CHEManager EUROPE

1–2/2011
January/February

THE NEWSPAPER FOR THE CHEMICAL AND LIFE SCIENCE MARKETS

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Strengthening Every Link in the Chain

Pharma Supply Chain Consortium Rx-360 Continues to Intensify Work in 2011

Looking Ahead – Rx-360 turned two years old in January, and the international supply chain consortium can look back on a host of achievements. The group now boasts over 50 organizations globally that have joined either as members or observers. Rx-360 has also been in intensive talks with regulatory bodies around the world, including the U.S. Food and Drug Administration; the European Medicines Agency; the World Health Organization; the Irish Medicines Board; and the Pharmaceutical Inspection Convention and Pharmaceutical Inspection Cooperation Scheme. Now that the group's infrastructure is set up, it is moving into its shared-audits phase. Brandi Schuster spoke with Rx-360's new chairwoman Lynne Byers about the group's visions for 2011.

Lynne Byers, chairwoman of Rx-360 and head of Quality Shared Services at GlaxoSmithKline

CHEManager Europe: Ms. Byers, what are your goals for 2011 within Rx-360?

L. Byers: We are looking to complete our pilot audit program by May. This comprises about 36 audits to prove that the processes we have set up and the standards we have developed are working to our expectations. Once that's completed, we will move into the routine operation of shared audits. We hope to complete an additional 100 audits under the joint program as well as an additional 100 audits under the shared audit program in 2011.

We are also planning to make existing audit reports from company members available to our Rx-360 members. We now have approval from the U.S. Federal Trade Commission that sharing this information among our members is permissible from an anti-trust perspective. This means that audits that have been done by member companies will be redacted of any commercially sensitive information.

That means there's no risk of inside company information being leaked to competitors through the sharing of the audit reports?

L. Byers: Yes, and also the suppliers who has been audited will be asked to permission before the reports are shared with our members. It is then up to them to decide which companies can receive a copy of the report. For example, they probably wouldn't permit a competing supplier to have access to the information.

What are your goals as far as your membership numbers are concerned?

L. Byers: We want to expand membership on the supplier and manufacturer side; specifically, we'd like to expand our membership to a total of 75 members, including ten pharmaceutical company members. Something else we are always working on is improving the worldwide knowledge and understanding of what Rx-360 does. We've been very focused on Europe and the U.S. during our first two years; now we want to extend our reach into Asia Pacific.

How specifically?

L. Byers: We are currently reviewing the possibility of holding conferences in China and India. We have shown presence there through members of our board who have presented at conferences in these regions. We are also planning on hosting an Asian Open Day in the fall.

A Japanese introduction is also planned …

L. Byers: We are working with one of our members, Takeda, to brainstorm ideas on how Rx-360 can best approach the Japanese market. Introductions are very important in the Japanese culture, therefore it's vital for us to work with a company based there.

What other efforts is Rx-360 undertaking to intensify the activities between all of the stakeholders Asia?

L. Byers: The SFDA, which is China's state food and drug administration, participated in training a few months ago, and one of our board members had the opportunity to give a presentation to the regulators on what Rx-360 is doing, which was well received. It's important for us that the SFDA is aware of our objectives, particularly because audits will also be done in China.

Does Rx-360 have plans to boost membership on the supplier side?

L. Byers: We exhibited at the CPhI in October in Paris, which gave us the opportunity to speak with suppliers. Also, we were able to drum up interest for Rx-360 at the EFCG dinner that was held during the show. The dinner brings together the most important leaders and decision makers within the world of fine chemicals. We were also grateful to have the support of the EFCG's chairman Guy Villax, who spoke about our efforts during the dinner.

What part of the pharmaceutical supply chain do you consider to be most at risk?

