes in workplace culture and strategic priorities. Now, however, the Covid-19 pandemic may be accelerating the pace of change.

What are the digitalization trends in the industry? What is the business case to develop and implement digital tools and digitalization strategies? And how can organizations introduce and use them?

CHEManager asked executives and industry experts to share their views on digitalization trends in the pharmaceutical industry and challenges on the way to realize the sector's digital transformation. We proposed to discuss the following aspects:

- What do you think are the key digitalization trends in the pharmaceutical industry?
- What do you consider to be the most important benefits of digitalization in the pharmaceutical industry?

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- Is your company involved in systematic, ongoing action to digitalize operations?
- At present, digitalization in the pharmaceutical industry is immature. In your view, what are the biggest obstacles that need to be overcome in the digitalization of the sector?
- How would you rate the digital maturity level of your company?

Read the insightful answers of the experts here.

Unlocking Treasures for Unmet Medical Needs

Michelangelo Canzoneri, Global Head of Digital and Data, Healthcare Business, Merck

"Digitalization will enable our industry to streamline its processes, increase speed to market, identify opportunities to reduce costs, and elevate performance."

We have unprecedented amounts of data at our fingertips, yet we're only scratching the surface of its value. To build industry-wide capabilities for deriving genuine and actionable insights from manufacturing data analysis for example is becoming increasingly success-critical in the industry. Some big questions here are 'How is my batch doing?' and 'Has this deviation affected product quality?' In the labs and manufacturing facilities of the future everything will be fully connected, with automated processes and data driven foresights too. Managing knowledge is where digital and data can elevate the connection between R&D and operations. It is not just about accessing and compiling the data. Everyone involved will require access to high qualitative information (re-integration of learnings from all batches) to build process and business excellence.

Secondly, the drive towards more resilient manufacturing. According to an Accenture report, two out of five cyberattacks are now indirect causing the industry tens of billions of US-dollars due to IP theft yearly. Companies in the pharma sector need to look beyond their own four walls to their broader ecosystems. Investing in robust cyber resilience, while bridging the gap between information and operational technology, will be key to prevent, manage, monitor, analyze and predict risks for attacks and intrusions and important to conduct counteractive protocols and report incidents, along with examining and evaluating security strategies and defense.

Digitalization will enable our industry to streamline its processes, increase speed to market, identify opportunities to reduce costs, and elevate performance. And if we continue to evolve and put the patient at the center of everything we do, then we will unlock treasures for unmet medical needs across the digital continuum. This will create opportunities for precision, personalized, and preventative medicine, and deliver tangible benefits to patients faster. Digital is not an end state — it's a journey.

Digital Transformation Journey

Balajikasiram Sundararajan, Chief Digital Officer, ACG

"We strongly believe in digital-enabled transformation. The future is bright. The future is digital."

At ACG, we began our digital transformation journey in 2017 with four broad objectives: How can we use emerging digital technologies to transform manufacturing operations, enhance customer experience, build smart products and services, and create new business models?

We started with projects focused on reducing machine breakdown and enhancing overall equipment efficiency (OEE). Today, 1,000+ machines are connected to our industrial IoT platform streaming more than 30,000 parameters, spanning process data, energy data, machine condition data, alarms, alerts.

What started with OEE enhancement has evolved into a range of digital initiatives powered by technologies, such as industrial IoT, advanced analytics, machine learning, computer vision, mobile robotics, augmented reality, and virtual reality. These digital initiatives have yielded significant benefits in reducing downtime, enhancing OEE, decreasing lead time, reducing defects, optimizing energy consumption, enhancing capacity, improving first pass yield, and much more.

We are also in the process of developing and deploying digital solutions aimed at providing delightful customer experiences across various touchpoints. These include technical services, factory acceptance tests, plant qualification, and product approvals. As a machine builder serving the pharma industry, "Smart Connected Products" is our strategic initiative to make machines smarter using Industrial IoT, edge computing, advanced analytics, and machine learning. These technologies allow us to provide insights to our customers to run the machines better and reduce unplanned breakdowns, enable service teams with insights to perform better field service, and help our design teams to optimize machine design.

At ACG, we strongly believe in digital-enabled transformation and see great potential in technology for delivering significant value to our customers, our partners, and to ourselves. The future is bright. The future is digital.

Data Science and Analytics Are Key Trends

Viola Meisterling, Digital Officer HPS&GQ, Boehringer Ingelheim

"In today's fast changing world, everyone needs to adapt to succeed."

Health is what we care about. We believe that digitalization helps us to develop new and innovative therapies for patients around the world. Data science and analytics are key trends. With digitalization and automation, the amount of data is constantly increasing. By making better use of data, we can identify patterns and tendencies and transform data into insights and smart decision making. This allows us to optimize our entire value chain. As a result, digitalization helps us to create exciting new opportunities to improve human and animal health.

Digitalization affects almost every aspect of the pharmaceutical value chain. To give you one example: The lead times between the research and development of new compounds and the market launch of the pharmaceutical product will become shorter. Accordingly, manufacturing capacities need to be available faster than in the past. We have created a digital roadmap to be prepared for these developments in operations and supply chain and to actively manage these processes. One example is our project "Real Time Release Testing" (RTRT), which is part of our BI dataland initiative. With RTRT we want to use data in operations to predict product quality and release in real time with minimum risk.

In today's fast changing world, everyone needs to adapt to succeed. We must change the way we think and act today and break out of the existing structures. If you want to be successful with your digital transformation, you need to think and act across the entire end-to-end value chain to achieve more resilience and flexibility.

Standardized Key Quality Systems

Markus Zeitz, Quality Innovation hub lead, Novartis

"Built on the renewed IT landscape an enterprise-wide data lake supported by a solid master data governance will be a key enabler for transformation projects."

For quality, the digital journey will continue to focus on the standardization of key quality systems (e.g. exception handling, change control, document management, batch release, lab systems). These systems will embrace the benefits of cloud computing wherever possible. Built on the renewed IT landscape an enterprise-wide data lake supported by a solid master data governance will be a key enabler for digital transformation projects.

The access to high quality data will be the foundation for transformational projects using state of the art digital tools like machine learning, artificial intelligence, internet of things and block chain. Some of these tools will require investment in new standardized platform applications on the enterprise level. Novartis Quality is embracing operational excellence and playing in all the abovementioned fields focusing on standardized key quality systems, insight generation based on high quality data and automation of transactions.

At Novartis Quality, we are leveraging data and digital to improve compliance and to increase efficiency at the same time. To be truly transformational and unleash the power of our people we embrace the Novartis values of being a workplace, which inspires curiosity in our employees and allows them to work in an unbossed way.

Seamlessly Integrated Planning across all Disciplines

Andreas Bonhoff, CEO, TTP Group

The planning of all technical projects of TTP Group is based on the building information modeling (BIM) approach. The trend is towards seamlessly integrated planning across all disciplines under one roof. This minimizes replanning efforts as well as costs and enables the creation of a digital twin of the plant. Actually, already part of our daily work.

To meet the BIM requirements for each project and define the scope and benefits, it is necessary to work closely with the client. It is critical that the process is considered as a whole and that the information/data requirements are coordinated and agreed upon by both parties. Through the BIM approach, changes in all phases of the building's life cycle are immediately visible to all parties and the impact is synchronized immediately.

During the construction phases, BIM provides contractors with data information that is shared via cloud data platforms, helping them save both time and money. In addition, construction managers can also track and control the entire construction progress using augmented reality.

"We have systematized the digitalization of processes by deploying specialized teams in the development departments."

At TTP Group, we have systematized the digitalization of processes by deploying specialized teams in the development departments. For example, at Pharmaplan, the Digital Factory department is divided into different areas that are responsible for the development of digitalization — which is unique: Digital Engineering Building, Digital Engineering MEP & Process, and Manufacturing IT & Automation. We use a cloud-based platform called BIM360 as our common BIM data environment, which allows us to share the work with all project participants as well as with our client. It provides not only the data management system, but also all relevant building data that is geometrically visualized as a virtual composite model and stored in a live database. Only in this way, the correct implementation of the BIM database from conception to facility management activities can succeed.

Pharma Industry Faces Specific Challenges

Teresa Minero, Founder & CEO, LifeBee

"Digital transformation is too often perceived to be only about technology. It is not. It is about people and information."

Pharma 4.0 embodies the same characteristics of Industry 4.0, but there is an extra dimension in its complexity: compliance with regulations for patients benefit. The Patients are waiting at the end of our supply chain for a medicine that must be more and more effective, safe, promptly available at sustainable costs. We must assure this with Pharma 4.0.

From what we find in ISPE, and also in my company LifeBee, we must underline that digital transformation is too often perceived to be only about technology. It is not. It is about people and information. The main benefit is to empower human beings with the right information at the right time, in order to act and make the best decisions, at every level in the organization, from the line operator to the lab analyst, to the supervisor, to the QA, to the CEO, up to the regulators. In pharma there is also an additional complexity: information needs to be managed in full "data integrity".

Regarding challenges specific to Pharma 4.0, they were deeply analyzed in a workshop in 2020, held at the ISPE European Pharma 4.0 conference. Results were clustered in six key topics as follows: 1. Compliance: the need to assure the company of the alignment between 4.0 and regulatory guidance; 2. Economics: costs of a 4.0 program versus the tangible value; 3. Knowledge: a wide spectrum of information on the 4.0 initiative must be shared with management and personnel from the outset; 4. Organization: the company organization will need to change — cut the silos — to benefit from and manage the 4.0 perspective; 5. Competencies: questions from management about workforce 4.0 features and workers' potential resistance to change; 6. Strategy: many companies have developed 4.0 pilots and projects, but there is a lack of a mid to long term strategy, with a definition of business targets and a sound road map.

The benefits are undoubtedly far more important for our patients compared to the complexity of challenges. Let's start the Pharma 4.0 journey!

Enormously Transformable Buildings

Rino Woyczyk, Head of Life Sciences, Drees & Sommer

"Modular digital construction planning offers maximum user orientation via defined modules that can be quickly exchanged as needed."

For construction projects in the life sciences segment, with its stringent safety, speed and flexibility requirements, two approaches are particularly promising when it comes to digitalization: modular construction and building information modeling (BIM). Linking these two methods forms a powerful digital duo that allows, amongst other things, faster, more reliable and more cost-effective realization of production buildings and labs.

The key to efficient modularization is the digitalization of the design using a BIM model, a process whereby a "digital twin" of the building is created. The building model is consistently modular. Recurring spaces and structures are only modelled once and stored as catalogue models. Examples of such modules are the furnishing modules for user-defined expansions, such as laboratory units, offices and meeting rooms, cloakrooms and kitchens, including their entire development and all of their technical equipment.

Modules from the catalogue are added to the project model according to user preferences. The result is a building design that is developed like a product. The components can be put together according to the customer's wishes within a coordinated set of rules, and the planning becomes more or less a configuration.

