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Bayer Technology Services
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Hermann Tietz, the first person to carry out the idea of the department store in Germany, was well aware that good quality ensures it is the customers and not the goods that come back. And he was right. Yet there is something else to bear in mind if the customers’ wishes are to be in harmony with the expertise offered by the company: quality naturally costs a little more, but a lack of quality costs much more.

Bayer Technology Services enjoys an excellent reputation not least due to the quality of the work it carries out. But where does this high quality actually come from? How does an investment project reach its successful conclusion to the satisfaction of all concerned?

I am convinced that a major role is played by the fact that we can offer a one-stop service. We not only develop innovative processes and products, but also manage investment projects worldwide, optimize production plants and products, and offer a comprehensive range of consultancy services. This is why Bayer Technology Services is justifiably considered a driver of innovation and the technological backbone of the Bayer group.

All the while, we are at work in a unique environment: Bayer is the only global company to unite expertise concerning the health of humans, animals, and plants under one roof. And it is this that we are busy researching across a diverse range of fields. Whatever the task, whether we are manufacturing phenol from waste products, or developing mathematical models for simulating the processes inside a cell or creating the basis for developing new medicines – we have a large number of first-class scientists and experts at our disposal: engineers, natural scientists, pharmacists.

They all combine their knowledge to create solutions of value to clients and society alike. And in so doing they demonstrate that the term synergy means much more than simply reducing costs. Because at Bayer Technology Services, more than anything synergy means maximizing quality. And you will find a number of examples of how we do this in this issue of technology solutions.

I hope you enjoy the read.

Yours, Dirk Van Meirvenne

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Magnification in a scanning electron microscope reveals a soybean leaf on which a rust fungus spore is thriving. Left untreated, such infections lead to heavy crop losses. This issue deals with effective fungicides, for example in the articles on biological pest control (p. 34) and expanding the production of active ingredients (p. 42)

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eared worldwide, soybean rust can destroy as much as 80 percent of a soybean harvest. Once infected, the fungus transforms healthy soybean plants into red, burnt-looking stalks within a week. The fungicide Flint, developed by Bayer CropScience,
successfully fights soybean rust. It works by combining two active substances, the first of which disrupts the metabolism of the fungus and thus its energy balance, while the second prevents new cell membranes forming, inhibiting its growth.

Bayer Technology Services has now used its expertise to make the production of one of these active substances even more efficient. This optimized process is currently being implemented at the Swiss production site in Muttenz (see page 42). The wide-ranging fungicide is used today in around 100 crops – alongside soybeans, also in the cultivation of vegetables, vines, berries, pomes, and hops, for example.

Magnified 4,500 times, scanning electron microscopy reveals here a rust fungus spore poking its germ tube through a gap in a soybean leaf.
What Exactly Are You Developing?

There is a recurring need for innovative technological solutions – whether in product development or production processes. This is where Technology Development at Bayer Technology Services can help. The head of this division, Dr. Günter Bachlechner, explains how this works.

solutions: Bayer considers itself to be an inventor company, and each subgroup has its own research department. So why is there still a need for a development department at Bayer Technology Services?

Bachlechner: To support the subgroups – in all interdisciplinary technological areas, from research right up to production. We’re a melting pot of ideas, if you like, extending beyond the boundaries of the subgroups and devoted to those future concerns that appear promising for the further technological development of the entire Bayer group.

Working with our subgroups HealthCare, CropScience, and MaterialScience we have defined five strategic topics: process technology, biotechnology, formulations, screening technologies, and the modelling of complex systems. All with the same goal of turning ideas into solutions that can be implemented in practice.

solutions: 2,300 employees who’re paid just to think? Bachlechner: To think and implement. This figure includes all the staff at Bayer Technology Services working in every division – from the development of technical processes, via designing and constructing plants, right up to methods and instrumentation for the safe and efficient operation of facilities.

So you see implementation is just as important as thinking. After all, our job is to create reliable and efficient solutions for the industry from excellent, new ideas. And this means we need people as well as technology.

solutions: New ideas – the first thing you think of is young people coming straight from university...

Bachlechner: Of course a new generation of first-class employees is crucial. Which is why we network very closely with the best universities around the world. After all, we’re also the Bayer entry and personnel development portal for engineers and natural scientists. It is only this interaction between promising talents and experienced experts that can lead to great innovations. I believe it’s here that the value of diversity becomes unmistakably clear.

solutions: Do you have any concrete examples?

Bachlechner: Loads of them. With our expertise in the field of process technology we’re continuously discovering possible optimizations – even with tried-and-tested methods – allowing for more products of a higher quality while reducing the amount of resources and energy needed. In this way we’re supporting the subgroups in their striving for market leadership. This also involves developing innovative methods to replace fossil fuels with renewable ones.

Furthermore, we make good use of our mathematical natural scientific expertise gained from the simulation of chemical reactions in complex facilities. For example, nowadays we can simulate the metabolic process in cells and organisms, such that one day it’ll be possible to better understand diseas-

The career path

Born in 1956 in Villach, Austria, Günter Bachlechner has been head of the Technology Development division since June 2011. With his doctorate in chemistry, he began his career at Bayer Crop Protection in 1987, starting with Environmental Research in Monheim. Seven years later he was appointed project manager in portfolio management, and in 2000 took over as head of the development division at Nihon Bayer Agrochem in Tokyo. Following this he joined Industrial Operations at Bayer CropScience, before returning to research. Between 2004 and 2011 he was responsible for the area of Research Product Technology at Bayer CropScience. The Technology Development division has a total of around 400 employees, working at various sites around the world.
es and so develop the appropriate medicines more quickly.

solutions: Would you say that people and their ideas are the real added value offered by Bayer Technology Services?
Bachlechner: Yes, that’s right. The key to success is the timely identification and correct development of our expertise. In my opinion it actually makes little sense to buy in expertise or seemingly profitable innovations without examining them first. They have to be evaluated and developed. Which is exactly what we’re doing. In life science research in particular it can take up to ten years to develop a new product and successfully launch it on the market. This requires enthusiasm, dedication and patience, alongside expertise and discipline. That’s why we’ve also introduced the project manager and expert career path in addition to the traditional manager path, which rewards responsibility for staff and budgeting.

This allows talented employees to devote themselves to their areas of expertise to the extent necessary that they become leaders in the field with a worldwide reputation, which is then rewarded like a managerial qualification.

solutions: And how many people at BTS take this opportunity?
Bachlechner: Over 200 of our employees have decided on this career path … solutions: … which they are then committed to permanently?
Bachlechner: No, not necessarily. You can also switch between the two. The decisive factor is that each employee is empowered to make an entirely individual contribution to our mission of “Science For A Better Life” in the best possible way. Because this is, after all, our task – and one we take very seriously: creating added value for Bayer by way of dedicated experts and technology.

solutions: But can’t you simply buy everything you need on the market these days?
Bachlechner: No, especially not in those important new areas where we want to make life better, as per our mission. You cannot buy our solutions for screening or bio-imaging, for example, on the market. Which is exactly what gives Bayer a competitive edge. And, to be honest, we’re happy with this state of affairs.

solutions: You originally worked at Bayer Crop-
Science, a customer of Bayer Technology Services. Did the switch to the other side change your own personal point of view?

Bachlechner: Not change so much, but certainly widen. Because BTS demands of itself that it always views the projects from the customer’s perspective on the path to success. To this must be added the fact that we always develop solutions together with the customer, too. This means cooperation is a substantial part of our work. Which is why there is no alternative: It is really all about furthering Bayer as a whole. And if you take me as an example, I can say that I’m now working with my colleagues for all three subgroups at Bayer.

solutions: Are the resources available to Technology Development sufficient to meet all the demands you’ve stipulated?

Bachlechner (laughs): I’ve yet to meet the head of research who considers his or her resources adequate. No, but seriously: In research it is above all quality that determines success. And fortunately we have an excellent team at our disposal …

solutions: … made up how?

Bachlechner: We’re a team made up of laboratory technicians, technologists, natural scientists, engineers, computer scientists, and pharmacists. Experts from 22 nations, incidentally. And all put together they form an important part of innovation at Bayer.

solutions: That sounds like you already have all the experts you need.

Bachlechner: There’s no doubt that we have a great team, one that I’m very proud of. But, no, to cover every aspect of every conceivable innovation we would really have to acquire very wide-ranging expertise – in subjects outside our area of core competence. So we prefer to cooperate with our trusted partners from among the world’s best. And it is they who contribute the expertise we need.

solutions: In other words: open innovation?

Bachlechner: That’s right. And it must be said that in many areas this is an efficient and useful way of dealing with the complexities of the task in question.

solutions: What have your experiences been like so far in this field?

Bachlechner: Outstanding. And I make no secret of the fact that we’re proud when our expertise is regarded so highly that internationally renowned partners want to collaborate with us.

solutions: For example?

Bachlechner: Only recently we founded the Joint Research Center for Comp-
tational Biomedicine with the RWTH Aachen. This is concerned with examining how diseases develop and treating them with novel active ingredients using computer models. The new research center will become a leading European institute for systems biology.

Or take our INVITE research center, for example. We’re working together with the Technical University Dortmund on the “Factory of the Future” and are testing the production of fine chemicals on a pilot-project scale.

Here, too, we are pioneers – and not only from a technological point of view, but also in terms of the type of cooperation.

solutions: How do you mean?

Bachlechner: Who would’ve thought ten years ago that European competitors would sit down at one table to work on new production standards? Or that the energy and chemical sectors would collaborate on the sustainable use of CO₂? We’re all working together on this under one roof in Leverkusen right now.

solutions: And are there any tangible results yet?

Bachlechner: Oh, yes. Very good ones even. Together with international partners we have paved the way for manufacturing using a minimum of resources. And the beauty of it is that we can already prove the resulting huge benefits using standardized and modular production plants.

solutions: Is this also a part of “Science For A Better Life”?

Bachlechner: But of course. Saving resources and thus working towards sustainability are more important than ever. After all, we have to think in terms of cycles now more than ever.

solutions: For example?

Bachlechner: As I said before, in the use of environmentally-harmful carbon dioxide as a raw material in the manufacture of chemical products, for example. And we don’t only intend to demonstrate that this is possible, but also that it makes economic sense. So we’re naturally a little proud when Klaus Töpfer, founding director of the Institute of Advanced Sustainability Studies and for many years executive director of UNEP, at the official opening of our pilot plant described closing the carbon cycle as a solution to one of mankind’s major problems.

solutions: A drop in the ocean?

Bachlechner: I’d prefer to say a step in the right direction. And, what’s more, one of many that have to follow.

solutions: But, in the public’s view, the chemical industry is not usually considered a pioneer when it comes to ecology.