L. Byers: I don't think there's any one part that's particularly at risk, but if I had to pinpoint one possible area, that could be the distribution from the manufacture to the pharmaceutical company. Understanding how materials are transported and finding out the answers to questions such as "Does the material go through an agent? Do they re-label or repack the material?" I think the real challenge is understanding all the facets of the supply chain and making sure every link in the chain is strong. It's also important that every link is assessed by Rx-360 or individual companies in order to further understand where any potential for risk may be.

What does Rx-360 do to raise awareness about possible weak points within the pharma supply chain? What can companies do to ensure that they are not this weak spot?

L. Byers: It's growing, unfortunately not completely unrelated to the series of tragic incidents we've seen over the last few years – adulterated glycerin with diethylene glycol found in cough syrup; contaminated Heparin; infant formula laced melamine, etc. Companies are now more aware of possible supply chain weaknesses and work to have a full understanding of the supply chain. Regulating bodies, particularly in Europe, now expect companies to be able to write a risk assessment on the whole supply chain. While that is currently only a pilot program at the moment, that is the sort of thing we can expect to be seeing in the industry in the future.

How would you describe Rx-360's relationship with national regulatory bodies, such as the U.S. FDA or European Medicines Agency?

L. Byers: It's a very cooperative relationship. We've had many meetings with different regulators regarding our plans for going forward, which have been met with positive resonance. They want us to secure the supply chain.

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About Lynne Byers

Lynne Byers has a degree in chemistry, is a chartered chemist and a fellow of the Royal Society of Chemistry. She has worked throughout her career in the pharmaceutical industry, both within industry, working for GlaxoSmithKline and UCB and also worked as head of Inspectorate and Licensing for the MHRA, the UK regulator. Her current role is Head of Quality Shared Services within GSK.

International Year of CHEMISTRY 2011

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CONTENT

CELEBRATING CHEMISTRY

When I accepted the job as editor of CHEManager Europe in 2005, my decision was met with amusement by some members of my family – namely from my uncle Ron, a NASA engineer. He has only known me as the bleeding-heart liberal that I am, and as someone who has been known to write angry letters to big corporations regarding environmental offenses (OK … I was 12 and appalled to find out that my asthma inhaler contained CFCs as a propellant.).

"Oh, Brandi," he grinned. "Now you're working for The Man." The Man being, for him, big industry.

Granted, the chemical industry doesn't always have the best image in the public eye, which is exactly why the International Year of Chemistry could not have come at a better time. The industry has been working hard over the last years to shake off its sometimes demonized public image and, in fact, it is long overdue that the public begins to recognize chemistry as the impetus for innovative solutions for many of the world's woes.

A good example of this is DSM, whose CEO Feike Sijbesma was named the UN's 2010 Humanitarian of the Year for his company's efforts to battle hidden hunger (see our interview with him on page 5). Chemical companies are constantly working to find ways to use their resources more efficiently, looking into the advantages of renewable feedstocks and working to help the end-consumer fulfill their part when it comes to being kinder and gentler to the environment – Henkel's laundry detergents that contain enzymes that enable efficient washing at 15 degrees Celsius is just one such example. Across the board, the industry's big players have integrated sustainability into their strategies and are visibly active in this regard.

It's a good start, for sure. And sustainability is for the industry, not to mention what it can do for a company's image. But it's not enough. It's not enough for companies to use catch phrases like "CO_2 footprint reduction" and "renewable feedstocks." Every single player in the industry must make sure that every link in their value chain coincides with the company's sustainability mantras. Consistently.

Chemistry is in the spotlight in 2011. There's no better time than now to consider what your company can do to improve its value chain and reduce unnecessary negative environmental impacts – while saving money as a positive side effect. Be inspired by fellow chemical companies – there are plenty out there who are doing amazing things.

And as far as my working for The Man is concerned: Uncle Ron, I'm not working for The Man. The Man is working for us.