The innovative modular planning approach in combination with a complete digital representation of the building is opening up new dimensions. The buildings of the new pRED research center in Basel, most of which are equipped with laboratories, are set up using this method, and the requirements are very high, due to the necessary laboratory installations and especially the demand for flexibility in the buildings.

Modular digital construction planning offers maximum user orientation via defined modules that can be quickly exchanged as needed. It allows for the quick conversion of labs instead of new construction or renovation. Even in highly customized architecture, the digital duo leads to economical construction and operation and reduces the planning effort as possible errors are already identifiable in the "digital twin". Thus, it enables a proverbial "quantum leap" towards enormously transformable buildings, perfectly tailored to a particular use and produced to the highest quality standards.

Significant Market Advantages

Ferdinand Biermann, Head of business unit Life Sciences Engineering, Fraunhofer Institute for Production Technology IPT

Digitization and networking are the central development concepts of production in the sense of 'Industrie 4.0'. For manufacturing pharmaceutical companies, these modernizations result in significant market advantages: One is that powerful systems for obtaining and evaluating process and product data in real time provide valuable information that can be used for optimization. Additionally, they facilitate compliance with regulatory requirements — from Good Manufacturing Practice (GMP) to EU directives on serialization and anti-counterfeiting. Furthermore, process chains can be organized more agile through digitization and networking. This results in a new level of flexibility that prepares pharmaceutical manufacturers for the challenges of the personalized medicine of the future. The modernization and development of production processes and process chains according to 'Industrie 4.0' is a core competence of the Fraunhofer IPT: Together with our partners, we develop individual solution concepts for the establishment of new technologies as well as for networking and adaptive design of production in pharma companies.

"Process chains can be organized more agile through digitization and networking."

Seamless Shift Integration

Digital Shift Management Cures Pharma Processing Communication Woes

The increasing complexity of drug products brings pharmaceutical companies significant manufacturing challenges arising from the pandemic. This includes disrupting supply chains and requiring changes to business and operational processes to accommodate social distancing, remote work and quarantining. The industry has been in constant transition from producing blockbuster medicines towards personalized medicine to breakthrough vaccines, which for production teams, means there will be increasing variations in the production processes.

These challenges mean that communication between members of the manufacturing team is paramount. This requires a lot of agility and the right tools and systems to automate and instantaneously capture key communications and critical information during shift handovers.

Shifts Communications in BioPharma

One biopharma company initially focused on automating microbial quality control quickly expanded after Covid-19 to deliver contaminant testing for pharmaceutical and vaccine manufacturing. The need for digitalizing shift management became more dire as this pandemic ignited the need to shorten the supply chain for critical drugs and vaccines while enabling biopharmaceutical companies to operate their manufacturing facilities with reduced staff.

In this example, the second shift of cleanroom automation operators required better communications with its third shift to ensure safe operations of its automation lines to target overall equipment effectiveness (OEE) conditions and deliver quality product. Any silo of communication could mean a decrease in quality and the potential loss of customers.

Cleanroom operators conduct manufacturing in a cleanroom environment and carry out maintenance tasks related to the automation line. It's vital that all manufacturing shifts communicate and work safely according to the company and OSHA guidelines.

A shift management system enables a smooth shift to shift transition and operators to identify past operating patterns or any background details to make proper machine adjustments, impacting quality and performance.

Automated shift handovers can be critical to complete timely validations and ensure paperwork completion. Continuous improvement efforts and accommodating a shifting work schedule for periods as needed is key.

A Break in the Clouds: Communication and Collaboration

The pandemic brought to light how we can strengthen our communication. For instance, it's important to make communication easy by making it easy to capture, collect and store shift notes, tasks and directives.

Andreas Eschbach, Eschbach

Pharmaceutical manufacturing teams usually require a lot of face-to-face communication and are used to working together. Therefore, it's important to develop up-front an approach on how information can be shared within the team and how the team-to-team communication should work.

Automating at a Pandemic Speed

Through automation, shifts can access an intuitive shift handover system that ensures all legal and compliance standards are being met. For instance, audit trails have accessible auditable data storage with chronological change history, since that often causes a note of contention. All those working in a shift find that it's helpful to have all events visible at any time. A shift hand over management system allows operators to easily conform to Current Good Manufacturing Practice (CGMP) Observance of CGMP regulations assures the identity, strength, quality and purity of drug products by requiring that manufacturers ensure adequate control of manufacturing operations.

The Result of Digitalized Communications

Digitalizing and automating shift handovers has become more important than ever because it can result in improved pharmaceutical production, increased performance, reduced risks and time savings.

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Recipes for Sustainable Success

Innovative Chemicals Enable Environmentally Friendly Solutions

Consumers have ever more demanding expectations when it comes to the sustainability of products, which brand manufacturers have to meet. As one of the most diverse supply industries, the chemical industry has a particularly important role to play in improving sustainability. The WeylChem Group is taking a proactive approach to this.

That's why the company has recently launched a variety of sustainable innovations including a family of high-performance polyether polyols based on 1,3-propanediol, which is derived from renewable raw materials. A life cycle analysis according to the ISO 14040/44 standard shows that this polymer's climate footprint is up to 50% lower than that of petrochemical alternatives such as PTMEG.

Marketed under the name Velvetol, the polymer is able to completely replace petroleum-based polyols in polyurethane systems, thermoplastic polyurethanes, dispersions and elastane fibers. „Its possible uses range from shoes, clothing and accessories like handbags and bracelets to sports equipment, delivering even higher performance in some cases," says WeylChem business manager Hendrik Fleßner. In the area of care chemicals, WeylChem is present with a particularly sustainable product family. The bleach activator Peractive TAED is produced using a solvent-free manufacturing process in which the only by-product is water. Since June, the Peractive AC White Eco variety has completed the portfolio. It does not contain any polymers considered microplastics by the EU and is easily biodegradable, thereby meeting the Ecocert criteria for detergents and cleaning agents. „With Peractive TAED, you can achieve the same cleaning and hygiene results at 30 or 40 °C that would usually require a 60 °C wash," says Konstanze Mayer, WeylChem's head of business development for care chemicals. "This saves energy and is good for the environment, while consumers still get perfectly clean laundry and dishes. Further environmentally friendly products are in development."

WEYLCHEM

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Working with Data Instead of Documents

Digitally Transformed Processes in the Chemical Industry

When it comes to digitalization in the chemical industry, we often hear that our industry is special and that implementation costs often exceed the benefits. But, interestingly, precisely because of its specifics, it offers countless opportunities for successful digital transformation. Recent research in real-life digital transformation cases shows substantial benefits for organizations, the entire supply chain, and the environment.

Imagine that you are working with a team on a vital project, developing a new product that is key for reaching your growth goals for the year. Your colleagues in charge of laboratory testing work tirelessly to get valuable data on various formulations. They measure many parameters and collect their findings on a spreadsheet. Finally, after thorough testing and a long wait, the result lands in your inbox. You open the report eagerly, but when you do you are confronted with a huge, sprawling, unwieldy spreadsheet that stretches over many pages. You want to make your own analysis, compare data against previous projects, add some columns and formulae, draw charts, but the problem is that the spreadsheet is in PDF form. You can't do any of the analysis you want to and put the data to use. This is frustrating and unnecessary as there are far better uses of your valuable time.

You mail to your colleagues and ask them to send you the spreadsheet as an Excel file, they say that this is not possible: the data can only be saved as a PDF file. Therefore, the only way to make use of the data is to transcribe the spreadsheet manually — which is frustrating.

I've heard countless anecdotes of cases like this happening in companies around the world. It seems to be such a fundamental problem that it should have been overcome long ago, and yet it remains the norm, not the exception. In many organizations, data is kept in various formats, scattered over various business functions and units. As soon as we move outside of that organization, only PDFs are sent from one company to another. The PDF is the primary medium for exchanging data, information, and knowledge in the supply chain.

On the supply side, a significant amount of effort is put into generating data and creating documents, as well as getting those documents to customers. On the customer side, the same level of effort is required to extract — which too often means manually transcribing — information from documents (usually PDFs) into usable and processable data. Moreover, it happens at every step in the supply chain and at every organization within it. Instead of focusing on creative work, highly educated experts are doing non-value-added work: copying PDF information into Excel.

The Chemical Industry Is Unique

In the chemical industry, formulators combine various ingredients from multiple suppliers to create a new product. Therefore, the output data of the supplier represents vital input data for the next company in the supply chain.

Raw material properties and parameters are important for a formulator when deciding which materials to use in their next project. Health and safety information (hazards, the presence of substances of very high concern, etc.) is vital for a health and safety expert to develop measures for the protection of workers using the new product. Knowing the concentration of volatile organic compounds (VOCs), ozone-depleting and other environmentally hazardous substances is essential for environment protection experts when assessing risks for the environment. Product information, like properties and parameters, is essential for a marketing expert when preparing or updating a catalog, a website, or a web shop.

Bojan Buinac, Bens Consulting

All this data and information is product-related. For example, raw material (product) information is vital for producers of mixtures, while mixture information is relevant to companies down the supply chain. More importantly, this data is required in most business functions, including but not limited to R&D, health, safety and environment, marketing and sales, storage, logistics and so on.

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How Digitalization Can Help

In general, digitalization means a process of leveraging data to improve (business) processes. In other words: no data — no digitalization!

This definition suggests that the chemical industry must first shift its focus from creating and sending documents to exchanging data and information. Documents must not be the focus but rather side products of digital transformation. Moving towards data exchange opens the doors to substantial time and cost savings and helps to reduce waste.

Where to Start

Recently, two digital tools that can save time and money and help protect the environment caught the attention of researchers. Allchemist is

a cloud-based web application that connects suppliers, formulators and downstream customers in the same digital environment. On the supply side of Allchemist, suppliers of raw materials digitize their materials and share them with formulators. On the demand side, formulators develop and optimize formulations using digitized raw material information in the shared database.

While Allchemist is for R&D experts, Chemius was developed with environment, health and safety (EHS) experts in mind. When a formulator creates a formulation in Allchemist, it automatically appears in Chemius. This allows the EHS team to directly use digitized formulation data to automatically create digital safety data sheets, safety instructions and labels — all within seconds. When done, they can easily share them with customers. This way, teams and customers work in a shared environment without sending documents back and forth.

Significant Time and Cost Savings

Recent research on digitizing the paints and coatings development process using Allchemist as a technical enabler for improved process shows a 48% shorter throughput time for the entire process when compared to a conventional one. The substantial reduction was achieved due to a 70% reduction of non-value-added activities.

Major results normally come at a high price. This raised the question of whether the faster development process also reduces process costs, or whether these actually increase due to implementation costs. A special study was therefore carried out to determine the implementation costs. The researchers showed that the renewed, faster process is also significantly cheaper than the conventional one. The costs were reduced by 48%.