Bachlechner: That is unfortunately how it appears. Which is why it’s all the more important that we repeatedly point out how much people benefit from our work and to what extent we really do contribute to improving the quality of life.

solutions: Yet this improvement to the quality of life refers to the most varied areas. From developing active ingredients for medicines right up to using CO₂ as a raw material in the production of plastics. Why are you concerned with so many different issues?

Bachlechner: They’re not that different. If you take a closer look at these fields, you’ll see that they all have a common basis.

As far as I know, Bayer is the only global company researching on such a broad scale all three biological systems: humans, plants, and animals. Because all three share one thing in common: the biochemical metabolism in cells. If we can understand these interconnections, then we can manipulate complex molecules using bacteria, develop active ingredients and biologics or, put simply, protect and treat humans, animals, and plants.

“As far as I know, Bayer is the only global company researching on such a broad scale all three biological systems: humans, plants, and animals.”
Southern Saskatchewan is practically nothing but prairies and wheatfields. Apart from some ridges, small lakes - and those long, icy-cold winters. Yet much has already been realized in just a few months as part of the K+S “Legacy” project, including the first boreholes in the earth, through which hot water will be pumped to force a highly concentrated solution to the surface.
Megaproject in the Prairies

Life can get pretty lonely in Saskatchewan. Yet this has not stopped several Bayer employees from relocating to the Canadian province. A subsidiary of K+S is building a potash mine there, and has commissioned Bayer Technology Services with managing the project.
Liu Jiang is used to driving for two hours each way to work. When traffic was bad in Shanghai, his daily trip to the Bayer plant in the Shanghai Chemical Industry Park, some 30 miles south of the Chinese metropolis, would take up to two hours. Even today, living and working in Canada, the chemical engineer spends just as long traveling to the K+S construction site in southern Saskatchewan. Driving in Shanghai, however, was a slightly different experience.

Liu now covers 125 miles in the same time, but unlike in Shanghai, just ten minutes into his journey he will have left the outskirts of Saskatoon behind him. From here onwards, all he sees from Highway 11 are endless fields of wheat and rapeseed.

The route towards the provincial capital, Regina, is at times so straight that Liu hardly needs to turn the steering wheel. Accidents with other vehicles are not a great danger, but falling asleep at the wheel is. If, on occasion, his journey does come to a standstill, it is not due to traffic jams, but rather to icy roads in the midst of a winter blizzard or slow-moving farm equipment in summer.

Liu still remembers the first trip he made to his new job site. About a year ago, all he could see around him was cropland, and he wondered where the construction site was going to be – especially one so large. The customer, K+S and its Canadian subsidiary K+S Potash Canada GP, would be investing around 4.1 billion Canadian dollars in developing a potash mine to be completed in 2016, a sum exceeding the total investment costs of all the Bayer plants that Liu had supervised during his ten years in Shanghai, including some world-scale projects. Yet aside from a few isolated signs referring to “K+S Potash Canada,” there was little to be seen for miles.

Little changed even after Liu had finally reached the K+S premises and passed the security checkpoint. Across the fields the first drilling rigs could be seen, which K+S would use to drill the wells from which the potash would later be mined. It was only after driving another 15 minutes along a gravel road that he found himself standing in front of some portable cabins used as offices, in the middle of nowhere. Apart from a huge water pipe and some digging in places, there was not much else to see.

“What a difference,” thought Liu. “In the middle of wheat and “big sky” and without any infrastructure.” The chemical plants he had previously worked at were small in comparison. Hardly surprising considering the plan was to tap into an underground reserve of an estimated 160 million tons of potassium chloride. Enough to provide every person on earth with more than 20 kilograms of potassium chloride each – and to fill almost two million railroad cars. A train this long would span the entire globe.

However, a lot of work has to be done before K+S can load the first railcars. Not only does the railroad connection exist purely on paper, but the potash also has to be mined from at least a mile underground. It is going to be a technical challenge.

“There was really nothing there,” recalls Dr. Gerd Dahlhoff, Head of Bayer Technology Services Canada, who started work on the site prior to his colleague, Liu Jiang. Other than the arrow-straight gravel roads that divide the fields of southern Saskatchewan,

“All human cells are reliant on potassium. In fact, our daily intake of nutrients should include at least two grams of this alkali metal. Plants need it, too: if they do not have enough, their leaves fade and their metabolism is affected. This is why potassium is considered the third most important nutrient for plants after nitrogen and phosphorus, and thus a basic component of many fertilizers. Studies have shown that fertilization using potassium can greatly increase the yield of corn, wheat and soybeans. In 2013, the global demand for potassium reached almost 60 million tons, over half of which was put to agricultural use. Furthermore, potassium salts play an important role in the industrial production of chlorine, for example, and in the manufacture of building materials and plastics, as well as in the pharmaceutical industry, such as for the production of insulin. One of the world’s largest manufacturers of potassium products is K+S in Kassel, Germany.

In 2011, K+S acquired the Canadian company, Potash One, so as to increase its own manufacturing capacities. Alongside the world-class reserves of around one billion tons of potassium chloride, this deal includes the relevant environmental certification for mining the 160 million tons of the Legacy project.

The need for potassium
This area of no man’s land in Saskatchewan needs an infrastructure before the huge reserves of potash can be mined. Starting with proper roads (above), which only then allow the material and machinery to be transported (below).
Saskatchewan like a checkerboard, it really was a lot of wheat and an endless blue sky. These roads were unsuitable at first, however, and had to be reinforced before they could support the heavy trucks supplying the necessary building materials.

The main task was developing the infrastructure for mining the potash and constructing the huge above-ground processing plants in this landscape with its many lakes. However, there was also the peak workforce of almost two thousand construction workers to think about. This meant installing offices and housing, a water and gas supply, a wastewater disposal system, and electricity. The project site even had to be connected to the cellular network.

Internally, K+S named the project “Legacy.” To ensure that a project of this size and complexity ran smoothly, K+S sought a project management and engineering partner for their “Owner’s Team”. They needed a partner who had both the technical expertise required as well as substantial experience in handling large-scale projects.

The decision to commission Bayer Technology Services began three years earlier at a meeting of Aachen University alumni. Dr. Jürgen Barge, then in an executive position at K+S, and Dr. Wilfried Kopp, head of ‘Chemicals’ within Project Management & Engineering at Bayer Technology Services were talking about their career paths since receiving their degrees. Barge mentioned to Kopp that his company had acquired the Canadian Potash One in 2011, and now had several exploration permits for potash, which were being combined into one megaproject. He also said that K+S was still looking for a partner to join the Owner’s Team to provide project management and related services.

This caught Kopp’s attention: “We have a lot of experience in large project development, so why not work with us!” Which is exactly what K+S did. This led to Dahlhoff, Liu and ten other colleagues from Bayer Technology Services relocating to Saskatoon – many of whom had already met on similarly large projects in Shanghai.

Dahlhoff had also worked in the Chinese metropolis for eight years, supervising several major projects there, before returning to Germany in mid-2012. He had not been back in Germany long when K+S confirmed the Saskatchewan project. At short notice, he put together a strong Bayer team for Legacy, established the Canadian division of Bayer Technology Services and was appointed as its manager. At the same time, he was made one of the three managers of the so-called “Execution Team” for the K+S project, responsible for engineering, procurement, and contract management, as well as the actual construction of the facility and the site development.

It is interesting to note here a further role played by Dahlhoff at K+S that is both unusual and another example of the deep integration of the Bayer teams: As Vice President Controls at K+S Potash Canada he also reports to the CEO there,
Making the grade

Unlike oil or natural gas, potash cannot be simply pumped from a depth of one mile underground. The method chosen for the Legacy project was potash solution mining. Initially, two large bore-holes of equal depth are drilled into the earth, 80 yards apart, into which inner and outer pipes are inserted. Hot water is then injected into the outer pipe to dissolve the sodium chloride seam, found under the potash seam. This creates a brine which is then pumped to the surface. At this stage, a special layer of hydrocarbons is injected into the potash seam to prevent its premature dissolution. Eventually, the cavities under both bore-holes become so large that they combine to form a cavern. Gradually, the potassium chloride is dissolved and the highly concentrated solution is then pumped up to the surface. Because this is a mixture of sodium and potassium chloride, further purification stages follow above ground. In order to reach customers around the world, the salt will be transported by rail to the port of Vancouver, 800 miles away. From there two further Bayer Technology Services employees are already preparing the entire logistics strategy.

Dr. Ulrich Lamp: “If you take a closer look, you’ll see this is absolutely essential for the day-to-day operations. Nonetheless, I consider this a special responsibility and proof of the great amount of trust involved.”

Liu Jiang, on the other hand, is a part of the “Owner’s Team”, which will play a key role in the design phase and in supporting the field engineering and execution on the construction site. He is responsible for the largest of the facilities on site – the “Evaporation, Clarification, Crystallization” units, which are currently being manufactured in China, among other places. This is where the extracted saline solution will be purified and crystallized. At the same time, he also needs to ensure that the “Early Cavern Development” division is ready by October of this year – a prerequisite for tapping into the potash reserves and starting operation of the main plant.

Gerd Dahlhoff is extremely excited about the project. “This is part of the future of K+S, and we can add our expertise.” The client is equally pleased with the project. “Bayer Technology Services suits us very well, starting with our common German background. They have a lot of experience in handling major projects, particularly on a global scale, and all-important specialist know-how in chemicals, which will complement our own expertise significantly,” says Lamp. He is also impressed with the way Dahlhoff’s colleagues cooperate and their dedication to the project: “If you didn’t know better, you wouldn’t be able to tell the difference between their staff and our own.”

The teams have already achieved a lot in the first year of the project. This is all the more impressive when you consider the long harsh winters in Saskatchewan, where the temperature can drop to -50°C, making construction work above ground a particular challenge from November through April. Nevertheless, there is a temporary cabin camp where the numerous skilled workers live, equipped with 1,500 beds, a kitchen complex, gyms and an entertainment center – kind of like a resort hotel. “It’s the largest settlement between Regina and Saskatoon,” Dahlhoff adds with a smile. “And even then they are still close to 200 miles apart.”

Liu’s Early Cavern Development is heading for completion in the last quarter of this year. Driving in the piles for the main complex is progressing at a good pace and the initial drilling into the reserves is almost completed. For Liu and his coworkers, the action will soon move away from the Saskatchewan office toward the Legacy construction site.

After all, there is still so much to do. By 2016, 36 caverns (see: “Making the grade”) will have been created. These will supply the initial tons of potash, which K+S plans to ship via rail to the export facility near Vancouver, and then via bulk carrier ships to K+S’s worldwide customer base. Just one year after that, K+S aims to produce two million tons, and in the years that follow, this will continuously increase to around three or even up to four million tons a year. It is estimated that it will take more than 50 years before the current deposits have been mined. Legacy is certainly a project of the century.