Brandi Schuster, Editor-in-Chief, CHEManager Europe & CHEManager Europe Online

P.S.: We will be featuring International Year of Chemistry topics throughout the year. Just look for this symbol:

2011 C CHEMISTRY International Year of CHEMISTRY 2011

Danisco's Jørgen Tandrup Responds to Looming Shareholder Revolt

Jørgen Tandrup, Chairman, Danisco

Danisco's chairman reaffirmed support for chemicals group DuPont's bid for the food ingredients and enzymes maker in what appeared to be his first public response to reports of a looming shareholder revolt.

Chairman Jørgen Tandrup's remarks in an emailed statement came in answer to questions from Reuters about a Danish newspaper report that said some institutional investors were teaming up to seek a higher bid or block the takeover.

"The offer from DuPont represents a fair value for the company," Tandrup said.

U.S. chemicals giant DuPont announced on Jan. 9 that it would pay $5.8 billion in cash or 665 crowns per share and assume $500 million in Danisco debt to acquire the Danish company with backing from Danisco's board. Tandrup said at the time of the bid that DuPont's was the best of several offers and gave shareholders a 25% premium over Danisco's all-time high share price set on the trading day preceding the DuPont offer.

But since then, media have reported that some Danisco shareholders have been unsatisfied with the offer and are ready to look for a better deal.

Recently, Danish financial daily Borsen said that "a handful" of big institutional investors who were not impressed with the DuPont bid were talking to one another and considering taking action against it.

"They want at least a higher bid, but are also considering whether there is not a better case for letting Danisco continue as an independent company and try to reap some of the improvements in profitability that Danisco has promised its shareholders," Borsen said, citing a source it did not identify. ■

SABIC Sees Higher Sales, Profitability in 2011, 2012

Mohamed al-Mady, CEO, SABIC

SABIC said it expects higher sales and profitability in 2011 and 2012 as production increases and petrochemical prices rise to pre-crisis levels. The world's largest chemical firm by market value said a new steel plant will begin operations by the end of the year and that its affiliate Saudi Kayan Petrochemicals will start commercial production in the second half of the year. "Growth will continue in 2011 and 2012," SABIC'S chief executive Mohamed al-Mady said in a press conference. SABIC earnings – a yardstick for rivals such as Dow Chemicals and Germany's BASF – announced its fourth-quarter results, saying it made a 27% rise in net profits to 5.81 billion riyals ($1.55 billion). The chemical maker said its sales for the fourth-quarter reached 41 billion riyals and that its biggest growth market is in China. High oil prices are positive for petrochemical firms because they increase petrochemical product prices, and SABIC usually does better in terms of profitability than rivals because it purchases feedstock at lower prices. Mady said there is no indication this feedstock price policy would change after the kingdom's Oil Minister Ali al-Naimi said last year the top OPEC producer was considering raising the price of gas to cover production costs.

"We don't have any indication, the feedstock is now fixed until the second round of review. We have not been really informed of any change," Mady said.

SABIC benefited last year from higher production after the addition of new capacity under its Saudi-based affiliates Yansab and Sharq and under its Tianjin joint-venture with Sinopec. ■

Business As Usual?

Strategy Development in the Chemical Industry in China

Differences – From a Western standpoint, business strategies should be based on an external and an internal perspective. The external perspective covers all aspects of the outside world, while the internal perspective focuses on the specifics of the company developing the strategy. While managers of Chinese chemical companies will likely to agree with this general view, there are substantial differences between multinational companies and Chinese chemical companies in the way this view is turned into reality.