Benefits for Suppliers

The above results and benefits directly apply to formulators who are on the demand side. But what are the benefits for suppliers? What can they expect in return for providing the data? The most obvious benefit is that they help their customers to be more efficient. As a result, the customers will likely do more business with them. The second reason, which is not so obvious, is that they can shorten their sales cycles. Another research project demonstrated that the digitally formatted sales process by using digital tools can be shortened by up to 32%. Simultaneously, more potential customers can be accessed using the common technology. Interestingly, the authors of this study suggest that a digital sales channel is different from an online sales channel (e-commerce). The latter is 15.9% faster than the personal "call me, mail me" channel and comes in handy for customers when buying already well-known products (commodities). However, when they decide to make their first purchase, they need reliable and detailed product information. This is where a common technical tool like Allchemist, which allows customers to access all product information and formulate online, makes a difference.

As a result, the digitally supported sales channel is 32.1% faster than the personal sales channel and 16.3% faster than the online sales channel.

Last but not least, digitally transformed processes also help reduce waste. Therefore, they contribute to cleaner environment efforts, which are at the center of the European Green Deal and its Chemicals Strategy for Sustainability.

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Chemical Industry — Surviving or Thriving in the Next Normal?

Taking Product & Service Portfolio, Profitability, Resiliency, and Sustainability to the Next Level

Digitalization continues unabated. Even in times of the Corona pandemic, innovative customer-centric business models emerge, supply chains are entirely redesigned in a world changing from global to multipolar, new business networks and multi-discipline consortia are formed and, last but not least, sustainability more and more establishes itself as a strategic goal. All these evolutions cause challenges but also provide opportunities for chemical companies to redefine their core competencies and future strategic direction. Stefan Guertzgen talked with Thorsten Wenzel, Vice President and global head of the industry business unit Chemicals at SAP, about most recent trends and developments shaping the future of the chemical industry.

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CHEManager: Mr. Wenzel, in light of recent dynamics and uncertainties which have been even exacerbated by the Corona pandemic, what keeps chemical executives up at night?

Thorsten Wenzel: In the value chain, chemical companies are the first to convert energy and natural resources into more than 70.000 different products. Located between the energy and feedstock suppliers on one side and manufacturing and consumer industries on the other side, chemical companies are facing both resource volatility and price pressure, tightened environmental regulations and challenging sustainability targets — e.g. Climate21 and circular economy. At the same time, they must adapt to changes in consumer behavior and expectations.

How do you see traditional strategies and business models being impacted?

T. Wenzel: Today, traditional strategic advantages such as proximity to customers and access to competitively priced feedstock or in-house intellectual property and technological know-how can no longer secure a sustainable competitive advantage alone. We observe a strong move beyond classical B2B-driven business models towards a more B2B2C-driven focus, frequently even in a co-innovation based "Segment of One" relationship.

As classical competitive advantages are losing their edge, and customer demand moves towards more sustainable and innovative solutions, both products, services and business must be reimagined, and corporate strategies need to be adapted. This requires chemical companies to prioritize new business models and to transform processes while ensuring sustainability, safety and integrity along the entire value chain and lifecycle of their products and services.

What main paradigm shifts are required for chemical companies to survive or even thrive in the "next normal"?

T. Wenzel: First and foremost, they start selling business outcomes instead of just products. This means connecting to and collaborating with their customers and suppliers via industry business networks (IBNs) on co-innovation and supply chains, understanding and becoming part of their value chains, and using digital technology to deliver innovative services and business outcomes instead of just selling products.

Secondly, they simplify their operations and focus on shrinking cycle times. Chemical companies run simulations and predictive models, enabling real-time sense and response, and leveraging IT and OT integration

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Thorsten Wenzel, Vice President and Global Head of Chemicals, SAP

and the IoT to reduce time to market, streamline operations, maximize asset performance, and minimize rework. The manufacturing and distribution logistics area have been in focus for digital transformation for many years. We see a recent emphasis on co-innovation, research, and intellectual property management.

> *"Predictive analysis will enable chemical companies to anticipate downstream supply chain disruptions and take corrective actions in real-time."*

Thirdly, chemical companies begin competing as entire ecosystems. Collaboration is also a focus as successful chemical companies capitalize on open co-innovation, use extended manufac-

turing networks, go beyond the boundaries of their existing value chain, and understand their customer's customer needs. The more chemical companies are focusing on co-innovation together with customers, the more partners are usually involved in an innovation platform approach. This frequently includes universities, research institutes, start-ups, logistics partners and other service providers.

Finally, we see them adopting strategic agility in response to market dynamics. Companies adjust their strategy and portfolio dynamically in response to market opportunities and needs, grow rapidly into new markets or segments, and capitalize on mergers, acquisitions, and spin-offs to secure continued growth. The chemical industry has outperformed most of the other industries in recent years by number of M&A and spin-off deals, due to the tremendous need to optimize overall portfolio profitability and performance.

What role does technology and data play in terms of realizing those new paradigms?

T. Wenzel: Digital is the new norm, with technologies such as the Internet of Things (IoT), artificial intelligence (AI), machine learning (ML), robotic process automation (RPA), blockchain, the cloud, and analytics providing new opportunities for chemical producers to cut costs by automating the back office and running low-touch operations.

As a next step, chemical companies will capitalize on structured and unstructured data — both operational and experience — from common platforms and open networks to understand and rapidly respond to market needs. Ultimately, this will result in differentiating, innovative products and services, such as benchmarking or proprietary recipes, or business models that support a higher purpose, such as precision farming or circular economy.

What's your view on the overall impact of the Corona pandemic on the chemical industry?

T. Wenzel: With regards to digital transformation and related projects, Covid-19 has been acting in many cases as an accelerator. Especially for ongoing projects, during the early days of Covid-19 the pandemic impact and related lockdown caused some delays due to the need to switch to home office and virtual environment. After that, the pace of those projects mostly picked up as before

> *"We observe a strong move beyond classical B2B-driven business models towards a more B2B2C-driven focus."*

with the result that ongoing S/4HANA implementation projects, for instance, have experienced very little delay.

What innovative business models do you see emerging?

T. Wenzel: Coming from a pure B2B-based push model in the past, as mentioned before, many chemical companies are applying B2B2C-based business models to deliver sustainable, co-developed applications, services and business outcomes instead of just products. Emerging new models will also include programs to monetize corporate knowledge, intellectual property, and data assets on new platforms, supported by extended partner ecosystems as well as intelligent technologies like e.g., machine learning.

> *"With regards to digital transformation and related projects, Covid-19 has been acting in many cases as an accelerator."*

Customer-centric R&D will anticipate customer and consumer demand, simulate product and formulation performance, and design products that minimize environmental impact and support a circular economy. Applying digital technologies in operations will help chemical companies analyze production process variables and asset performance in real-time and simulate their impact on product quality, costs, and yield. Predictive analysis will enable chemical companies to anticipate downstream supply-chain disruptions and take corrective actions in real-time.

What chemical segments do you see leading the pack in terms of innovation?

T. Wenzel: Within the broad chemical industry portfolio we clearly see the agrochemicals & seeds segment leading the pack, and this started already more than ten years ago. With digital farming the traditional value chain has steadily moved from B2B to B2C, considering the single farmer as customer, instead of agricultural cooperatives and wholesale & distribution channels. In this environment, companies are moving towards direct sales to farmers, with product sales supported by companion product and service offerings provided by business partners.

What's your view on the role of business networks as game changers?

T. Wenzel: Industry business networks (IBN) are cloud-based collaboration offerings that can help transform disconnected supply chains into unified, collaborative, and intelligent networks that remove barriers and centralize data. This will be one of the most strategic topics for the chemical industry in the next decade. Enterprise resource planning focuses on single corporations and companies. In the future we will see a strong emphasis on cross-company and cross industry data exchange. One recent example is Catena-X, initiated by German automotive companies working together with their suppliers and partners.

Catena-X members share the vision of a continuous data exchange for all contributors along the automotive value chain. Prominent members of the chemical industry, BASF and Henkel, are founding members and a few other chemical companies are evaluating membership now.

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The Future of Biopharma

How to Create a Flexible and Efficient Biopharmaceutical Production Facility

Biopharmaceutical production is in a transition phase. The recent pandemic has shown that it is becoming more and more critical to react fast and be flexible in production. The trend is towards smaller single-use bioreactors and continuous bioprocessing. In addition, digital solutions like AI-guided production planning and steering drive efficiency. In this article, we present a vision of a high-end smart biopharmaceutical production unit and a corresponding operating model.

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Four factors lead to so far unsolved challenges in biopharmaceutical production. First of all, the Covid-19 pandemic has shown that sudden outbreaks of diseases require biopharmaceutical production, which is flexible, simple to scale, and readily adaptable to various technologies. New vaccines — mRNA-based or attenuated viruses — and antibodies need to be developed quickly and produced in large scale. Secondly, managing stock levels becomes more important for pharmaceutical companies in order to keep free cash flow and margins high in an environment that requires enormous investments in R&D. This becomes increasingly challenging as complexity grows along with the number of stockkeeping units (SKUs), which have increased since 2006. This is enhanced by wide variations in volume demand. Thirdly, a paradigm shift is driving the pharmaceutical industry to modular construction. Conventional facilities have proved to be costly in construction and difficult to repurpose. Faster innovation cycles require adaptable production facilities. Lastly, policies are driving the industry towards greater flexibility. Among these policies are national immunization programs and regulatory aspects like updates to the GMP regulations and new laws, e.g., the Drug Supply Chain Security Act (DSCSA).

Increased Productivity and Flexibility

The answer to the challenges listed above lies in smart and flexible biopharmaceutical production units. The design of these manufacturing units is influenced by seven trends.

Some 45.5% of decision makers in pharma are committed to single-use bioreactors, which reduce changeover times by minimizing cleaning effort. Modeling an mAb production process in E. coli indicates that the number of batches produced per year can be increased by 117%.

While single-use technology addresses the mechanical aspects of flexibility, the plug and play concept addresses the software part of flexibility. Plug and play provides interoperability by enabling standardized communication among devices from different suppliers. Furthermore, it provides information transparency by standardization of naming of parameters and report data.