However, Bayer Technology Services will not be staying that long. Dahlhoff estimates that for most of his employees work will be finished by 2016, or at the latest by the beginning of 2017. If everything continues to run as smoothly as it has until now, the head of Bayer Technology Services Canada will not have to worry about the project: “Budgeting and scheduling a megaproject of this kind is undoubtedly a challenge. But the team from K+S is well organized, has a great deal of technical expertise and an experienced local contractor. Our first ton of potash will be delivered to the customer on time in 2016.”

“Our experience in handling major projects will complement our own expertise significantly.”
Dr. Ulrich Lamp, Chief Executive Officer, K+S Potash Canada
Leslaw Mleczko is Bayer’s catalysis specialist. As a key expert, he scours colleges and universities the world over for new developments that could be of interest to the group. And he keeps a lookout for new talent. In a way, he is like a catalyst. He triggers processes, monitors them for a while, and then, as fresh as ever, moves on.

Mleczko searches the world over for suitable catalyst specialists for Bayer, using his numerous international contacts to professors. “After all, they know their students and send me their best.” What he modestly fails to mention is that, more importantly, the professors also know him – and his standards. And they are demanding. As he says, “I’m looking for really creative people.” Mleczko, who is originally from Poland, is well acquainted with the academic environment. He has been lecturing since 2002 at the Ruhr-University in Bochum, Germany, and has been a visiting professor since 2008 at the East China University of Science and Technology in Shanghai. Mleczko considers his own life to have been “more or less a series of fortuitous coincidences.” After earning his doctorate with a thesis on a subject from process technology, he received an invitation to go to Germany. He was doing postdoc research at the University of Hanover when he received an offer from Toronto. But he turned it down and went instead to Bochum to the Ruhr-University, because he was enticed by the offer of heading the Catalytic Reaction Engineering Group. In 1996, he qualified as a university lecturer in reaction engineering. And one year later he joined Bayer. “Actually, I only wanted to stay one year,” he says and adds with a chuckle, “and now here I am, still here.” But this was no coincidence. There are a myriad of activities in the company that fascinate him. “They have developed many new processes and implemented them here. You don’t see that at universities,” he notes. A particularly positive aspect, he feels, is being able, thanks to his work in research, to maintain contact with universities and students, many of whom he has been able to lure into the company. He knows that “young people bring fresh ideas with them. That stimulates your own creative juices.”

This is why he is held in such high esteem outside the company, too. “Professor Mleczko is one of the world’s foremost catalysis experts,” notes Prof. Andrzej Górak, Prorector Research at the Technical University Dortmund, which works closely with Bayer Technology Services. There is a simple reason why Mleczko’s expertise is in such demand in the chemical industry: catalytic processes are one of the key technologies. The majority of the roughly 25,000 processes that produce basic chemicals today are run exclusively with the aid of catalysts. And the experts are convinced catalysts can do far more than is known so far, for example, realizing the dream of converting the harmful greenhouse gas carbon dioxide into an economical chemical resource.

This, however, would require completely new catalysts, and to develop them, Mleczko emphasizes, you have to understand...
since 2011. Partnering this project are the energy provider RWE Power, the RWTH Aachen University, and the CAT Catalytic Center. The Bayer experts tested over 200 catalysts until they found a suitable one. The industrial production of raw materials for polyurethane using this unusual resource will begin at the end of 2015.

A second example of seeking to make use of this climate pollutant goes one step further. The initiative, CO2RECT, founded in 2010, is taking the approach of storing surplus power from alternative energy sources. With the help of this power, hydrogen is produced from water. Together with CO₂, with the aid of a catalyst, this can be converted into intermediates for polymers - either carbon monoxide or formic acid. RWE, Siemens, and a number of prominent institutions are contributing their expertise and experience to this project supported by the German Federal Ministry of Education and Research. Bayer Technology Services and the group headed by Leslaw Mleczko have the overall responsibility. They are developing catalysts designed to accelerate the reaction of hydrogen and carbon dioxide. “The research project is running superbly,” he says. But he cautions against any high hopes for success in the near future, “It’ll be many years before we see its technical implementation. Some time after 2020.”

Key technology

Around 90 percent of all chemical raw materials are produced with the aid of catalysts. Without them we would have neither fuel nor plastics, there would be no pharmaceuticals or pesticides and also no auxiliary materials for the electronics and semiconductor industries. Catalysts facilitate innumerable chemical reactions; many would be impossible without them. The expert selection of a catalyst has a major influence on the results of a reaction. This is the reason chemists strive to fine-tune these facilitators so that only the desired result is produced.
“Downtime? Not with us!”

Chemical equipment should be ready to go into operation whenever needed and then deliver top quality. The Asset Lifecycle Management unit at Bayer Technology Services is there to ensure both, on a sound economic basis.
hen Carlos Hedler recently purchased a new mixer for his kitchen, he did not just look at the price. Being an electrical engineer with a Master in Business and Administration, it was far more important to him that the new device was solidly constructed of robust materials. “I’ll gladly spend more money for that,” says the native Brazilian. An extra expense that pays off in the end. “What’s the use of saving money if I have to buy a new mixer again in a year?” That not only costs more money but also time. And maybe even nerves, if, for example, the appliance stops working at the exact moment you need it most.

A seemingly banal example taken from a domestic household, but one that clearly reflects the underlying philosophy that plays a key role in Hedler’s everyday professional life. Hedler is in charge of the Asset Lifecycle Management (ALCM) unit at Bayer Technology Services. One way to describe the task of his around forty-member team is that, together with their partners in the Bayer subgroups, they ensure all facilities enjoy the maximum of availability and reliability. This includes reactors, distillation columns, and agitators, as well as such smaller components as pumps, compressors, valves, and pipes. And here, too, it is a question of finding the right solution and not necessarily the cheapest. This is especially true when it comes to ensuring the high operational availability and the long service life of a production facility.

The ALCM team’s work begins as early as the designing of a new facility. For example, the preparations for Bayer MaterialScience’s new, world-scale TDI production plant in Dormagen (see technology solutions 2013, p. 26). Toluene diisocyanate (TDI) is an important raw material for the flexible polyurethane foam used in upholstery, mattresses, and car seats. People from Hedler’s team were called in when, among other things, various materials were evaluated for certain components that were potentially susceptible to corrosion. “In such cases, we carry out meticulous corrosion testing,” explains Hedler. This involves complex computer modeling covering not only the planned operational conditions but also the characteristics of the individual materials with which specific parts of the system come into contact. “Based on such calculations, we changed the
culcates the ranges of the individual “right conditions” in a system and also about the “integrity operating windows” (IOW). “Those are the areas in which a plant can be operated with notably little wear and tear, ensuring a long operating time,” he points out and adds, “A major concern is corrosion because of the many metal components. We specifically look for thresholds above which the risk of corrosion significantly increases.” Then, among other things, alarm systems are installed that react when these limits are exceeded. Just like a car’s tachometer needle goes into the red when the driver revs the engine too high. Such “operating windows” have long since been standard when dealing with safety concerns. “Now we’ve extended this approach to include reliability aspects,” states Hedler. His team calculates the ranges of the individual “right conditions” in complex models and simulates standard operating conditions, along with further scenarios such as a system’s start-up and shut-down. The overall objectives are clear: to increase the operating time of the system’s components and prevent system downtime due to damage.

What Success Creates

Part of this design for reliability concept is also determining the optimal ranges for certain operating parameters, such as temperature, pressure, and humidity, in the various system segments. Hedler likes to talk about the “right conditions” and also about the “integrity operating windows” (IOW). “Those are the areas in which a plant can be operated with notably little wear and tear, ensuring a long operating time,” he points out and adds, “A major concern is corrosion because of the many metal components. We specifically look for thresholds above which the risk of corrosion significantly increases.” Then, among other things, alarm systems are installed that react when these limits are exceeded. Just like a car’s tachometer needle goes into the red when the driver revs the engine too high. Such “operating windows” have long since been standard when dealing with safety concerns. “Now we’ve extended this approach to include reliability aspects,” states Hedler. His team calculates the ranges of the individual “right conditions” in complex models and simulates standard operating conditions, along with further scenarios such as a system’s start-up and shut-down. The overall objectives are clear: to increase the operating time of the system’s components and prevent system downtime due to damage.

Naturally, a plant’s operation is never completely without some turnarounds. For example, there are mandatory inspections by authorities, which take place at set intervals, depending on the particular country. Advising and supporting the clients so as to ensure such downtimes are conducted as flawlessly and efficiently as possible also falls within the ALCM’s area of responsibility. This, again, is something the experts keep in mind when planning a new facility. In the case of the Dormagen TDI plant, for example, the team took into consideration from the beginning places where the thickness of a wall would have to be measured later on or the tightness of a seal tested. “Now we construct such spots to be easily accessible right from the start and, for example, insert a window in the insulating material for just that purpose,” Hedler explains. In short, forward thinking that was previously not necessarily the case.

Another element has also become standard in the meantime. Whereas until now the wall thickness at critical points in a system would only have been measured during an inspection, these days ALCM conducts such a measurement program prior to the initial system start-up – a “baseline measurement” so to speak. Having these reference points proves to be a great advantage – at the latest by the time of the first inspection. “We then not only see if all the numbers are still OK, but also immediately see the changes over time,” says Hedler. Just as a car driver only knows when he is losing oil if he has already checked it once beforehand, plant operators can learn much from a baseline; for example, where the thickness of a material has shrunk faster than elsewhere.

The inspection program itself has also changed. Hedler’s team now practices risk-based inspections (RBI), a procedure that is comparatively new within the chemical industry (see technology solutions 2011, p. 20). Instead of across-the-board set intervals for inspection, the probability that something can occur is determined for each individual component and what the consequences would be. This results in a kind of risk matrix and the intervals for inspection are set accordingly. “For some inspections, once every ten years is enough,” says Hedler, “while more critical spots will conceivably be examined in shorter cycles.”

The expert compares it to a company’s fleet of vehicles, “Instead of checking the vehicles every two years, for example, it make more sense to inspect those used the most every year, while inspecting those less used every four or

“We had 60 percent less costs during our latest inspection and, as a result, also reduced our production losses.”

Erwin Dieterich, Head of the Antwerp aniline plant, Bayer MaterialScience
five years.” In the final analysis, the effort and expense is perhaps even less than a biennial inspection of all the vehicles. And even availability could profit in the long run, since the vehicles used the most would be checked more often and thus be less prone to break down.

The experience made with RBI has been good. For example, the head of production at Bayer MaterialScience’s aniline plant in Antwerp, Erwin Dieterich, was extremely pleased following the latest inspection: “We had 60 percent less costs and also reduced our production losses due to downtime.” The water pipes in the new TDI plant in Dormagen will also need to be inspected less often in the future thanks to the choice of stainless steel, since the risk of corrosion is lower than with normal steel.