Dr. Bernhard Hartmann,
Managing Director,
A.T. Kearney China

Dr. Kai Pflug,
CEO, Management
Consulting – Chemicals

External Perspective: Understanding The Market

Analyzing the market environment is arguably one of the most challenging parts of strategy development for the chemical industry in China. The reasons are manifold:

- Market demands, competitors and customers change much more rapidly in China than in developed markets
- The type of market participants in China is broader than in the West, including multinationals, private domestic companies and state-run entities (SOEs)
- Government policy has a stronger influence than in Western markets. For example, some MNCs have recently considered setting up production in China's western provinces in order to align themselves with government policy of promoting these areas
- Reliable data is still hard to come by in China. Any data available – whether customs statistics or data coming from industry organizations – has to be checked for its consistency and reliability
- There are many unofficial but sometimes extremely useful data sources that may or may not be available, e.g., customer lists of individual chemical companies
- Due to the lack of official data, other sources such as phone interviews, face-to-face interviews, fair visits etc. are more relevant than when examining Western markets

With regard to market analysis, local chemical companies tend to be better placed than MNCs, as they often have better access to local industry organizations, customers etc., and a better inherent understanding of the difficulties of getting reliable information in China. But their data collection process frequently lacks the rigidity that Western companies apply, and sometimes fails to uncover gaps between a company's perception of the market and market realities. Correspondingly, Western companies do better concerning the formalization of the analytical process but have a harder time getting difficult-to-access information or evaluating unreliable information.

Internal Perspective: Company-Specific Aspects

Keeping in mind that strategic choices are best derived from a fit between internal capabilities and external opportunities, an analysis of internal strengths and weaknesses is vital to gain competitive advantage. However, domestic Chinese chemical companies and MNCs operating in China show fundamental differences.

MNCs do include this analysis into their strategy development. For example, LyondellBasell established polypropylene compounding sites in China not only because of the market opportunities, but also because the company has knowledge in making these compounds that is superior to that of domestic companies.

In contrast, Chinese chemical companies spend very little time on the evaluation of their internal capabilities. Among them, there seems to be a strong feeling that if the market environment is right, a business opportunity should be grasped regardless of whether their own company has any specific competitive advantage in this area.

There are several possible reasons for this focus of Chinese companies on external factors rather than internal ones.

- Many companies, particularly SOEs, have a very broad business scope, which encourages a similarly broad-based search for opportunities. For example, Sinochem is not only active in chemicals but also in real estate, logistics, fertilizers, energy and finance. In contrast, a Western specialty chemicals producer such as Altana has only a limited number of focus segments.
- In addition, particularly for private domestic companies, there is limited company history that could serve as a guideline for future strategy.
- However, the key element probably is that Chinese chemical companies rely less on immaterial (and thus hard to gain) internal capital such as intellectual property, strong R&D or the technical knowledge of their employees than MNCs.

There is an obvious consequence to the limited importance Chinese chemical companies place on internal capabilities. The analysis of chemical markets should give comparable results independent of which company conducts the analysis. If this is the sole factor determining company strategy, Chinese chemical companies should all pursue similar strategies. Indeed, this "strategic crowding" can frequently be observed in the Chinese chemical industry. Often there is a rush towards seemingly appealing areas (past examples include PE, PP, coal chemistry and vanillin) by many companies and the subsequent creation of substantial overcapacity.

Let us now take a look at the outcome of the analysis and the subsequent development and selection of strategic options.

Striving For Localization

In their published strategies for China, a number of chemical MNCs emphasize localization:

- BASF claims that "local innovation and local production are driving business growth in this region". As a consequence, BASF is to increase local production to a target of 70 %
- Bayer aims to "grow in step with China's economic and social development"
- DSM focuses on internationalization of its asset base and workforce to create a better balance between sales by origin and sales by destination. China is specifically mentioned for its rapid sales growth
- DuPont counts growth in emerging markets among its four main strategic trends
- Dow China's president states that "our development in China is in the third stage, which is to build full local capabilities and capacities"

On the level of business strategies, this is reflected in multitude of activities along the value chain, including the establishment of local production, increased local hiring, moving into direct distribution or establishing local R&D activities.