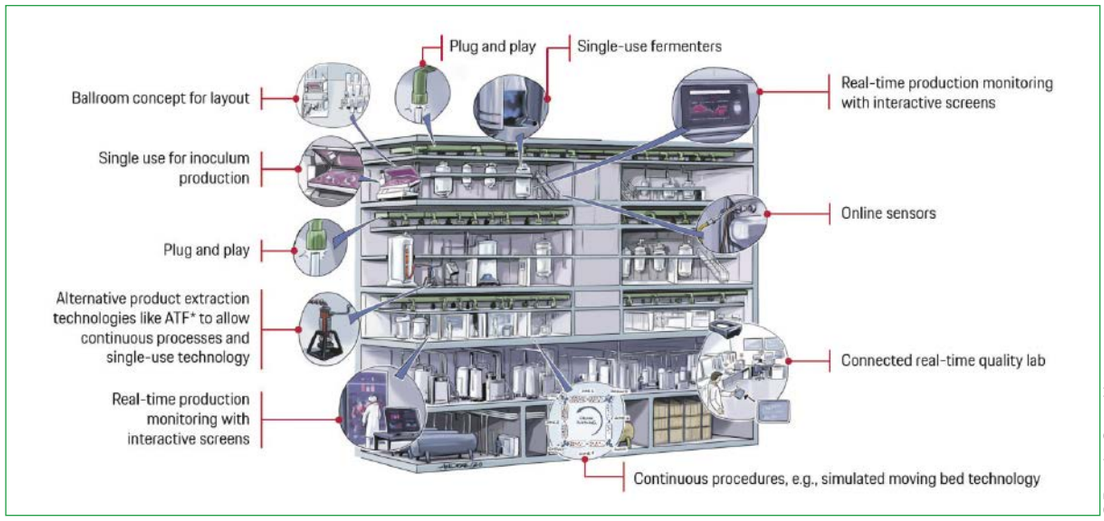
The third trend is modular construction, which is usually realized with a "ballroom" concept opposed to the classic "dance floor" concept. A ballroom is more compartmentalized. Partial areas with the corresponding heating, ventilation, and air conditioning are raised to the cleanroom class required for the respective process step. On average, the required space is reduced by 38%. Durations rather than volumes primarily govern continuous processing production.

Till Giese,
Porsche Consulting

Production can simply be ramped up by extending campaigns and incorporating additional compact continuous processing units. On the other hand, it exhibits more process variability, and the process complexity increases. 25% of decision makers are committed to continuous processing in the upstream area, while 17% are committed to it in the downstream area.

Key components of the fifth trend — green design — are: reducing waste, energy, and water consumption. For example, energy can be made more green by utilizing renewable energy (e.g., solar panels) and using waste for energy. A heat, ventilation, and air conditioning system that automatically reduces air changes during non-operational hours can reduce annual utility costs by 10%.

Quality is shifting from a risk-avoiding approach to a risk-managing approach and risk-based compliance. The latter requires much more knowledge about the processes and potential risks. However, the value is a leaner and more educated ap-



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Target picture of a smart biopharmaceutical production facility (* Alternating tangential flow)

proach to quality without any compromise on patient health.

The seventh trend is lean manufacturing. Margins were traditionally high in the pharmaceutical industry. As pressure continues to increase, the focus is more and more on efficiency. Lean principles have to be considered in all elements of smart biopharmaceutical production.

Overall, for the implantation of trends and technologies it is always important to consider the individual challenges and possible solutions. A decisional framework is essential for the planning of a smart biopharmaceutical production.

A Holistic Operating Model for Biopharma Production

At the start of the development of smart biopharmaceutical production, the objectives have to be specified clearly, e.g., time to launch, number of products per asset, COGS. The Porsche Consulting operating model for smart biopharmaceutical production then guides the way towards facility implementation. It all starts with the strategy and organization, which needs to be defined for the new facility. This first action field defines the vision and the mission of the new facility. Moreover, future processes and the respective organization are defined.

In the second action field, the transformation enablers need to be installed. Structured and purpose-oriented communication, which focuses on the "why," supports the change management and motivates the employees. Competence management is important to identify and develop the skills required in the new facility. This goes hand in hand with the design of the future way of working. A specific upskilling program is essential to prepare the employees. Important transformation enablers are partners, e.g., for planning and building the new facility.

The third action field is the target picture of the smart biopharmaceutical production facility. Design principles guide the direction. These principles are derived from the specific objectives and the latest trends, described previously. They lead to a vision image like the one shown in the figure, which serves as orientation and for communication purposes.

Finally, the details need to be defined. This includes the infrastructure, buildings, and means of production. Creating a 3-D model of the facility supports the optimization of the layout. Defining the IT system early on is relevant for integrating digital solutions. In line with design principle 7, "AI-supported decisions", installing automated production planning and scheduling increases the overall efficiency of the facility. This becomes more important if the focus is on flexibility and an increased number of products per asset, as this increases the planning complexity. Further relevant digital solutions are digital batch records and AI-supported data analytics.

In conclusion, the challenges of the modern world require new smart production facilities. When designing these, the latest trends have to be considered and a structured approach for planning has to be taken.

References to this article can be requested from the author.

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Managing Supply for Complex Biotherapeutics

Drug Substance Manufacturing of Antibody-Drug Conjugates (ADCs)

Antibody-drug conjugates (ADCs) are complex bioconjugates typically used as vector-based chemotherapy, allowing the selective delivery of a nanomolar potent cytotoxic agent within a tumor. For drug substance manufacturing, the cytotoxic agent and the targeted monoclonal antibody are chemically linked via a linker. The drug product for an ADC is typically filled and lyophilized to distribute the drug in a stable form.

ADCs are complex, and their manufacturing supply chain contains five different technologies with specific asset needs: monoclonal antibody, cytotoxic payload, linker, bioconjugation and fill & finish. Even with the necessary expertise, the combination of disparate technology requirements to manufacture the five ADC components creates supply complexity. It can take years of effort to establish a reliable, high-performing logistics network to manufacture ADCs. Many companies, therefore, consider outsourcing to experienced contract development and manufacturing organizations (CDMOs) as an option to accelerate development and limit risk.

The Global ADC Portfolio Continues to Grow

Antibody-drug conjugates have shown an exciting pace of development, especially over the last 10 years. Today, we have 10 approved ADCs and more than 80 candidates in different clinical studies. There are substantial learnings from the successful candidates, but also from over 50 candidates that were abandoned in the clinic over the same time for reasons of toxicology and efficiency. Advancing technology has improved and will further improve the probability of success by better allowing control of toxicity and a wider therapeutic index. According to Lonza's market data analysis, ADC sales will rise to over $15 billion over the next decade.

Lifecycle and Supply Considerations

Successfully managing the supply of the various components of ADCs requires a sophisticated understanding of the technological development process and access to a range of large- and small-molecule manufacturing assets.

In the early stages of development for monoclonal antibodies, it is important to create processes that are adaptable and resilient through later stages. Proper control of quality attributes with analytical methods ready for the purpose must also be established. The use of established expression systems and platforms substantially reduces risk and the time needed to submit an Investigational New Drug (IND) application.

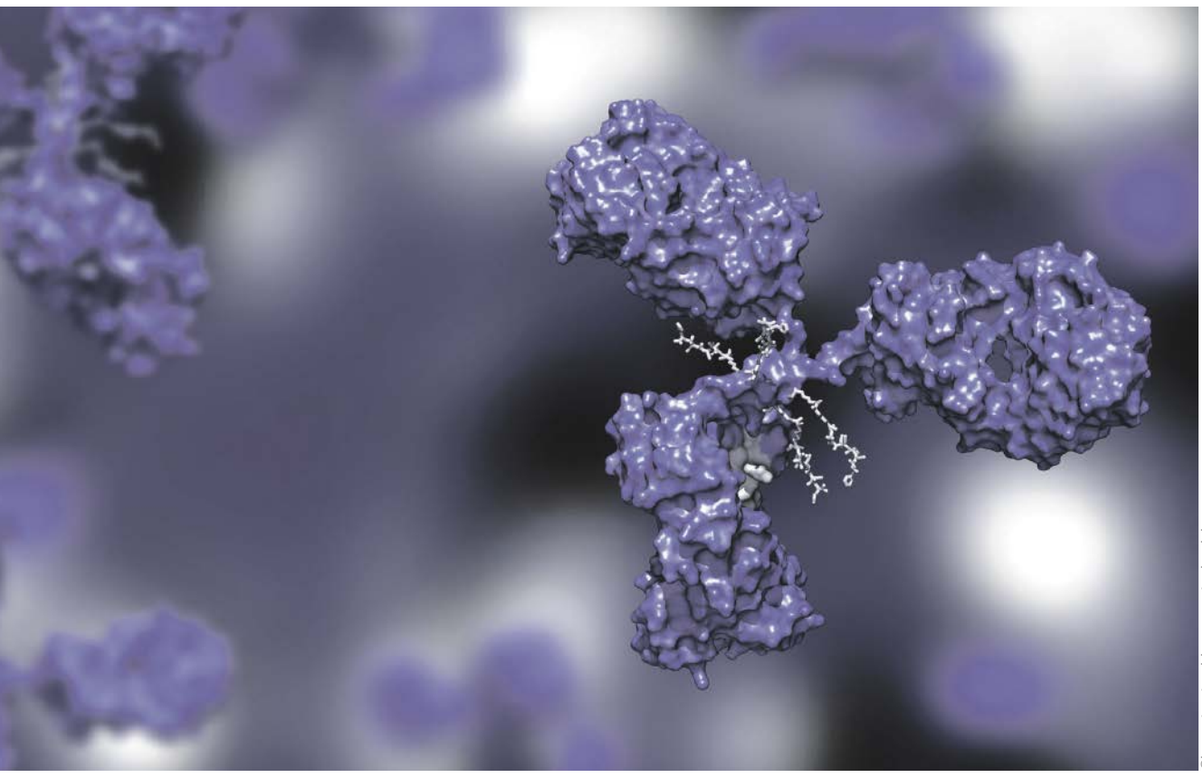
Small molecule assets are required to deliver the linker and cytotoxic payload. While the linker can typically be manufactured in an asset without special highly potent capabilities, the cytotoxic payload requires special safety control. Payloads for ADCs come with an inhibitory concentration (IC50) which is typically below picomolar concentrations.

Iwan Bertholjotti, Lonza

This toxicity is translated into occupational exposure levels, which are typically below 10 ng/m^3, requiring proper strategies for substance handling during manufacturing. Substantial resources are required to invest in cytotoxic-dedicated infrastructure, and define and implement processes and control strategies. Proper training and control measures are continuous efforts through development.

Beyond infrastructure and established safety concepts, the supply of cytotoxic payloads requires development and technology transfer capabilities that support process implementation at the required scale. Because the effort to execute activities for cytotoxics is high, good planning and effective execution are key.

Regarding bioconjugation, the handling of cytotoxics in a bioburden-controlled environment requires special attention from a safety and quality perspective. Specialized biologics assets must be equipped to fulfill these requirements. Bringing the two worlds of small molecules (payload) and biologics (antibody) together in bioconjugation typically requires a dedicated workforce specially trained in this expertise. Process definition, implementation and control are critical since high-value intermediates need to be conjugated. The bioconjugate is isolated in the final and stable liquid formulation as bulk material is stored frozen for control. Storage and shipment processes need to be in place to prevent any unplanned supply interruption. The conjugation can be made in different ways and with the high number of bioconjugation technologies developed over the recent years,



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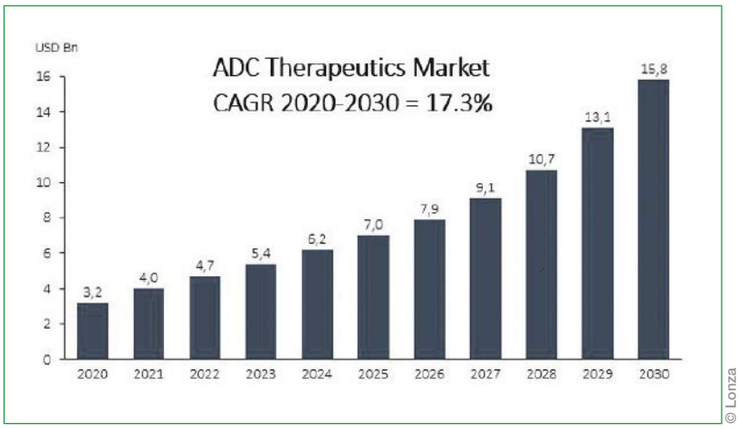

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ADC market sales prediction 2020-2030. Source: Roots analysis

the early development of lead candidates needs special attention.