When Carlos Hedler talks about his work, he likes to refer to other industries. The engineers in the aviation industry, for example, naturally aim to minimize the time their fleets spend on the ground. When it comes to Lufthansa Technik, Hedler virtually goes into raptures, exclaiming, “They have systematic online data collection and analysis and know exactly when each part has to be replaced to keep their planes in the air.”

Data and its uses – now that is a subject with a lot of potential still. The systematic analysis of data collected worldwide is also set to aid Bayer in gaining valuable insights into asset management. According to Hedler, modern database models, data mining concepts, and self-adaptive systems will make integrated asset monitoring possible in the future. Results from individual plants that perhaps have not revealed much until now are more than capable, with a global perspective, of providing significant information. “For example,” declares Hedler, “when we suddenly realize that a certain pump always breaks down prematurely under certain operating conditions.” If he has his way, intelligent computer programs will soon be helping to derive such information from the volume of data accumulated worldwide.

Hedler has also found the automotive industry to be a source of inspiration for his work. At first glance, an automobile assembly line has conceivably little to do with the designing of a chemical plant. Nonetheless, there are many comparisons, as Hedler points out: “They also reflect on ways to prevent downtime on their production line. They use an extensive database of past events to calculate failure probabilities. They then estimate the effects of such failures and search for prevention strategies. So there are many things in their fundamental procedure that are exactly like our own.”

And, in the final analysis, it is also not that much different at home with the Hedlers. The kitchen mixer, at any rate, has been operationally available 24/7 since its purchase – thanks to life-cycle based investment planning.
In the Face of Adversity

Despite the devastation caused by Hurricane Sandy, the new Bayer HealthCare USA headquarters was completed within a mere 14 months. This was due entirely to the supreme commitment of all concerned.

Built in just over one year: the new Bayer HealthCare U.S. headquarters in Whippany, New Jersey.

Lost their homes, and were forced to live temporarily in tents as their neighborhood had been severely damaged. And of all the times for this to happen, it had to be at a stage when construction was meant to proceed quickly. After all, the building was intended to be opened and occupied one year later, in October 2013.

For a project costing 300 million U.S. dollars, one year of construction is extremely short. Fortunately, the two people leading the project at Bayer Technology Services, Rob McElhany and Egbert Heinze, were supported by a highly motivated team – not only their Bayer colleagues, but also the many employees involved from other companies. “Although many of them were living in temporary accommodation after the hurricane, they continued working at top speed while adhering to the safety requirements – and with no less enthusiasm,” recalls Heinze, still visibly impressed.

The project has long since been completed for Heinze. Despite all the difficulties, the building was finished according to schedule – and within budget. The first employees began moving in at the end of June 2013, with the rest following by October, after a construction period of just 14 months. The headquarters provides office space for some 2,400 Bayer HealthCare staff over a total area of around 65,000 square meters. The open-space layout is spread over two separate buildings, linked by a glass atrium. With its 25-meter-high ceiling, the atrium proved to be a particular structural challenge for the engineers. “The design was completely without pillars, meaning it had to be self-supporting,” Heinze explains. “In the end we solved this with huge sheets of glass weighing over 350 kilograms, which were joined together using a special adhesive.”

The project team also paid constant attention to such aspects as energy efficiency and sustainability in terms of the architectural design itself as well as the building materials used. This is reflected in the many LEED certificates issued for the new building. LEED stands for Leadership in Energy and Environmental Design and is commonly used in the USA to evaluate environmental friendliness and sustainability within the construction industry.

With its new U.S. headquarters established in Whippany, Bayer HealthCare has closed down and merged some of its locations in Morristown, Montville, and Wayne (all in New Jersey), as well as in Tarrytown (New York).
YOUNG TALENT HONORED

Bayer Technology Services has honored the outstanding graduates from the biochemical and chemical engineering programs at TU Dortmund University. Those honored were Malte Fittkau (second from the left) for biochemical engineering and Sebastian Rieks (second from the right) for chemical engineering, who graduated with a grade point average of 1.4 and 1.2 respectively, on a descending scale of 1 to 6. The awards were present by Dr. Günter Bachlechner, Head of Technology Development (left). Bayer Technology Services further strengthens its partnership with the renowned college, which provides a significant percentage of the young engineers who join Bayer each year.

NEW REGIONAL HEADS

As of July 1, 2014 Jan-Peter Schmelz has been responsible for Bayer Technology Services Mexico. He replaces Dr. Thomas Sperling, who is now heading part of a major investment project in Wuppertal. Dr. Yun Chen has been head of Bayer Technology Services Asia since the beginning of 2014 and is also Managing Director of Bayer Technology and Engineering (Shanghai) Co. Ltd. The chemist has been working at Bayer since 1994 and succeeds Dr. Martin Franke, who now holds an executive function in Dormagen. BTS Asia runs projects in East Asia, especially in China. Samme Wang took over as head of Bayer Technology Services Singapore in October 2013, replacing Dr. Olaf Stange. BTS Singapore manages projects in South East Asia, Australia, and New Zealand.

INVESTMENT IN BIOLOGICS

Bayer is currently investing around 500 million euros at its sites in Leverkusen and Wuppertal to expand manufacturing capacities for hemophilia-A products – so-called recombinant factor VIII products. Until now Berkeley, in California, USA was the sole Bayer site manufacturing the blood clotting factor VIII, a protein used in treating hemophilia A.

Bayer Technology Services supports Bayer HealthCare in the technology transfer needed for the biological manufacture of the active substance as well as in the planning and construction of the new facilities. In Wuppertal alone this means the construction of three new buildings for the production and storage of the factor VIII products, as well as a quality testing laboratory. The sterilized bottling and packaging is to be carried out in Leverkusen. As a result of these investments, an additional 500 jobs are to be created by 2020.

Coming to Germany: the production of factor VIII at Bayer HealthCare (here in Berkeley, California).
Each person is unique—we are quick to recognize that. But it is harder to recognize the differences in cell molecular activity in an individual. Yet, once this is achieved, it might be possible to customize therapy.
Some cancer patients are given the same diagnosis. Despite this, the pathomechanism in their cells can be different. High-performance analytics from Bayer Technology Services help in identifying these differences. The final goal is to personalize patients’ treatment.
he statistics are merciless. Colon cancer claims over 600,000 lives worldwide—year in and year out. It is the fourth most common cause of death among all types of cancerous tumors. Yet many patients would live longer if they could be diagnosed early enough and treated with existing, readily available drugs. The problem is, however, that not every drug has the same effect on every patient. For this reason, physicians would love to be able to test a drug’s likely effectiveness for a particular patient in advance.

And this is a task for OncoTrack. OncoTrack is a project financed by the EU-wide Innovative Medicines Initiative (see page 38), headed by Dr. David Henderson of Bayer HealthCare and Prof. Hans Lehrach at the Max Planck Institute of Molecular Genetics. Collaborating on this project are close to eighty scientists from both industrial and academic research. One of the ways they are developing a test is closely examining tumor cells from some thirty patients with colon cancer.

This involves employing a very special technique supplied by Bayer Technology Services. The researchers call it RPPA, which stands for reverse-phase protein array. Bayer Technology Services has developed its own RPPA platform based on know-how gained several years ago through its acquisition of a Swiss company, Zeptosens.

What makes RPPA so interesting is that it can identify a whole series of different proteins from a single sample and, at the same time, even register variations in the concentrations of a single protein compared to control samples. This technology has a myriad of applications in a number of fields, such that Bayer CropScience also makes use of it in joint projects. Dr. Mathias Gehrmann is well aware how concerted evidence of several proteins can be of great significance, particularly in cancer patients. He works at Bayer Technology Services in the field of Enabling Technologies in the Bioanalytics group, which is also responsible for the RPPA platform. “The composition of the proteins in the cells provides information about whether a signal path is active or not,” he explains. When scientists refer to a signal path they mean a type of molecular cascade that ultimately transmits specific commands. The messages are transferred by chemical means from one molecule to the next, which are, as a rule, proteins, until the messages eventually reach their destination, for example, the cell nucleus. When such signal paths are out of control, it can lead to uncontrolled cell division, even though this is not physiologically necessary, or to a breakdown in apoptosis, also known
Each tumor can appear differently on the cellular level. Tissue samples (above) provide information. A detection procedure from Bayer Technology Services makes certain protein patterns visible and shows which signal paths are impaired (below).
What Affects the World

“Compared to other methods, our approach is a whole lot faster – and also more sensitive.”

Dr. Mathias Gehrmann, Bioanalytics, Bayer Technology Services

as programmed cell death. Both of these malfunctions are typical of many tumor cells.

The special problem among tumor patients is that even when people are suffering from the same type of cancer, it does not necessarily mean that the same signal paths are disrupted. Or, as the biochemist, Dr. Henderson expresses it, “Two people can have colon cancer that is completely different on the cellular level.” This is also one of the reasons why some medications are effective with one patient and not with another. Many drugs have been developed to have a regulatory effect on specific signal paths – but have no effect on others.

This is where RPPA comes into play. The particular signal paths that are dysfunctional in a specific tumor are also expressed in the degree to which a certain protein has been modified. RPPA technology can determine the extent of this modification – and, as Dr. Gehrmann puts it, do it “for a lot of proteins in a single go.” As he sees it, this method is even “a whole lot faster and more sensitive” than other comparable methods.

The researchers use antibodies to identify a protein in a sample, since an antibody can be found for almost every protein that it bonds well with. This means that a whole series of antibodies can be used in protein analytics, depending on how many proteins are to be identified in a sample. If these proteins are actually present, the corresponding antibody gets caught, as if on a fishing hook.

If the antibody molecule is previously coupled with a fluorescent dye, the protein can even be made visible. And what is even more important for these researchers is that it makes the relative concentration of the protein much more easily measurable when compared to (healthy) cells, because the stronger the light signal, the greater the amount of a specific protein in the sample.

By itself, that is nothing new. Actually, this is normal practice in protein analytics. Yet, RPPA technology is substantially different from other methods. In most of the procedures, the antibodies are first placed on a carrier plate, a so-called array, and then the sample is added. With the RPPA approach, it is exactly the opposite, first the sample and then the antibody – hence the term “reversed phase.”

The advantage is that “In this way, a large number of different samples can be examined at the same time on a single array,” explains bioimaging expert Daniel Rechsteiner, who played a decisive role at Bayer Technology Services in the further development of the RPPA method. The biochemist further emphasizes that this approach makes the analysis substantially more flexible because, once prepared, an array can handle any antibody.