Strategies Of Chinese Chemical Companies: Avoiding Limitations

In contrast, published strategies of Chinese companies tend to be less specific than those of MNCs. This is a consequence of the unwillingness of these companies to limit themselves in grasping market opportunities, though it is related to the lower perception of a company having specific core competencies. For example, Sinochem's strategy, also known as "One-Two-Three-Four-Five Strategy" is extremely non-restricting with its five components

- "One ability" – Sustainability
- "Two fundamentals" – Internal management/external expansion
- "Three joints" – resources, technology and market
- "Four measures" – Innovation, integration, M&A and collaboration
- "Five key areas" – Energy, agriculture, chemicals, finance and real estate

Consequently, the business activities of Chinese chemical companies are much harder to put into a strategic framework. Instead, decisions are driven much more by opportunities in the market (e.g., a high price for a specific chemical leading to many Chinese companies extending production capacity) or governmental influence (e.g., the rush into coal chemistry by Chinese companies). This is despite the claim of most Chinese chemicals to indeed have a strategy – a claim that is more likely to arise from the demands of the shareholders than from the desire to provide a guideline for the company. In reality, the vast majority of Chinese chemical companies do not seem to have a stable strategy.

Up Next

Read about the specifics MNCs in China in our April issue.

Conclusion

MNCs and domestic chemical companies differ in their approach to strategy development. While MNCs tend to have somewhat consistent business strategies based both on internal capabilities and the external situation, local companies focus much more on market opportunities and overall are less limited by strategic decisions. While this may partly be the result of cultural differences, it can also be explained at least partly by the specifics of Chinese companies such as the combination of good market knowledge and less clear-cut core competencies.

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Redefining Roles

The U.S. Chemical Industry's Position in the World

Is the worst over? – A cautious but growing consensus among economists and industry analysts suggests that after more than two years of turbulence, the global economy in general and the chemical industry, in particular, are entering calmer waters.

At the same time, this recovery presents its own set of challenges for U.S. chemical companies. The growing size and diversity of emerging markets, the increasing influence of chemical producers in the Middle East, Asia and Latin America, the increased burden of environmental regulations and many other factors have created a new global playing field in which U.S. companies are no longer taking their technical, financial and market advantages for granted. In fact, "business as usual" will never be the same again as the U.S. chemical industry moves into a post-recession global economy. U.S. chemical companies are redefining their traditional role as chemical producers and literally reinventing themselves as the global industry's leading science and technology companies for the 21st century.

The U.S. and Emerging Markets

U.S. chemical companies are increasingly focused on emerging markets, recognizing their tremendous market potential. As consumer spending increases in China, the demand for differentiated products is expected to follow suit, driving the chemicals market toward specialty chemicals.

Equally significant market opportunities exist in India. The country is currently the second-biggest market in Asia with a population of 1.12 billion. However, by 2025 the population of India will approach that of China, and India's population will continue to drive increased levels of consumption. By 2015, over 63 million Indian households are expected to reach a household income of over $6,500 annually, ensuring demand for food and healthcare products as well as consumer goods.

For the moment, most U.S. chemical companies see Asia and Latin America primarily in terms of market opportunities, not competitive threats. However, that perspective will most likely change in the near future. The American Chemistry Council (ACC) expects chemical industry output in emerging nations to increase 7.6 % in 2011, surpassing expected growth rates for the U.S. To maintain their competitive advantage, many U.S. chemical companies are taking steps now to realign or expand their global initiatives and strategies. Recent activities include the following:

- In November 2009, Air Products opened a new specialty amines plant in Nanjing, China, which will complement its existing local capabilities.
- ExxonMobil Chemical has announced that the majority of growth for its products in the near future will be in Asia, especially China and India. The company intends to supply these markets from its global network, including its Singapore manufacturing facilities.
- Chevron Phillips Chemical Company (CPChem) is increasing its production capacity in the Middle East with two new joint ventures between affiliates or subsidiaries of CPChem and companies in Saudi Arabia and Qatar. CPChem already owns three plants in the region, with another one under development.
- In March 2010, Eastman announced the acquisition of Genovique Specialties Corporation, a global producer of specialty chemicals. Through the deal, Eastman acquired operations in the U.S. and several countries overseas, including a joint venture in Wuhan, China.