For the fill and finish of ADCs, assets need to be equipped to handle cytotoxic drug formulations. Since formulation and processes need to be developed and implemented, companies delivering drug product need to have the necessary infrastructure and knowledge to cover process development and manufacturing. For product testing and stability testing, there is a significant overlap with drug substance. Depending on the level of integration of the offering, synergies can sometimes be realized to streamline the effort.

Simplified Supply Chain with the Right Partner

Proper management of the complex ADC supply chain is an important success factor in making these life-saving drugs accessible for patients. Since the supply of monoclonal antibodies, cytotoxic drugs, bioconjugation and fill & finish require expensive assets and expertise, small biotech companies typically do not have the required in-house capacity. At the same time, established pharma companies understand the advantage of outsourcing to secure a reliable and efficient supply.

Bringing the entire lifecycle together under one roof simplifies the supply chain substantially. This integration removes complexity from an overall chemical manufacturing control (CMC) management. A high level of integration allows for easier planning, contracting, quality systems, program management, analytics, storage, shipment and improved timelines.

Currently, there are few CDMOs that have invested in capabilities across all the technologies required for ADCs. Fewer still have mastered manufacturing processes at the level needed for reliable production. Lonza entered the ADC market in 2006 and is today the most advanced supplier to provide an integrated supply for ADCs under one roof. The fact that Lonza is part of the supply chain for the majority of the 10 commercial ADCs, having completed over 750 successful cGMP batches, illustrates the importance of outsourcing and experience for this product class.

The Future of ADCs

The dynamic market outlook for ADCs is very positive. With ten commercial ADCs in production and a healthy clinical pipeline in place, sales are projected to surpass $15 billion in the coming years. ADCs are widely approved for the treatment of solid tumors and will offer an answer to many unmet medical needs outside oncology as non-cytotoxic bioconjugates are advanced. However, bioconjugates currently have one of the most complex supply chains in the pharmaceutical industry. By outsourcing to a reliable CDMO, pharma & biotech innovators may access the expertise, infrastructure and flexible business models needed to secure supply. An experienced and reliable CDMO partner can provide access to supply under one roof and help deliver new, innovative drugs to market and to patients sooner.

References for this article can be requested from the author.

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A Digital Twin for the Cold Chain

De-risking Temperature Controlled Logistics by Simulation

The virtual cold chain is a modern software approach to save time and minimize costs in the cold chain. Pharma companies use it to simulate the shipment of temperature-sensitive goods and determine the lane-specific optimum level of thermal protection, to only invest in what is necessary. This computer-based approach is faster, cheaper, and more reliable than classical physical testing, because it requires no physical shipments and can be used to test thousands of potential scenarios.


Stefan Braun, SmartCAE


Jan Walbrecker, SmartCAE

The global distribution of temperature-sensitive ingredients and products is a central challenge in modern supply chains. Lately, the criticality became particularly apparent during the distribution of Covid-19 vaccines. The pharmaceutical products had to be kept between 2 °C and 8 °C, below -20 °C, or even as low as -70 °C, during delivery across a multitude of origins and destinations.

One core task for a reliable and efficient cold chain is to determine the optimum combination of packaging and logistics service: too little thermal protection leads to unacceptable temperature excursions, compromising the quality of the payload; too much protection results in unnecessarily high costs and carbon emissions. Given the variety of thermal conditions in which goods are shipped, there is no one-fits-all optimum solution; each setup has a specific optimum. Some might require an expensive container and pharma-level logistics, others might work in light protection and general cargo. Often the optimum lies somewhere in the middle, and a decision has to be made to invest in better container insulation, or to book higher logistics service levels with temperature-controlled facilities.

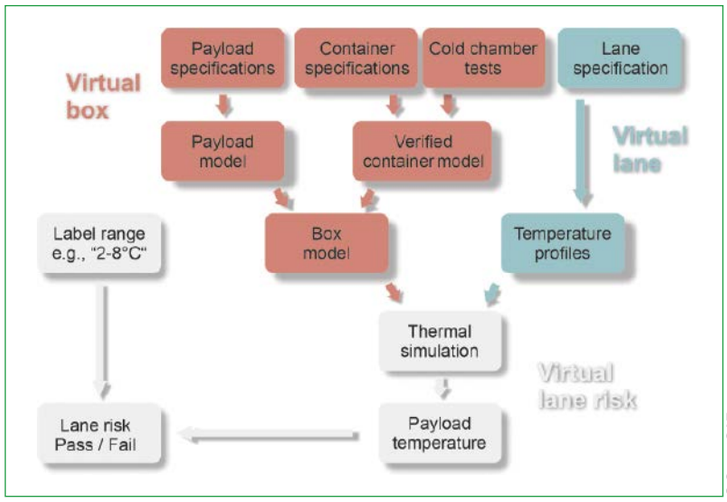

Fig. 1: Digital twin of a cold chain distribution process to quantify the lane risk.

Physical Testing is Limited by Nature

The quest for finding and validating the optimum combination can be attempted by physical testing against expected temperature conditions. This classical strategy is naturally limited, because it provides only a snapshot of the real conditions a shipment will experience: In reality, ambient conditions are different for each month and each departure time, there can be flight delays, re-routings, traffic delays, temperature-controlled storages might not be available. To capture each scenario would require thousand of tests, which is impossible to achieve — unless you are taking the virtual approach.

Virtual Lane Risk Assessment

The virtual approach is based on accurate thermodynamic simulation of

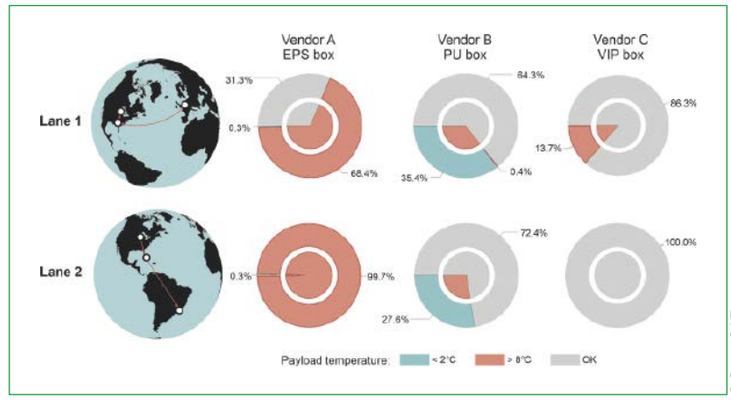

Fig. 2: Virtual lane risk assessment for three container options on two lanes. Results are based on the equivalent of 12,000 historical shipments, obtained in a few hours of computer simulation.

the distribution process. It takes only a few minutes to simulate a lane of, e.g., 100 h duration. With parallelized simulations, thousands of scenarios can be tested in a matter of hours. In contrast, physical testing cannot be accelerated: it always takes 100 h to physically test a 100-h-lane in a climate chamber or by dummy shipments.

To run a virtual lane risk, a digital twin of the distribution process is established, as illustrated in fig. 1: (a) The container is represented by a virtual box model; its thermophysical parameters are validated to ensure that the model is a suitable representative in any realistic ambient conditions. (b) The lane is virtualized using specifications from the logistics provider and combined with potential risk scenarios. Lane segments in which the container is exposed to ambient conditions are modeled by including historical ambient temperature data from proximate weather stations for the last years. Delays, lane variations, solar irradiation are included as additional scenarios, if relevant. All potential scenarios are evaluated by thermodynamic simulation software, thus generating the equivalent of thousands of historical test shipments.

Total Cost of Ownership

The simulation results show if and under which conditions a temperature excursion is to be expected. Figure 2 shows a summary for an example assessing the performance of three container options on two lanes. To determine the most cost-effective solution, the analyst can combine risk and costs for any container in their supplier's portfolio and run a total cost of ownership analysis to single out the optimum solution. This approach can be executed for any lane, and all containers on the market: simple passive containers, vacuum-insulated boxes, pallet shippers with phase-change materials, dry ice containers, and reefers.

Fast Analysis of Large Data Volumes

A major advantage of this approach is that it is not necessary to collect big data from physical shipments. All data are available before any shipment has been carried out. Statistically, virtual lane risk assessments are even more reliable because thousands of scenarios can be tested, unlike in physical testing. If a thousand of scenarios is not enough, make it a million. Everything is possible. At the end the question is not "Why should I use a virtual approach?", it is "Why not?": the virtual cold chain is faster, it can be used before any physical shipments, it is more reliable because it uses more data, it strengthens the scientific foundation of your qualification process to augment your conformity with GDP guidelines, and it is cheaper, because it only involves the costs of the software without any physical shipments or testing.

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PET Recycling on a Large Scale

Efficient Processes in Response to Rising Recycling Rates

For more than 20 years, recycling plants have been processing PET bottles into new raw materials, thus conserving resources by closing the loop. In the reprocessing process itself, many plants face the challenge that the volume of PET products is increasing, and the existing systems are reaching their capacity limits. Therefore, a smooth interaction of the individual process steps is required in order to work safely and efficiently even on a large scale. With its technologies, Zeppelin Systems not only provides an economical answer to this challenge for high throughputs, but also offers a complete solution from conveying technology and homogenization to elutriation and storage.

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Shampoos, shower gels, oil or juice bottles — it's no longer just the classic beverage bottles that are made of PET. A study by the Society for Packaging Market Research shows the growth of recyclable plastic packaging in 2019 by 8.1% compared to the previous year. The increasing volume requires economical recycling processes to avoid high intermediate storage costs. In this context, it is important to understand the different recycling processes of PET deposit bottles which are collected from the deposit cycles and other PET packaging in order to guarantee the optimal interaction of the system components in each case. Sorting, grinding, washing and drying are necessary for both material streams. However, their differences in shape, color and residual foreign substances lead to different process requirements in the recycling plant: while the PET flakes from deposit bottles can be processed directly, the other material is preferably processed by chemical recycling.