All this happens completely automatically and with a high sample throughput. The hardware needed is also supplied by Bayer Technology Services, with some of this highly specialized equipment having been developed in-house. Among these is the optical procedure that makes proteins visible and measurable after bonding with antibodies. The RPPA approach by Bayer Technology Services also scores with a further advantage that is thanks to, as Rechsteiner calls it, a “twist of physics.” This is his way of describing what is known in scientific circles as an integrated planar waveguide. This is what causes the laser beam, which excites the dye on the captured antibodies, to

Shine a light

Light can not only be “contained” in round glass fibers (as used in modern broadband data transmission), but also in flat layers. And it is these planar waveguides (PWG) that Bayer Technology Services is using for protein analysis. Sample arrays are coated with a layer of tantalum pentoxide just 0.2 micrometers thick, through which a laser beam is directed diagonally (right). This leads to an electromagnetic field close by – causing all the dye molecules on the array to shine. And this is namely wherever antibodies have bonded to the proteins in the sample. The intensity of the fluorescence in each case depends on the amount of dye – and can be measured using a CCD camera. Other methods where the laser beam scans the array from above have two disadvantages compared to planar waveguides: to begin with, they are considerably less sensitive due to light scattering, and part of the laser beam is reflected by the array, concealing the signals sent by the luminescent dye.
propagate through only one layer of the array, the one that conveniently happens to be the layer with the sample molecules and antibodies (see box). “In this way, random signals can be circumvented and the sensitivity of the whole procedure is substantially increased,” emphasizes Rechsteiner.

Sensitivity in this case primarily means that decidedly small amounts of samples are enough to identify the proteins. In concrete terms, a mere 0.4 billionth of a liter of a sample is spotted on the array. That is such a minuscule amount that about 100,000 of these samples would fit into a single drop of water. Other methods require considerably more sample material.

But no matter how small the amount of sample may be, only those proteins can be identified for which the researchers have a matching antibody available. And they do not grow on trees but are in fact the result of further expert research. And this is yet another major advantage of the RPPA platform: the experts at Bayer Technology Services have an outstandingly large pool of antibodies for various applications. “For cancer alone, we have over 300 tests for specific tumor-related proteins,” Rechsteiner points out.

“This expertise will help us to break down the individual differences in the formation of cancer,” says Dr. Christian Regenbrecht, molecular biologist at the pathological institute of the Berlin Charité hospital and head of an OncoTrack subproject. At the moment, patients are being sought whose tumor tissue can be examined. “We will use highly validated antibodies to identify, for example, specific protein modifications produced by dysregulated enzymes,” explains Dr. Gehrmann. This, in turn, will allow conclusions to be drawn about the individual, impaired signal paths. “Ideally, this will reveal which specific mechanism leads to cancer in which patient,” he says.

And that would be a vital clue in answering the question as to which medication can really help in which case. Thousands of lives may depend on this knowledge.

Scattered blue light makes two lines visible (left). The arrays are then prepared along these lines such that a laser beam is directly channeled into the planar waveguide. This is also where the samples are to be found, which have been added to the array using a special device (right).
The wine-crate-sized container looks surprisingly like a beating heart. Surrounded by surveillance monitors, hoses and pumps, it swings back and forth every second, keeping its liquid contents in constant motion. In fact, the object that swings so steadily in the E 41 building at the Leverkusen Chempark is a heart – the heart of an innovative concept for the production of biologics.

Biologics? Dr. Andrea Vester positively glows at the mention of the word. Sitting just a few feet away in her office, she gladly explains the term: “Biologics are large, very complex molecules that can only be manufactured biotechnologically.” The best example is antibodies for cancer therapy. As active pharmaceutical ingredients, biologics are becoming increasingly important, which is why their efficient manufacture is equally gaining in significance.

Together with her team at Bayer Technology Services, Vester is currently working on optimizing the industrial production of biologics – with the aim of more diversity and lower manufacturing costs. This is the great advantage of these innovative active substances: in future, many drugs will be manufactured in small quantities for specialized therapies, and thus will be beneficial for the patients as they will receive the optimum treatment available.

However, as opposed to small active substance molecules, biologics cannot be created using conventional chemical syntheses. “The molecules have very complex structures, for example, certain patterns in groups of atoms that cannot be produced chemically,” says Vester. Fortunately, certain bacteria and cell cultures are able to take on the production process. This is because most biologics are proteins whose genetic blueprint can be transferred by way of DNA snippets into the genetic material of organic producers.

Together with a nutrient solution, cells prepared in this way are placed in a type of incubator, called a fermenter. Once the conditions are right, the cells will start producing the desired biomolecules. Finally, once this process is completed, the product is separated from the nutrient solution and purified.

It may sound simple, but in practice, it is an extremely sensitive and inflexible procedure. Starting new production inside the equipment, or even changing to another active substance is extremely time-consuming. “All the parts that have been in contact with the previous product have to be meticulously cleaned,” Vester explains. “This is carried out according to an officially approved cleaning protocol and subject to thorough examination. New processes cannot go into operation without these validation procedures. This ensures that the process and the equipment used can be reproduced to result in the desired product every single time.” The authorization process alone can take as long as twelve months.

Minimizing this time-consuming step is exactly what Andrea Vester and her team are working on. The concept the group is investigating, together with its laboratory version swinging every second, is called MoBiDiK. The abbreviation is derived from “modular bioproduction – disposable and continuous.” While MoBiDiK may have nothing to do with a white whale, it could still make large waves and revolutionize the industrial manufacturing of biologics. “The individual process stages, such as synthesis, filtration, and purification, are carried out in separate modules, which we’ve designed as sterile one-off systems made of plastic,” says Vester. Exactly as previously stated: modular and disposable. The advantage of this system is that at the end of the production process, all those components that came into contact with the product can be simply exchanged for new components. This omits the need for time-consuming cleaning and validation. “This type of production saves resources, time, and costs,” she explains.

Dr. Maria-Luisa Binda, Head of Innovation Management Product Supply, Bayer HealthCare

“This new procedure could bring significant advantages for the production of antibody preparations.”
The 37-year-old is obviously in her element. Biologics production seems second nature to Vester. But then she did gain her PhD in biological process engineering in Munich after completing a mechanical engineering degree in Aachen. She particularly enjoys the fact that she and her current team can work across disciplines, developing solutions with other engineers, as well as with chemists and microbiologists. And there is something else that she likes: the strong links to academia five years after graduation. MoBiDiK is a collaboration with INVITE, the joint research company run by Bayer Technology Services and the Technical University Dortmund, and with other university institutes. The 30-member team not only includes colleagues from Bayer, but also from the universities in Dortmund and Aachen.

Biologics are currently manufactured in a batch process. Production takes place in fermenters, which can occupy several stories and contain up to 30,000 liters. Once sufficient product molecules are formed within a single batch, they are isolated, filtered and purified. Meanwhile production comes to a standstill. Only when this process has been completed does production start again with the next batch. Vester and her team aim to be producing continuously soon, no longer in batches. Instead, the liquid will be constantly removed from the fermenter during the production process and the active ingredient separated. The production cells are retained and, together with a fresh nutrient solution, returned to the reactor.

With the next generation of active ingredient molecules the task of conventional fermenters will be replaced by much smaller disposable bioreactors, some of which, holding 200 liters, are barely larger than a bathtub. These small fermenters run continuously and can supply the same amounts of active ingredients as their larger counterparts.

This new concept is currently undergoing rigorous testing in Leverkusen. Bayer HealthCare is also following developments closely, since the number of biologics among the company’s pharmaceutical range of products is constantly growing. “This new procedure could bring significant advantages for the production of antibody preparations,” stresses Dr. Maria Luisa-Binda, Head of Innovation Management at Bayer HealthCare Product Supply in Leverkusen.

While the new concept is still being scrutinized, Vester already has a further development in mind – small, automated production lines that manufacture high-quality products at a low cost, independent of volume and location. Does this mean MoBiDiK is paving the way for personalized medicine? “This is certainly an important goal,” says Andrea Vester. Moreover, being able to provide patients around the world with affordable, tailor-made drugs would lend her profession a real sense of purpose.
n his early years as a process engineer, Dr. Helmut Brod could hardly have imagined doing anything more complicated than what he was already doing: spinning elastic thread of consistently high quality from a polymer solution. Now, more than ten years later and having seen his career at Bayer take him from purely chemical reactors to biotechnological fermenters, Brod knows that it can get a lot more complicated than that. Suddenly he was introduced to hamster cells that synthesize a gigantic protein. “The number of chemical reactions that take place in a living cell is many times greater than those in a purely chemical system,” Brod observes today. That made a lasting impression on the engineer, who only began to take an interest in biology at a comparatively late stage in his career.

Over the years, he has gathered an ever-increasing amount of knowledge and experience in the field of biotechnology, such that he is currently in charge of the Fermentation & Cell Culturing group at Bayer Technology Services. In addition, he is chair of a company-wide committee in which Bayer bundles its expertise relating to biotechnological production. And its expertise is diverse. Bayer HealthCare produces in its fermenters active substances for treating hemophilia and diabetes, for example, as well as the intermediate stages of hormonal contraceptives. Fermenters are also becoming more important for Bayer CropScience. It has only been two years since the company first began developing its biological pesticides division by way of acquisitions, and already the plan is to expand the capacity of the reactors. Now, when the question is asked – “What does the ideal large fermenter look like?” – Helmut Brod’s team is able to provide an answer.

“We are very fortunate to have access to such high caliber expertise within our own company.”

Dr. Hong Zhu, Biologics Process Development, Bayer CropScience

“Usually a chemical reactor can simply be replaced by a taller one,” says Brod, “but in a biotechnological process, you have to look at a couple of parameters first before you can undertake an upscaling like that.” This primarily has to do with the fact that biotechnology involves dealing with living cells, and they are very particular about their environmental conditions. These include the concentration levels of dissolved carbon dioxide – and this is where the height of the fermenter has a direct effect. “Most cells release CO₂ as part of their metabolic process, and this gas escapes since it is only dissolved to a limited extent within the reactor liquid medium,” explains Brod. In a taller fermenter, the lower layers are subjected to greater pressure – and more CO₂ is dissolved and does not escape. “The question then is whether this has an impact on the activity of the cells,” remarks Brod.

In a past project for Bayer HealthCare, for example, when new and larger fermenters were needed to replace the old, smaller ones, the issue of increased pressure led to them being made wider instead of taller. Jörg Kauling, a member of Dr. Brod’s team, remembers the experiments at that time, “Tests had shown the productivity of the bacteria involved was seriously diminished above a certain concentration of CO₂.” The conclusion drawn from this was that fermenters should not exceed a certain height and so were constructed wider. The fact that this is not the general rule is due to the difficulties involved in transporting wider reactors.

In the meantime, Bayer Technology Services has also examined the CO₂ issue relative to the bacteria in the Bayer CropScience fermenters. All that was needed here were lab tests using a one-liter fermenter. “We simply specified varying concentrations of CO₂ and then measured the resulting product yield,” explains Brod. The result was an all-clear: higher amounts of carbon dioxide in the fermenter’s liquid medium would in no way impede the production of the particular crop protection agent concerned. This meant that a
new fermenter could be built taller than its predecessor, thus providing the assurances needed for future planning.

“It was very impressive to see how quickly Bayer Technology Services was able to simulate the effects of CO₂,” extols Dr. Hong Zhu, who researches biological crop protection agents at Bayer CropScience. He adds, “We are very fortunate to have access to such high caliber expertise within our own company.” Dr. Lothar Döllinger, who is responsible for global technology activities at Bayer CropScience, is of much the same opinion. “Thanks to recent acquisitions, we now have quite a few biotech production plants. Being able to access the relevant know-how in other areas of the company is very useful when it comes to upgrading these sites.”

However, the fermentation experts at Bayer Technology Services help not only in the designing of new bioreactors, but also in optimizing existing biotechnology processes. When Dr. Brod talks about these tasks, he repeatedly uses the term, “debottlenecking.” What he means is identifying the bottleneck in the process as it has been managed up until now and eliminating it. An example of such a bottleneck might be when a depletion of a specific nutrient occurs somewhere in the reactor during a fermentation process. The cells in such a zone are then left on the back burner.

The capacity of production fermenters is anywhere from several hundred liters up to hundreds of cubic meters, depending on the product. “Of course, we cannot do our optimization tests on that scale,” notes Brod, since, as he points out, the cost of the nutrients alone would make it too expensive. “At the moment, we are working on defining the operation of small fermenters with ten or sixteen liters in such a way that we can draw reliable conclusions, which we can then apply on a large scale.” Defining a representative downscaling like this, however, is anything but a trivial matter. The precise downscaling of simply the stirring, which is meant to provide an even distribution throughout the fermenter, is a demanding task in itself. Another issue being investigated is the formation of foam, typical of many microbiological processes. In addition, to making their experimental work as effective as possible, the team is also attempting to simulate the complex reactor events in computer models to derive useful predictions.

And there is yet another trend in biotechnology that Brod and his team are currently supporting with their expertise: the transition from classic batch production to continually operating systems that produce a constant product yield (see p. 32).

In this respect, Dr. Brod is positively overjoyed at the diversity of expertise related to biotechnological production at Bayer. “We all compare notes regularly, meet at the relevant production sites, and learn from each other.” Although he still fondly recalls his time in polymer process engineering, he has long since become a passionate biotech process engineer.
Can you imagine moving to Berkeley for a few years?” When Dirk Fischer was first asked this question at the beginning of 2007, he had to pause to take a deep breath. The process engineer employed by Bayer Technology Services had an interesting job at the Wuppertal site and in his private life, he and his wife were just thinking about having a second child. How can you transfer to California at such a critical point in your life?

At the time the then 34-year-old had already been to Berkeley several times and had spent a few weeks there helping with an important development project. However, it increasingly became clear that this might not be enough. “As the site was preparing for growth, we needed more permanent support from Germany,” says Dr. Scott Probst, who then was with Bayer Technology Services in Berkeley. So, Probst asked Fischer the crucial question.

The project focused on an improvement to the existing rFVIII product manufacturing process. Bayer HealthCare has been synthesizing Factor VIII in bioreactors in Berkeley for the past 20 years. The recombinant factor VIII treatment, synthesized from modified hamster cells, helps people with hemophilia A around the world to lead a nearly normal life. Bayer HealthCare works continually on process improvements, and Bayer Tech-
nology Services has been an important partner in many of these projects (see technology solutions 1/2011).

In this case, the project involved a new additive that was meant to protect the hamster cells from mechanical stress. Bayer HealthCare wanted to substitute this new substance for the protein used up until then – for which the company was dependent on a very specific supplier. The new additive is more readily available and cost effective – two important factors to strengthen the competitiveness.

However, it was a long path from the idea to the technical implementation on an industrial production scale. It was precisely here that colleagues from Bayer Technology Services could help. “The entire manufacturing process had to be adjusted, as some of the classical process steps no longer functioned as before,” explains Probst, who was the leading process engineer.

In the solution that is continually harvested from the bioreactors the factor VIII is present in a highly diluted form. “Traditionally, the concentration is achieved through ultrafiltration,” says Probst. The ultrafiltration process separates water, salts and low molecular weight species from the clarified harvest, thus concentrating the factor VIII in the solution. “With the new additive this filtration is only possible to a limited extent,” explains Probst. “The substance precipitates out of the solution and would therefore end up blocking the pores of the filter.”

Bayer HealthCare already developed the idea for an alternative technology to ultrafiltration some years ago: membrane adsorption. With this process step, the bioreactor harvest flows through a filter membrane that has chromatography ligands on the surface. Under the load conditions, the factor VIII attaches to the ligands, and under the elution conditions, the factor VIII desorbs from the ligands. Through this step, the factor VIII is concentrated and impurities are removed.

Such was the theory; however, the technical implementation was anything but simple. Although you can freely purchase modules for membrane adsorption, it is not possible for them to be integrated immediately into your particular process technology with all its special features.

It is here that Dirk Fischer’s expertise was going to come into play. Thankfully, the German consented to the move. He and his wife agreed quickly, and by April, the family had settled into their new home on the west coast of the United States. At the time the process engineer had already amassed eight years of experience in various biotech projects, all of which involved the production of active ingredients. As a result, Fischer was well acquainted with the strict regulations of the pharmaceutical industry’s Good Manufacturing Practices, which also proved to be very useful in the work on membrane adsorption technology.

First of all, Fischer carried out detailed research to determine what is essential for the integration of the membrane adsorption process. As it turned out, membrane adsorption systems were meant to be connected to the feeds of six bioreactors in total. It was also necessary to connect the system to all of the chromatography and cleaning solutions required for the process. Due to space limitations, some of these solutions could only be stored as concentrates. “That means we had to be able to dilute them in the system itself,” says Fischer. Another requirement was that the entire system had to be able to tolerate hot steam sanitization procedures. The system also had to carefully control fluid temperatures and flow rates. In the end 105 automated valves were installed to regulate all of the required flow paths and system functions. The membrane adsorption recipe sequences are completely automated because they must be executed very precisely. Automation also saves labor, which reduces costs and, once again, increases competitiveness.

Product concentration by means of membrane adsorption is not only a practical alternative to the conventional ultrafiltration process, but it also offers a number of other advantages. “This technology platform is also much faster,” lead process engineer Probst is pleased to say. But that is not all. At the same time, it also fulfills two tasks as part of the purification process that, using the conventional technology, have to be carried out separately. This shortens the overall processing, which is beneficial. “Factor VIII molecules are relatively unstable and can disintegrate over time,” explains Probst. “Therefore, with every minute saved and the faster the product can be frozen, we also increase the production yield.”

“The project team is proud of something else too: the new manufacturing process was built right next to rooms where GMP manufacturing operations for a high-value product were ongoing. “Over and over again we had to carry out safety analyses to ensure we would not jeopardize normal production,” recalls Probst. For example, special considerations had to be taken into account when modifying utility lines that were directly adjacent to those utility lines supporting ongoing operations. “We had to be very careful to make sure that we were cutting the correct pipes because the alternative was potential disaster,” says Probst. Even though the new process is now ready for start-up, it still has not received authorization for use. Due to the modified process technology, the rFVIII therapies produced in this way must first be tested in clinical trials.

In the meantime Dirk Fischer is back in Wuppertal, where Bayer HealthCare is building another production facility for rFVIII therapies. Fischer will be able to make use of his experience from Berkeley. And so can Scott Probst. Much like in Fischer’s case, one day he was asked, “Can you imagine a move to Germany?” His family agreed quickly as well, and Probst accepted the offer.

“Once again, we have jointly realized an important process improvement.”

Jörg Heidrich, Senior Vice President Product Supply Biotech, Bayer HealthCare
What Affects the World

Anyone who can make high quality plastics from carbon dioxide has killed at least two birds with one stone. For one thing, this means using a raw material that would otherwise end up in the atmosphere as a greenhouse gas damaging the climate. For another, it saves on a raw material traditionally used for plastics: crude oil. And that is a limited resource.

What sounds visionary is also a task that ultimately no one player can manage alone. And so it comes as no surprise that important breakthroughs achieved on the way to turning CO₂ into a useable resource were accomplished through teamwork. Among those involved in this collaboration were Bayer MaterialScience, Bayer Technology Services, the RWTH Aachen University, CAT Catalytic Center Aachen (a joint project run by RWTH and Bayer), and RWE. Each of these partners brought an area of expertise to the table that contributed to the success of the project. For example, the teams from CAT and from Bayer Technology Services further developed an important catalyst. It was only with its help that the use of CO₂ molecules in manufacturing polyol is possible, while only producing negligible by-products and also saving energy. For its part, Bayer MaterialScience provided the expertise for the synthesizing of the polyols and their conversion to polymers. And RWE developed a method of treating the waste gases from coal-fired power plants such that they provide ample amounts of the desired raw material in a quality sufficient for industrial-scale production.

The German Federal Ministry of Education and Research (BMBF) also played a significant role in this success. The BMBF now supports a whole series of interconnected group research projects on the use of CO₂ with grants. Thomas Görgen stresses that although this public support was generally small in comparison to the total financial expenditure of the industrial partners, the outside involvement was important: “There are many research subjects that are risky from a business point of view; for example, because the chances of success are still too uncertain,” explains the chemist. “Often this risk must be shared by many shoulders if visionary projects are to be attempted at all. The public sector forms a safety net for such projects and promotes the formation and cohesion of such research alliances.”

Görgen heads the public funding group at Bayer Technology Services, a kind of interface between the company’s research departments and the external government boards that promote research projects. “For one thing, we help the government to direct its focus on supporting those issues that industry can actually handle,” Görgen adds. “For another, we are an important contact point for our own researchers, when, for example, it is a question of if and where Bayer research overlaps with that being subsidized from outside. Meaning ultimately, where applications for funding make sense.”

Currently, Bayer has over 100 research projects in Germany alone that are being supported by public funding. In 2013, the total sum of these subsides amounted to some eight million euros. Ten years earlier, the number was just two million euros. As important as these public-private partnerships are for individual research projects, Görgen is quick to stress that it is the company that pays the lion’s share of its own research and development. Bayer spends around three billion euros annually on it, with three and a half billion planned for the current year.

A new concept of funding has been put into practice in the
Open for business. Today’s R&D departments are more open – and exchanging their knowledge.
Experts from a number of pharmaceutical companies are jointly investigating whether a suitable computer model can reduce the amount of experimentation involved. “If they succeed, both producer and patient will benefit, because then innovative drugs can be developed more quickly,” according to Görgen. This is also in line with Bayer’s overall mission statement, “Science For A Better Life,” according to which, research, and the products resulting from it, are intended to improve people’s lives.