Intelligent Storage for Continuous Material Flow

A look at the overall plant shows that after the washing and drying process, the PET flakes first have to be stored temporarily before being transported to the processor. PET flakes are among the poor-flowing bulk materials and tend to form bridges when stored in silos, which can bring the material flow to a standstill. As plant engineering specialists with proven expertise in silo design Zeppelin Systems has equipped its silos with intelligent discharge devices, such as vibratory discharge bottoms or discharge screws, which activate the bulk material flow.

This ensures a reliable, continuous material flow. Zeppelin Systems also provides a suitable answer to the large quantities of PET flakes: storage silos with a volume of up to 800 cubic meters.

Optimum Homogeneity as the Basis for Product Quality

Due to quality fluctuations, the homogenization (mixing of the flakes) takes place before processing or chemical recycling. Many companies use mechanical mixers for this purpose. Since these mixers are limited in size, several ones are used in parallel. The mechanical mixers have the disadvantage of moving internals, so-called mixing screws, which cause fines generations when the flakes are mechanically stressed and also suffer from heavy wear, especially in the bearing area of the screw. Their repair and maintenance cause downtime for the plant, which affects productivity. In addition, multiple mixers do not achieve an optimum homogeneity of large product amounts, since single batches from the smaller mixers' contents stay separated. Gravity blending silos such as the Centro-Blend from Zeppelin are the low-maintenance, the low-wear and high-capacity alternative. Its central blending pipe with intake openings and deflector plates extracts the bulk material simultaneously from different heights, in equal amounts. The inclination of the deflector plates prevent product build-up or dead zones. The entire design is for mass flow. The homogenous blending is achieved by combining flakes from the blending pipe with flakes from the annular space in the blending chamber. This guarantees a high homogeneity for a volume of up to 300 m^3.

High Throughputs Thanks to a Clever Interaction of Components

However, the silo alone is not the decisive factor for an efficient process. The conveying system and all other components must be combined as an integrated solution. In many recycling plants, throughputs of 5–10 t/h are state of the art. This will no longer be sufficient in the future with the increasing quantities of PET. Plants will have to reach conveying rates of up to 30 t/h and overcome long conveying distances of up to 1,000 m. Zeppelin Systems has carried out tests at its test center in Friedrichshafen, Germany, proving that it works — and without any technical risk. In particular dilute phase conveying at reduced velocities and low conveying pressure has proven to be the reliable and efficient process.

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Artificial Intelligence for Drug Discovery

A Technology Platform for Deep-Learning-Based de novo Drug Design

Digital tools are a key to shortening the development of active pharmaceutical ingredients and thus market-ready drugs and therapies. Big data and artificial intelligence (AI) can significantly accelerate many processes and make them more efficient. The Paris, France-based start-up Iktos is developing a proprietary AI technology for ligand and structure-based de novo drug design, focusing on multi parametric optimization (MPO). Yann Gaston-Mathé, co-founder and CEO of Iktos, explains the company's technologies and provides an outlook on the further development of the company.

Yann Gaston-Mathé, CEO, Iktos

Personal Profile

Yann Gaston-Mathé holds an engineering degree from Ecole Polytechnique Paris and a master's degree in biology, genetics and biochemistry from AgroParisTech. He held several positions in the pharmaceutical industry (at Servier, Ipsen, Integragen), and in consulting companies Capgemini, BearingPoint and Cepton. With an excellent knowledge of the pharma sector, he has a global vision of the pharmaceutical industry's challenges as well as a broad understanding of methods, approaches and tools of data science. He led Iktos' development since its foundation, incl. capital raising, business development and team recruitment.

CHEManager: Mr. Gaston-Mathé, what was the starting point and motivation for founding Iktos?

Yann Gaston-Mathé: Iktos was founded in 2016 by Quentin Perron, Nicolas Do Huu and myself with the aim of developing an innovative and user-friendly deep learning-based technology platform for de novo drug design. The technology platform was built by leveraging a proprietary algorithm developed by Quentin and Nicolas who initially wanted to apply deep learning generative models to chemistry that were previously used in fields such as image recognition and natural language processing.

Our objective is to make our technology accessible to everyone, and to be the first company to release a user-friendly and high-performance de novo design software for multi-parametric optimization, that can be used by any medicinal or computational chemist, whatever their level of expertise in deep learning and computer programming.

What does the company name Iktos actually stand for?

Y. Gaston-Mathé: The name Iktos stands for 'God of dream catcher' in the native American mythology.

What problem does Iktos's technology specifically solve, or what previously untapped opportunities does it open up?

Y. Gaston-Mathé: We leverage big data and artificial intelligence (AI) to bring radical improvements and efficiencies to drug discovery process. Iktos is developing a proprietary, disruptive, AI-based generative modelling technology for ligand and structure-based de novo drug design, focusing on multi-parametric optimization (MPO). Our proprietary technology is built upon the latest developments in deep learning algorithms, not only for de novo design but also for AI driven synthesis planning.

Our generative modelling technology coupled with synthesis planning can be applied to the early stage drug discovery value chain ranging from hit generation or scaffold hopping projects to lead generation and lead optimization. In a very short timeframe, it can design novel, diverse, druggable and synthesizable molecules, that are optimized to match the target product profile (TPP) of the project.

Iktos has a strong expertise in deep learning based de novo design for medicinal chemistry: superior technology, experience and skills, and technical infrastructure. In a few weeks, we can provide solutions that help to accelerate collaborators research projects.

Who are your customers and in which markets do you find them?

Y. Gaston-Mathé: As a company specializing in AI for drug design, Iktos is developing and commercializing several software products in the field of generative modeling and retrosynthesis. We license our software platforms and interfaces — Makya, Spaya and Spaya API — on an annual SaaS licensing model.

Iktos predominantly operates in the early stage drug discovery sector. Our typical customers are from pharma, biotech, agrochem and academic sectors. Since 2017, our technology has been tested and validated in several real-life projects with bio-pharma collaborators globally. We either have been working or delivered 40 plus projects with bio-pharma collaborators.

What have been the most exciting projects so far?

Y. Gaston-Mathé: We are working with a large number of biopharma collaborators, for us every project is exciting. Here are a few examples where we can share the project details:

Iktos is the first company to report a successful application of deep generative modelling technology in a real-life drug discovery project. We have presented the results of our collaboration with Servier as a poster at the 2018 EFMC meeting and recently published a ChemRxiv preprint.

We have successfully applied our structure-based generative modelling approach to design novel compounds for a kinase target in line with the target-product-profile. Iktos has delivered molecules with well-balanced activity and physio-chemical profile, the MPO project work is progressing well with our collaborator Oncodesign.

What do you see as the main drivers for your success and what is the feedback from the industry?

Y. Gaston-Mathé: Iktos' technology and know-how in generative modelling are key drivers to our success. Our team is composed of 40 talented individuals meeting the key skills required to succeed in our business: medicinal and computational chemistry, machine learning and deep learning, data science, data engineering, open-source big data IT architecture, software development and business development.

Iktos is recognized as one of the key players in this emerging field of generative modelling. Our proprietary technology platform simultaneously tackles de novo design and synthetic planning of the molecules to match the desired blueprint of drug discovery projects. We have been able to sustain long term relationships with existing customers and secure collaborations with new customers on regular basis.

Business Idea

Reinventing Medicinal Chemistry

New drug design is long (5 years), costly ($50-100 million) and unproductive (1% success rate from hit to pre-clinical candidate). Iktos leverages big data and artificial intelligence (AI) to bring radical improvements to this process.

Founded in 2016 and located in Paris, France, Iktos is a company specializing in AI technologies and software applied to chemical research, more specifically new drug design, with two proprietary technologies:

- Generative AI technology and software (Makya) for de novo drug design and multi-parameter optimization (MPO)
- AI for synthetic planning with Spaya, a fully data-driven retrosynthesis software which provides plausible synthetic routes for any given compound in a very short time frame.

Iktos has acquired a unique know-how at the interface of AI, medicinal chemistry, and informatics with a solid expertise across multiple areas such as data science, deep learning, machine learning, cheminformatics, molecular modelling, synthetic chemistry, medicinal chemistry, data engineering, high-performance computing, cloud environments and software development. The company has built a talented team of engineer graduates from the French Grandes Ecoles, PhDs in AI, chemistry, specialists in physics and computational chemistry, and computer engineers.

A Tested and Validated Technology

Iktos has been recognized since 2018 as one of the leading players in AI applied to drug discovery.

The company was awarded several competitive grants for innovation and has acquired more than twenty pharma customers, including some of the most prestigious European and USA pharma companies such as Janssen, Merck, MSD, Pfizer, Lundbeck, Servier, UCB and Alkermes.

So far, Iktos's technology has been tested and validated in 40 plus different real-world projects in the pharmaceutical industry. In 2019, the company has established a US subsidiary, Iktos Inc.

- Iktos, Paris, France
  www.iktos.ai

Elevator Pitch

Deep-Learning-Based Drug Design

Iktos is developing a proprietary and innovative AI solution based on deep learning generative models, which enables, using existing data, the design of molecules that are optimized in silico to meet all the success criteria of a small molecule discovery project. The use of Iktos' technology enables major productivity gains in upstream pharmaceutical R&D.

Milestones

2016
- Foundation of Iktos

2017
- Winner of the Innov'Up Proto challenge, sponsored by the Paris region, securing a €100,000 non-dilutive funding
- Raising €700,000 in equity from a pool of private investors

2018
- Winner of the Concours Mondial d'Innovation, a €900,000 competitive innovation grant funded by the French Government

2019
- Research collaboration with Almirall in AI for new drug design
- Research collaboration with Janssen to utilize Iktos' AI technology to increase speed & efficiency of small molecule drug discovery
- Collaboration with Merck for use of Iktos AI technology across three drug discovery projects
- Successful closing of a collaboration with Servier in the field of AI

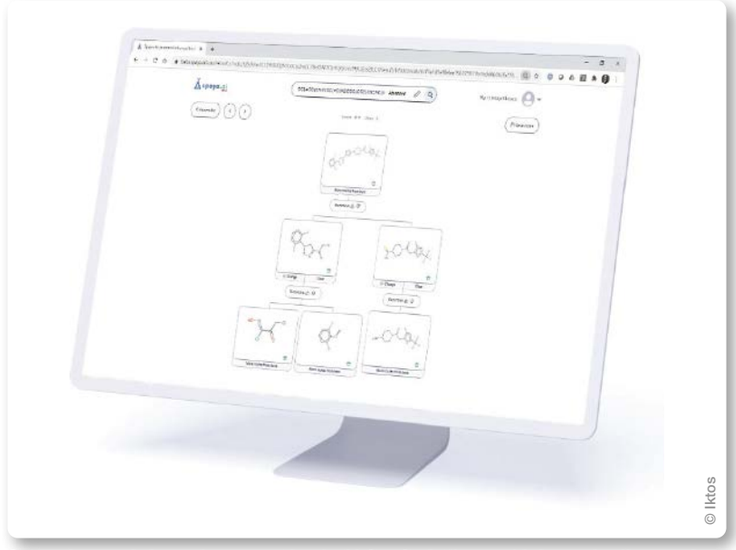
2020
- Additional Collaboration with Merck in AI for new drug design
- Collaboration with SRI International to combine AI and novel automated discovery platform for accelerated development of new anti-viral therapies

2021
- Collaboration with UCB in AI for retrosynthesis
- Collaboration with Kadmon to use AI for new drug design
- Collaboration with Facio Therapies to use AI for FSHD drug design
- Collaboration with Pfizer in AI for drug design

Roadmap

Iktos is seeking to establish new collaborations with pharmaceutical and biotechnology companies interested in the application of its AI technology to their drug discovery projects. It is also developing a SaaS software that aims to make its technology available to medicinal, computational chemistry and informatics groups.