Over fifty IMI projects have already been initiated. Researchers from Bayer HealthCare are directly involved in twenty-four of these, and in five of them as project coordinators. With a total volume of around 540 million euros, these twenty-four projects account for more than a quarter of IMI’s overall budget. Among the projects headed by Bayer HealthCare is OncoTrack, which involves the search for biomarkers suitable for customized tumor therapy for individual patients (see p. 28).

Another project led by Bayer is EU Lead Factory, a joint Eu-
The RWTH Aachen is another one of Bayer’s academic partners. RWTH scientists and researchers from Bayer are not only collaborating on projects at the CAT Catalytic Center mentioned earlier, but are also working side-by-side in the Joint Research Center on Computational Biomedicine that was established in 2013 by RWTH and Bayer Technology Services. Here, for example, they are working together on a computer model that allows the simulation of biological processes, with the aim of developing medicines and therapies even more efficiently.

There are also similar partnerships on specific research topics, among others with the German Cancer Research Center (DKFZ) in Heidelberg, with the University of Beijing, and with the Broad Institute in Boston. “Collaborative research with external partners from academia and industry is an integral part of our innovation strategy,” says Kemal Malik, responsible for innovation on the Board of Management at Bayer AG, in explaining the importance of all these partnerships.

“Naturally, no company is going to simply provide access to all of its intellectual property,” concedes Thomas Görgen from Bayer Technology Services, “but much can be achieved with the knowledge we make available to our partners along with their individual contributions.” After all, for some tasks you need a certain critical mass, namely enough colleagues, because you simply cannot manage it on your own. This is true of many IMI projects. Or you need the cross-sector expertise that no single company has at its disposal. As is the case with the use of CO₂ as a raw material.

Of course, there has been cooperation in research before now. But the difference here is that companies are systematically organizing their knowledge transfer across company borders. “The common goal of all partners must be to make the pie as large as possible,” says Görgen. “This makes an equal distribution easier, since the whole is often more than the sum of its parts.” It is a matter of give and take, and the bottom line is that progress should profit, and ultimately the general public, as well, as they are the beneficiaries of technical innovation, improved medicines, and sustainable products.

There are currently very differing approaches to open innovation in research practice. The CO₂ projects and the IMI program are examples of public-funded, cross-company cooperation. Moreover, for a science-based company like Bayer, direct networking with academic research is also important. “We maintain close relationships with a large number of universities, in Germany, the USA, and China, for example,” explains Görgen. Bayer Technology Services also supports the establishment of such networks within the Group.

Bayer Technology Services maintains an especially close relationship with the Technical University Dortmund. In 2011, both partners founded a joint research center, INVITE, which has been working on future production processes (see technology solutions 1/2012). This research is also being carried out with partial funding from the public sector and in cooperation with such competitors as BASF and Evonik.

Open Sustainability

Whenever possible, produce raw materials and energy from renewable sources and use as efficiently as possible. Recycle waste. Close material cycles. With all these measures, the initiative Sustainable Process Industry through Resource and Energy Efficiency (SPIRE) aims to contribute to sustainable industrial processes in Europe. Close to forty companies (including Bayer) from eight sectors, twelve associations, as well as some forty-five academic institutions have joined this public-private partnership (see p. 47). The president of SPIRE is Dr. Klaus Sommer, who is head of the Customer & Product Management division at Bayer Technology Services, as well as chair of SusChem, the European technology platform for sustainable chemistry.

The association has set itself a number of goals to be reached by 2030 — which convinced the European Commission to make SPIRE an integral part of the EU research program, Horizon 2020. In total, this initiative will receive funds amounting to around two billion euros.
Dirk Königsbrügge loves a challenge. At the moment, the engineer is on assignment in Switzerland. His task is not only to convert one synthesizing process into another but also simultaneously increase its capacity – all during ongoing production.

Königsbrügge happened to be in India on business once again when he received a call from Europe. He was not surprised when the voice at the other end of the line asked, “Say, could you take over a project in Switzerland?” As a mechanical engineer who has been working for Bayer Technology Services now for a quarter of a century, Königsbrügge has received many such calls during that time. Sometimes an offer might come at an opportune time and he was able to take off immediately. Christmas 1996 was one such example. He had just wrapped up a project at the Bayer site in Brunsbüttel, near Hamburg, Germany, and so could accept the job immediately and catch a flight to Jakarta. He had no idea at the time that he would be spending the next three years in Indonesia.

When the call came from Switzerland, Königsbrügge had to stall for time, since his consulting project at Bayer CropScience in Vapi, India, was not yet completed. Nonetheless, he accepted.

He arrived at the Muttenz plant in July 2012. It is here, southeast of Basel, that Bayer CropScience produces three substances for important crop protection products. One of these is trifloxystrobin, a substance that lends Bayer fungicides like Flint, Nativo, and Stratego their high efficacy against many types of fungal diseases. To meet increasing global demand, Bayer CropScience wanted to double its capacity. At the same time, the first of a total of seven steps in the synthesis process was to be converted to another method that makes use of more economical feedstock. Bayer CropScience and Bayer Technology Services had developed this alternative method while collaborating on a previous project (see technology solutions 1/2012, p. 36). The project had so resulted in a special treatment for waste products. This had come about because tests revealed that the waste contained chemicals related to trifloxystrobin, which could easily be converted into the active agent itself. This process step alone will increase the production capacity by seven percent.

Königsbrügge’s challenge now was to manage the technical conversion on a large scale. Dr. Wolfgang Bäcker, Bayer CropScience’s site manager, is delighted with the support and the anticipated effect: “Thanks to this, we can save up to 26 million euros a year.”

At first glance, increasing the capacity appeared to be a routine job: a couple of new mixing tanks here and there, some heat exchangers in all the right places, the usual pumps and piping. But on closer examination, it became clear that this project was more complicated than meets the eye. “The new and larger plant couldn’t simply be set up next to the old one,” explains Königsbrügge. “A key requirement was that as many components as possible from the old facility were to be integrated into the new process.”

This, too, would have been routine, if the old system could be simply shut down and the re-engineering process carried out without undue time pressure. “But we didn’t have that luxury,” says Königsbrügge. Bayer CropScience produces trifloxystrobin in only one location in the world and that is Muttenz. For this reason, there could be no long gaps in production. To put it another way, for Königsbrügge’s team it was like switching horses while galloping at full speed.

The first phase was comparatively harmless. It centered on constructing a building to house the equipment needed for the new synthesizing step as well as two additional reaction stages. Although there was also a tight schedule for this phase of the project, at least it did not collide with the ongoing production in the neighboring building.

The second phase of the project is a little trickier. This involves setting up the equipment for expanding the synthesis...
stages two through five in the existing production hall. “We want to switch over completely to the new system in August 2014 and, naturally, as smoothly as possible,” says Königsbrügge. Ideally, it will only require opening a couple of stopcocks and valves to redirect the stream of material into the new part of the system – but it will have to work on the first attempt. And it is this perfect integration of the individual project steps that represents one of the special challenges for 58-year-old Königsbrügge.

Integration equally fits the image Königsbrügge uses to describe working with his Swiss colleagues at Bayer CropScience: “Like clockwork from the very start.” A Swiss clock, of course. And, although Königsbrügge has been involved in many successful projects during his 25 years with the company, this perfection and precision delights him still.

There is something else that pleases Königsbrügge about the Swiss project. He can catch a train to Cologne on a Friday evening and spend the weekend with his wife. It was not always this easy. During his time in India and Indonesia, for example, his family life was limited to telephone calls and quarterly visits. He could often only experience his children growing up from a distance. This is why he recommends that colleagues “try to organize lengthy stays abroad to include your whole family.” In retrospect, he would have done the same. Sometimes it worked out, but not in the case of his three years in Indonesia. This was because originally he was not meant to stay that long, but one thing led to another.

All things considered, however, Königsbrügge is content with his nomadic professional life. Why else would he have recommended specializing in plant engineering to his son, Jan? After all, engineers who follow this career path can expect to be transferred somewhere else every couple of years. But, in his opinion, if you manage to balance this with your private life, there is nothing to beat it. “Besides, it’s not only extremely diversified but also very satisfying.” The final result is always a finished plant that is of concrete benefit, such as the one in Muttenz. After all, substances are produced here that help the whole world to secure crops and fight hunger. “Having been a part of that is really a fantastic feeling,” concludes Königsbrügge.
Building Bridges to the Future

The Indian subsidiary of Bayer Technology Services just keeps on growing. It not only supports the other Bayer companies in India, but also external customers. For example, Ferring Pharmaceuticals from Switzerland.

With this letter I would like to express my appreciation to Bayer Technology Services for their incredible support.” It is not every day you receive a business letter that opens with such warm words, which is why Balaram Khot was especially happy when he received this one. Khot, Head of Bayer Technology Services India, was lucky enough to receive two letters of this kind in 2013. Both were sent by Jouke Tuinhof, and in both letters the Director of Global Engineering at Ferring Pharmaceuticals conveyed his delight over the current progress of the investment project in India. “Milestones [...] that wouldn’t have been possible without the support and perseverance of the members from the Bayer Technology Services project team,” Tuinhof wrote each time.

The Ferring manager was referring to the construction of a production plant for an active pharmaceutical ingredient. At the end of 2010, Ferring, a Swiss company, decided to meet the growing global demand with the construction of a further plant. The location chosen was Ambernath in India, a town just northeast of Mumbai. This stood to reason as Ferring already had research and development labs as well as marketing and sales offices there. However, some issues still needed to be clarified; for example, the tropical conditions and the regulations set out by the Indian authorities had to be taken into account.

To resolve these issues, Ferring sought an engineering partner. One who knew a lot about production plants for the chemical and pharmaceutical industries, and one that was familiar with the specific conditions in Asia, in particular India. This was when Jouke Tuinhof thought of Bayer Technology Services, the company he knew from his time in Singapore. He was sure he would find the expertise he was looking for there. The fact that the Bayer company had its own subsidiary in India and its main office less than an hour’s drive from Ambernath was ideal. Tuinhof made contact.

Balaram Khot enjoys receiving requests like these. Although he is repeatedly faced with the challenge of how to supply all the required resources, this is an enviable problem. While many managers all over the world are streamlin-
ing their organizations and having to reduce staff costs, Khot is on the constant lookout for more engineers to expand his team. It is less than seven years ago that the Indian subsidiary of Bayer Technology Services was set up as a three-man team. Since then the workforce has increased more than tenfold, and by the end of the year may have grown to over 40.

The Ferring project has been contributing significantly to this expansion for some time now. “We were able to convince Ferring that we have the necessary experience,” explains Balaram Khot. To this end, the Head of Bayer Technology Services India told his future client about the engineering projects that his staff had already undertaken, for example, for Bayer MaterialScience and Bayer CropScience. This is why Ferring chose Khot’s team as an engineering partner.

Modern India (below: Mumbai), modern environmental standards. Bayer Technology Services has developed a special waste-water solution for the new Ferring plant.
“That wouldn’t have been possible without the great support of Bayer Technology Services.”

Jouke Tuinhof, Director of Global Engineering, Ferring Pharmaceuticals

course, due to the tropical climate we have to partly use very different materials,” Solanki adds.

In terms of the materials used, it goes without saying that as Owner’s Engineer, Bayer Technology Services is not only responsible for developing a fully functional plant. “We also want it to remain operational for a long period of time,” explains Solanki.

This is why the conditions that have to be endured by every process and utility system used in the Ferring project were evaluated, as well as which materials would ensure durability. “This means that we may give preference to glass-lined equipment rather than high-density polyethylene vessels in particular cases,” says Solanki. While this may initially prove more expensive, it pays off over the course of the expected service life. Explaining the general procedure, Solanki says, “All measures of this kind were discussed with Ferring and approved on an individual basis.”

Before the construction phase could begin, the important issue of wastewater treatment had to be addressed. For example, both the two-stage synthesis of the active substance as well as the subsequent purification of the finished ingre-
**CENTER FOR SEEDGROWTH**

Bayer CropScience was able to complete its new Australian Seed-Growth Center for wheat and oil seeds in less than twelve months after the ground-breaking ceremony. Following a construction period without a single accident, the center was officially opened in February 2014 (see photo). The new facilities in Longerenong College near Horsham, Victoria will house some 20 employees working on novel wheat and oil seeds with enhanced properties specially developed for Australian agricultural conditions. For Samme Wang, head of Bayer Technology Services Singapore (2nd from the left), this project reflected “his team’s ability to manage investment projects with the right degree of quality.”

**NEW OFFICES OPENED**

Bayer CropScience can now enjoy the presence of Bayer Technology Services at two more of its sites. Since the start of this year, BTS has been running its own office in the north-west Indian town of Vapi, an important production site for Bayer CropScience. This allows Bayer Technology Services to support the company even better and more intensively in both its investment projects and issues concerning waste water treatment.

Then, in May 2014, Bayer Technology Services opened its own offices at the industrial park in Frankfurt-Höchst, where the company will primarily be offering its services in the fields of plant and process safety, process analysis, and life-cycle management.

**LICENSE FOR ART TECHNOLOGY**

Ehrfeld Mikrotechnik BTS GmbH (EMB), has acquired the license for the global manufacture and marketing of ART reactor technology from Alfa Laval, a Swedish specialist in the field. With these millistructured plate reactors (see photo above), which are used in laboratory and pilot plants as well as production facilities, EMB is now the leading supplier of metal micro- and millistructured reactors and apparatus. This technology offers substantial advantages for particular processes within the pharmaceutical industry, as well as in the fine and specialty chemicals industries, for example, such as in heat transfer and with demanding reactions. EMB is a subsidiary of Bayer Technology Services GmbH.

**SUSTAINABILITY ALLIANCE**

For the very first time, eight leading European industrial sectors are forming an innovation partnership, with the aim of tackling the urgent issues facing the European Union. Sustainable Process Industry through Resource and Energy Efficiency (SPIRE) is the name of this initiative, which has the support of the European Commission (EC). As part of its research program Horizon 2020, the EC has earmarked around one billion euros of funds for the partnership. This alliance was sealed on December 17, 2013 with the signatures of SPIRE President, Dr. Klaus Sommer (see photo, 2nd from left) and EC Vice President, Neelie Kroes, among others. In future, the European process industry intends to work on completely new manufacturing methods in an interdisciplinary manner and more closely interconnected. The main goal is to manufacture new products using less energy and fewer resources and thus strengthen competitiveness. Bayer has been promoting this development for many years now as part of SusChem, the European Technology Platform for Sustainable Chemistry, which is also chaired by Dr. Klaus Sommer.
Inch by inch, the silver-gray container is hoisted into Leverkusen’s wintry sky. The thought crosses one’s mind: “Just don’t let it drop.” The anxious faces of other colleagues can be seen at a window in the neighboring building following the progress of the operation, obviously thinking the same thing. They are all members of the Bayer team who created the extremely valuable contents inching skyward inside this non-descript box. Everything runs smoothly. The crane sets the 14 meter-long container safe and sound on the semi-trailer truck and the journey can begin. There is an audible sigh of relief.

That was December 2013. In the meantime, the container has arrived in Changzhou Yangtze Riverside Industrial Park, to the northwest of Shanghai. Lanxess, a chemical company, is currently constructing a facility there for the production of EPDM rubber. This will also need reliable process analyzer technology (PAT), to monitor the process using specific substance reference values and controlled so that it delivers a product conforming to specifications. It is this PAT that Bayer Technology Services was shipping in the gray container.

For decades it had been standard to install the necessary PAT directly in the plant. But around 20 years ago, Bayer built a plant in Belford Roxo, Brazil, that required complex analyzer technology. “At the time, we had no PAT experts in Brazil,” recalls Dr. Thomas Sauter, who is in charge of PAT Engineering at Bayer Technology Services. “So the idea occurred to us to build all of the analyzer technology in Germany, check its functions, and then ship it to Brazil.” Analyzer technology to go, so to speak. Naturally, this had to be in a form that was not only easy to transport but also user-friendly on site and simple to integrate into the production system. This was the inception of the container concept at Bayer. However, it was not enough to simply install all of the measuring technology: the PAT container also had to interface with the plant’s own systems. No matter whether electricity, water, gas, or even optical signals – the workers in the plant had to be able to simply hook it up. After a short period of introductory training, the Brazilian operation was up and running. Plug and play is what we would call it today.

Since then, this approach has proven itself around the world dozens of times. The PAT team at Bayer Technology Services in Leverkusen supplied the 80th container earlier this year, while the Lanxess container shipped off in December was one of seven built by Bayer Technology Services in 2013 alone.

These PAT projects have the typical characteristics of an engineering project – conceptual design, basic engineering, and detail engineering. The experience gained in over four decades at Bayer Technology Services is put to good use from the very start. During the conceptual design phase, the experts have a repertoire of over 60 different measuring techniques to choose from – from a pH meter to complete gas chromatography. Once the implementation planning is finalized, the Center for System Integration and Prototyping, headed by Karl-Heinz Niehsen, comes into play. This is where the concept on paper drawn up previously by the PAT engineering team becomes reality.

“My team really can ‘read’ these plans,” explains Niehsen, and one can sense the electrical engineer’s admiration. Because “read” means that his experts, looking at lines and symbols, not only identify which measurement system or which connections for feeding in the substances and samples are needed, but “They can immediately visualize it spatially, as well,” he adds. This should be the most compact space possible, since, while the largest PAT solution to date took up 19 containers, the aim is to store all of the measurement technology inside as few containers as possible.
In some cases, this results in the walls of a container being so crammed full of wires and tubing that the technicians have to reach deep inside their bag of tricks. “Here, look at this,” exclaims Niehsen, pointing to a mass of tightly packed, stainless steel tubes in another container. Many of them curve around to avoid contact with neighboring lines. “You can’t even buy tubing with such bends. So we manufacture them individually in the workshop,” says Niehsen. With pride, he adds that customers are continually praising both the technical and optical quality of their design. “It’s not something everybody can do.”

The Center for System Integration and Prototyping has its own assembly space and workshop in the Leverkusen building with close to 1,000 m² of space available to preassemble all the components and install them in the containers so as to meet the customers’ individual needs. This is where those parts are produced that cannot be found anywhere else on the market. As a result of the team’s decades of experience, they now not only produce PAT modules but also, for example, modular production equipment for F³ factory containers (see also technology solutions 2012, p. 24 f.).

This vast reservoir of experience is equally appreciated at Aliseca. The Lanxess subsidiary is, among other things, responsible for Lanxess’s global initiatives, and, therefore, for ordering the container for the plant in Changzhou. “Many companies are able to work in measuring technology,” points out Frank Grümbel, head of PAT at Aliseca, “but also understanding how to adapt this to the complex demands of our chemical plants, now that is rare. Bayer Technology Services has this expertise because they have a high degree of owner’s experience themselves. The perfect partner.”

In the meantime, the PAT team in Leverkusen has long since been busy on their next projects. Even if many containers appear similar on the outside, inside everything is one-of-a-kind measuring technology, tailor-made for each individual plant. And every time another container is loaded by crane, some team members are sure to be seen standing at the window thinking, “Just don’t let it drop.”
Would You Believe It?

0.19 is the number of recordable incidents leading to lost working time per 200,000 employee working hours (or Lost Time Recordable Incident Rate, LTRIR) reported at Bayer Technology Services in 2013. This number was even below the ambitious target of “under 0.22.” Last year’s global LTRIR for the entire Bayer group was 0.26, which was not only down on the previous year’s rate (0.27), but also the lowest ever. Clear evidence of the success of numerous safety campaigns at Bayer, including the annual Safety Day and regular instructions, such as the one shown here in Shanghai (photo).

0.00000000004 liters of a sample are enough for bioanalysts at Bayer Technology Services to determine relevant proteins. The protein pattern of biological samples can provide such important information as which enzymes and biological processes are active within a cell. This tiny amount of 0.4 billionth of a liter is equal to the contents of a few cells taken from body tissue, for example removed from a tumor. The protein profile in tumor cells (photo) can tell us something about the individual disease mechanisms – and help to identify the optimum treatment option (see also page 28).

49 nationalities are represented among the global employees at Bayer Technology Services, a cultural balance that is equally reflected in the new colleagues joining the company. The 108 men and women who started work in 2013 come from 20 different countries. Most of these were in the USA (36), followed by Germany (35) and China (26). The number of women joining the staff was almost one third at 31 percent. By the end of 2013, among the total workforce at Bayer Technology Services nearly one quarter (24 percent) were women. The percentage of women is particularly high in China, namely 35 percent of the 447 employees. Overall, the 2,300 colleagues at Bayer Technology Services are working at sites in ten countries (right).

FORWARD-LOOKING STATEMENTS: This publication may contain forward-looking statements based on current assumptions and forecasts made by Bayer Group or subgroup management. Various known and unknown risks, uncertainties and other factors could lead to material differences between the actual future results, financial situation, development or performance of the company and the estimates given here. These factors include those discussed in Bayer’s public reports, which are available on the Bayer website at www.bayer.com. The company assumes no liability whatsoever to update these forward-looking statements or to conform them to future events or developments.
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