Makya is a web-based SaaS platform for ligand-based generative modeling focusing on multi-parametric optimization (MPO).



Spaya is a web-based retrosynthesis AI SaaS platform which can be licensed as a paid version and/or deployed on customer premises and customized.

Redesigning Tomorrow's Plastics Today

Start-up Develops Bioplastics Library to Ensure Inroads to the New Plastics Economy

B4Plastics is a Belgium-based biotechnology start-up and a polymer architecture company looking to catalyze the introduction of novel biomaterials and growing them from niche to bulk applications. Based on their technology platforms, they enlarge the B4P bioplastics library with unique backbones and search for the most advanced ecological solution for plastic materials. Stefaan De Wildeman, founder and director of B4Plastics, talks about the origin, mission and future plans of the company.

B4Plastics founder, Stefaan De Wildeman, in polymer architecture laboratory.

CHEManager: Mr. De Wildeman, you founded B4Plastics 7 years ago. Did it start just then or is there a story before the story?

Stefaan De Wildeman: It really started in 2008 when I quit my biocatalysis scientist role and became a bioplastics scientist over the weekend instead. I first came up with a list of potential building blocks which would form the links for building up new polymer chains that could be turned into novel bioplastics. That finally resulted in our name: bio-based building blocks (B4) for plastics. Later, using cupcake forms and a second-hand oven, I started to "bake" the first biomaterials in the greenhouse at the back of my yard.

What was your aspiration to start a company of your own?

S. De Wildeman: B4Plastics started in my head as the pressure on the plastics industry was increasing, and sufficient competences in companies were visible to make a change. However, it is not because novel bioplastics are being discussed and promoted on social media that it also happens automatically in industry and in real life. Therefore, I was attracted to the idea of creating a start-up firm, as I believed that those were not bound to running assets but used bio-spirit as fuel instead — for some time at least, and also since I was convinced that this was the only feasible way to really initiate the change that was necessary.

What kind of support did you receive, and which obstacles did you have to master so far?

S. De Wildeman: In 2017-2018, the company entered into three new Flemish and European partnerships which provided the funding to develop new plastics and biocatalysts. We also released our two initial product lines, Compost3D and Biorix, and attracted the first employees to join the B4Plastics team. Since then, we grew to a strong expert team, countering the technical challenges daily. Underway, we bootstrapped towards the first million EUR of turnover, backed up by some loans and subsidy projects. The biggest obstacle has been to leave the golden cage as an engineer in the old industry and radically go for still vague signals that a totally new plastics economy is unavoidable — and someone has to start (co-)creating it.

When did the start-up enter into the growth phase and where are you now?

S. De Wildeman: In 2020, B4Plastics has seen an unprecedented growth phase, marked by the build-up of a new laboratory, the launch of our new website, reaching a headcount of 10 employees, selling 14 million compostable Biorix straws in shops across Belgium, and being selected by the European Innovation Council to join the 2% top league of European Green Deal Scale-Ups. One year later now, B4Plastics has made a dedicated team operational to develop key competencies in R&D, sales and production, while expanding further into biotechnology with a new lab.

What is the USP or differentiating feature of your company?

S. De Wildeman: B4Plastics offers the highest accuracy and speed bringing designed bioplastics from gram to ton scale. This is made possible by relying on our technology diagram. We use (local) rest streams and transform them into valuable bio-based building blocks that can be readily implemented in the polymer backbones. Being polymers architects, we design these novel biomaterials in such way that they fulfill the application requirements offering the best balance between function, ecology and cost.

What have been the most exciting projects so far?

S. De Wildeman: The BBI JU project Vipriscar has ended in June 2021 and validated the industrial production of the monomer isosorbide bis(methyl carbonate), or IBMC, which opens up a bright future for the development of new non-toxic polycarbonates and non-isocyanate polyurethanes. Currently, another BBI JU project, Glaukos, has also received a lot of attention due to the impact of plastic waste, as there we focus on the design and development of new bio-based and biodegradable fishing nets and textiles.

What will be the next steps to develop the company?

S. De Wildeman: At B4Plastics, we want to further deepen our polymer architecture roots as a biotech company and keep on enlarging our bioplastics library with unique backbones, with our technology platforms as strong basis. Next to that, we want to continue enforcing our team strength and expertise with a large diversity in age, capabilities and gender — women represent 50% of our team. From there, we are underway to establish the first specialty bioplastics production site in the world in Belgium.

Personal Profile

Stefaan De Wildeman graduated as a Bio-engineer (KULeuven, 1998) and finished his PhD after discovering a new dehalorespiring bacterial species (Ghent University, 2002). He joined DSM in 2002 and increasingly explored new biobased building blocks (B4) for novel materials. From there, Stefaan co-developed the Master "BioBased Materials" and created the Chair of Building Blocks at Maastricht University. His hunger for social impact made him the founder of B4Plastics — a polymer architecture company designing novel polymeric backbones from new B4, with highest speed and accuracy. Since 2020, B4Plastics joined the top-2% league of Green Deal Scale-Ups in Europe and is one of the fastest growing bioplastics companies worldwide.

Business Idea

A Fast Move from Idea to Market

Just as an architect creates anyone's dream home, the B4Plastics team creates dream plastics. They design and scale the materials to give a customer application the best balance between function, ecology and cost. This is done in three phases: screen — scale — supply.

The screening stage happens at the prototyping level (TRL1-4). First, the team defines and lists the key requirements of the bioplastic in its application based on green, optical and mechanical characteristics.

With this information, the experts design the polymer architecture and develop prototype sample materials in the lab within a time frame of several months.

When the prototype boxes are checked, the project enters into the second phase. In the scaling phase, the project moves up to pilot scale (TRL 5-8) to pilot the material for in-house tests or trials with renowned brand owners for validation and certification.

Finally, when all is validated and certified, and supply agreements are made, the team pushes the novel materials and their products to (kilo)ton scale in the third and final supply phase.

Currently, B4Plastics is developing the first specialty bioplastics production site to secure the manufacturing and finishing of the first commercial-grade materials and their products.

Relying on this business strategy, the products have already demonstrated the power of the start-up's technology platforms:

- FortePlastics: The strongest materials in the world that are still degradable in a natural habitat.
- TriggerPlastics: The best-controlled degradable materials in the world. Commercialized examples being the B4Plastics 3D filament, Compost3D, and home-compostable drinking straws, Biorix.
- RubberPlastics: The ideal elastomeric materials to help our New Plastics Economy land softly.
- LowEnergyPlastics: The lowest-energy- consuming materials during production.

- B4Plastics, Dilsen-Stokkem, Belgium
www.b4plastics.com

B4PLASTICS

Elevator Pitch

Reduce. Refuse. Rethink.

Stefaan De Wildeman founded B4Plastics with the aspiration to create new environmentally friendly plastics for a better planet. The Belgian start-up company has already opted for "reduce" and "refuse": pushing the old fossil plastics towards the new plastics economy. Being convinced that there is a whole new redesigned plastics universe waiting for use they "rethink" the plastics industry by building materials on a molecular level, to give them the best balance between functionality, ecology and cost. At B4Plastics, new polymer ambitions are in the hands of a team of bio-based-materials engineers, masters and experts — educated to create new material value chains, from the field to the product, and back.

Milestones

2014-2016
- Foundation of B4Plastics
- Development of first prototypes, transparent degradable plastics

2017-2018
- First Flemish and European partnerships, product lines (Compost3D and Biorix)
- First employees

2019-2020
- Construction of new polymer architecture lab
- Launch of new website
- Opening of new headquarters
- Staff growth to reach 10 employees
- Supply of 14 million Biorix straws
- Selection by EIC to join the 2% top league of European Green Deal Scale-ups
- Creation of technology platforms, validated leads with world-leading brands

2021
- Development of R&D, sales and production assets
- Establishment of a biotech lab

Roadmap

2021
- Q4: Expansion of the pilot park, final designs of the specialty production site in Belgium

2022
- Q1–Q2: Construction start of the production site
- Q3–Q4: First commercial ton-scale products launched based on newest technology platform materials.

By using in-house designed and developed technology platforms B4Plastics is able to create new, tailor-made eco-plastics.

Transforming the Scale-Up of Biobased Molecules

Toll-Processing Service for Scaling Up Chemically Modified Natural Polymers Production

Producing industrially relevant quantities of material for application testing has been a continuous challenge for scaling up new bio-based products. The solution offered by Finnish start-up company Mega Cellulose is a kiloton-scale open-access toll-processing service. The founder Jere Koskinen and the idea originator Ali Harlin explain the idea and the strategy behind Mega Cellulose.

Ali Harlin

Jere Koskinen

CHEManager: When did you found Mega Cellulose, how did it all start?

Jere Koskinen: The company was started in 2019 and pitched for the first time at the European Chemistry Partnering event in Frankfurt in February 2020. We were able to complete a number of smaller customer projects. But due to the pandemic, we put the project on hold for the remainder of 2020 and started operations again in early 2021 with revitalized vigor

What is the idea and driver behind Mega Cellulose?

Ali Harlin: During my career, I have seen a number of good chemical inventions that never made it out of the laboratory or small-scale pilot. Many of these inventions were lacking proper industrial demonstration. The facility that would be needed to produce sufficient volumes for industrial product validation require significant investment in terms of time and money. If this is done for each project, molecule or material, the costs are just too high. Ground-breaking novel concepts, where the process differs from the traditional platforms are especially challenging. This is why a multipurpose factory is needed, which is large and flexible enough to share the fixed costs between several projects. Natural polymeric materials, especially from lignocellulose origin, are in our focus. This makes the Mega Cellulose facility one-of-a-kind.

What is the USP or differentiating feature of Mega Cellulose? What makes your technology unique?

J. Koskinen: We are not working on our own products. Our concept is to offer scale-up for chemically modified natural polymers as a toll processing service. A kiloton-scale industrial demonstration plant of this kind will easily require €40–60 million in investment. Also, it will require some years to build. Moreover, one needs to recruit and train a team of specialists to operate the plant. When all this is available as a service, our customers will save time, capital and the effort of recruiting at the demonstration stage. This lowers all the risks associated with the industrial application testing and product validation. If they are not successful, there is nothing to write off the books later on. If there is success, the customer can move on to preparing the full-scale investment. This is the first time when the customers will need a larger dedicated in-house investment project team and a larger investment of their own capital. We estimate time savings of some 5 years and CAPEX savings of some €50 million to validate each molecule or material. When realized, this should accelerate the creation of a true bioeconomy in Europe.

Which obstacles did you have to master so far and what challenges are you seeing to get your start-up company up and running?

A. Harlin: There was a big push this year to get the first small-scale assignments from customers from order to delivered results. Prior to its main investment, Mega Cellulose is still working with borrowed and rented equipment. It needs to rapidly grow our operation in meaningful but prudent steps. The next step will be increasing the annual capacity to approximately 200 t. The site selection for this is under way in Finland and Germany.

Mega Cellulose is adopting novel processing technologies and process concepts, targeting compact, flexible and economically viable solutions. According to our vision, the future biorefineries should be simple to start up, and as easy to scale up when the initial market ramps up. This requires an interactive way of working with several parties, including customers, equipment suppliers and other partners.

What are the next steps for the company?

J. Koskinen: The next steps will be: Building a pipeline of customer cases. Building the 200-t installation in either Finland or Germany will start in 2022. Planning the larger 1,000-t plant with the experience from the preceding step will already require a steady workflow from customers. Moreover, we need to grow the team beyond the initial five members to some 25 by the end of 2022. In addition to building successful business cases for our customers, we will continue talks with potential investors. Securing financing for the growth path is the third leg we need. The fourth one is to create a network of collaboration to in- and outsource services. The fifth element will be marketing existing intellectual property rights from our partners to customers to enhance their commercial and industrial development in bioeconomy.

Personal Profiles

Ali Harlin studied chemical engineering at Helsinki University of Technology and earned his doctor in science (DSc) degree while working as a process development manager at Borealis. He is a materials scientist and research professor at VTT Technical Research Centre of Finland, and has previously acted as a professor at Tampere University of Technology and adjunct professor at Lappeenranta University of Technology. He is an inventor of several patents and also involved with several start-ups in circular and bioeconomy, most recently in Infinited Fiber Company and Rester.

Jere Koskinen earned his PhD in physical chemistry at Helsinki University, Finland. His early career encompasses academic research at Purdue University, the Empire State Paper Research Institute at the State University of New York in Syracuse, and a faculty position in paper chemistry and recycling at the Georgia Institute of Technology. For the past two decades he has worked in and with the forest and agricultural products industry. In 2014, he started off as an independent entrepreneur with Ecotradex, active in consulting circular and bioeconomy initiatives in large corporations, as well as in trading and developing new biobased materials e.g., for the packaging industry.

Business Idea

Accelerating Product Commercialization

Mega Celullose aims to accelerate bio-based product commercialization and reduce the industrial demonstration and product validation costs by half.

There are tens of thousands of working years' worth R&D work done for development of new biobased molecules in Europe alone. Many have cleared the laboratory, bench and pilot scale testing but there is no cost-efficient way to produce truckload quantities required for industrial product validation. Building a kiloton-scale demonstration plant for each molecule separately would take disproportionate amounts of time and capital. Mega Cellulose offers this step as a toll processing service along with a number of associated expert services to shorten the time and reduce the capital expenditures for scale-up.

The company's core expertise is in high-consistency chemical derivatization of natural polymers. The feedstock can be cellulose, starch, hemicellulose, lignin, chitosan or any other natural polymer. The raw materials that can be handled include industrial side streams (peels, shells and hulls), agricultural side streams (straw and husks) and recycled materials (paper, textiles, deinked pulp), and lignin and hemicellulose from new biorefineries.

Typical examples of the chemistry involved encompass cellulose hybrid ether esters, e.g. propyl hexanoate cellulose, and allylated cellulose derivatives. Similarly starch esters and ethers belong to the core menu of derivatized polymers. Hemicellulose ether esters, as well as cationic and anionic polysaccharides in general, are further examples of the type of derivatives that can be produced. Similarly modified microfibrillated and microcrystalline cellulose could also find significant industrial applications in the near future.

The company's goal is not to develop own products but to offer the demonstration plant as a service to customers. All product-related intellectual property rights would also be handed over to our customers during their demonstration campaign. Our service will also include engineering, laboratory, regulatory and IPR (intellectual property rights) service and consultation. These will be partly produced by Mega Cellulose itself but also with network partners and suppliers.

- Mega Cellulose Oy, Espoo, Finland
  www.megacellulose.com

Elevator Pitch

Toll-Processing Service for Biobased Products

Mega Cellulose was established in 2019 in Espoo, Finland. First customer projects were completed in the spring of 2021. The business is a CDMO for toll-producing chemical natural polymer derivatives. The start-up company was founded to accelerate the industrialization of new biobased products. Currently the team comprises the two founders, a business developer, a process engineer, and synthetic organic chemist with a significant amount of the work outsourced to partners and suppliers.

Milestones

2019
- Foundation of Mega Cellulose Oy

2020
- Pitch at the 4th ECP in Frankfurt, Germany (February)

2021
- First customer projects completed, also leveraging hardware from network partners for customer testing at this stage

2021
- Stepping up marketing and investor discussions
- Actively engaging customers, partners, and investors.

Roadmap

2021
- Recruiting round to complement the team
- First capital round to consolidate the status quo
- Setup of permanent laboratory facility in Finland

2022
- Site selection for 200-t/a plant (Finland or Germany)
- Financing for this first plant
- Reel in first major customer projects
- Engineering and construction of 200-t plant

2023
- Site selection for 1,000 t/a plant (10 candidates in Europe)
- Financing for 1,000-t capacity
- Developing operation of 200-t plant to a continuous pipeline

2024
- Engineering for 1,000-t capacity

2025
- Construction of 1,000-t plant
- Further financing round

2026
- Both 200 and 1,000-t plants in full operation

Mega Cellulose plans to build and operate a modular multi-product synthesis plant for chemical modification of natural polymers.

Mixed bulk reactors are particularly well suited for modification of natural polymers.

CIEX 2021 — Hybrid Event

Taking place in a hybrid format on Oct. 6–7, 2021, in Frankfurt, Germany, the conference is aimed at R&D and innovation experts from the consumer, industrial and specialty chemical sectors. By bringing together all players across the value chain, the event is a unique platform for participants to learn, exchange ideas, and collaborate. Participants will hear from and discuss with industry leaders, international experts and innovative thinkers from around the globe.
http://ciex-eu.org

Interphex 2021

This event is to take place on Oct. 19–21, 2021, in New York, NY, USA. The pharmaceutical, biotechnology, and device development and manufacturing event will be attended by industry professionals from pharmaceutical, biotech and device facilities and service providers. Interphex brings over 10,000 global industry professionals and 625+ leading suppliers together through a combination of technical conference, exhibits, demonstrations and networking events.
www.interphex.com

Bio-Europe 2021 — Virtual Event

This year's BIO-Europe will be held digitally on Oct. 25–28, 2021. The event is expected to bring together over 4,000 executives from more than 2,000 life sciences companies spanning an estimated 60+ countries. The program content in business development, therapeutic areas, startup innovations, digital health, and more will be available on demand beforehand as well as in live sessions during the conference.
www.informaconnect.com/bioeurope

CPhI Worldwide 2021 — Hybrid Event

CPhI Worldwide, taking place in Milan, Italy, on Nov. 9–11, 2021, is the leading networking event and exhibition 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.
www.cphi.com

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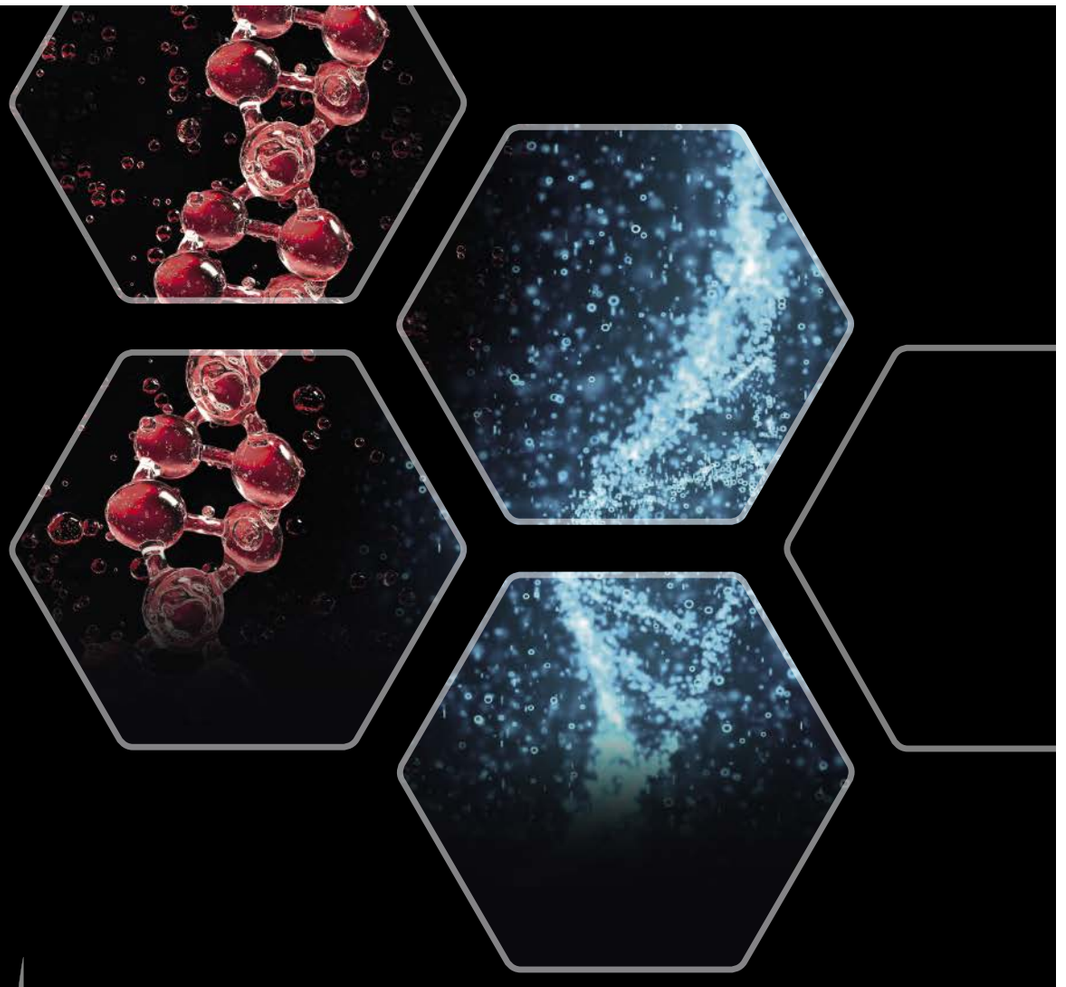

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