New oil and gas discoveries in Brazil have put the petrochemicals sector and the country on a path to strong growth and development. The promise of Petrobras' pre-salt hydrocarbons program, demand from China and the success of tax reductions for autos and consumer appliances have increased confidence in the region. By 2014, Brazil is estimated to receive investments of over $26 billion for the chemicals industry, according to a survey by the Brazilian Association of Chemicals Manufacturers (Abiquim). The investment is expected to generate 5,800 direct jobs.

Opportunities in Brazil have not been overlooked by U.S. chemical companies. In the first quarter of 2010, Dow Chemical's sales in Latin America increased 25.5 % year-over-year from $1.13 billion to $1.41 billion. DuPont witnessed a 21 % increase in its Latin American sales in the first quarter of 2010, to $800 million. Latin American sales contributed 9 % of the company's global sales.

The growing economic importance of Brazil to the U.S. is reflected by the complex trade relationships between the two countries. Of particular importance to the U.S. chemical industry is a long running dispute between Brazil and the U.S. over U.S. cotton subsidies. This dispute has led to the possibility of "cross-retaliation" penalties by Brazil involving the suspension of patent and intellectual property rights on goods including agricultural chemicals, biotechnology products, and pharmaceuticals.

Overcapacity, Emerging Market Competition

Although the U.S. chemical industry is clearly recovering from the global recession, production facilities in China and the Middle East are being built at a rapid pace. Global overcapacity, particularly at the commodity end of the industry, is a strong possibility, even with increased demand from emerging markets.

To an extent, the U.S. industry is sheltered from these dynamics by its feedstock advantage. Natural gas, which in 2010 enjoys a cost advantage of 20 to 1 over crude oil provides the basis for approximately 70 % of U.S. ethylene, while in Europe, for example, 70 % is derived from oil-based products. If the U.S. chemical industry becomes more proactive at identifying and rationalizing un-economic plants than its European competitors, it may be better placed to face these new challenges.

Undoubtedly, however, global overcapacity and emerging market competition will continue to change the market dynamics of the U.S. chemical industry. At the same time, the U.S. chemical industry is being presented with huge areas of opportunity by the emergence of a number of global mega trends, such as climate change, sustainability and population growth. The U.S. chemical industry has not remained idle in the face of these challenges, and many companies have already started to adapt through rigorous portfolio rationalization and a drive to advanced specialty chemicals, which focus on providing the solutions for the needs of a changing world.

The actions taken by U.S. chemical companies during the downturn may have given them a head-start over their European counterparts in terms of realigning their business models to fit the needs of their long-term strategic goals. To remain competitive, U.S. chemical companies must continue and even increase their drive to develop and productize world class scientific research and technology.

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A Philosophy Of Innovation

Clariant Makes Frankfurt Its Global Hub For R&D

New Architecture for New Innovation – A warm, open building with an inviting aura as a home to R&D laboratories for the chemical industry – visitors strolling through any given industrial site aren't likely to happen upon such juxtaposition. That is, unless, we find ourselves in Industriepark Höchst in Frankfurt, Germany, at the end of 2012. That's when Clariant's new innovation center will officially open, making it the home of the Swiss-based company's global chemical R&D activities.

Martin Vollmer, Chief technology officer and head of Group Technology Services, Clariant

Hariolf Kottmann, CEO of Clariant

The 23,000 m² center, which represents an investment of more than €50 million, will cooperate closely with the company's R&D satellite sites in Gendorf, Germany; Lamotte, France; and Suzano, Brazil as well as 40 application centers around the world. Five R&D centers will call Frankfurt home – colorants; surfactants and alkoxylates; effect chemicals and intermediates; specialty polymers; and formulation technologies.

The center's open architectural office and laboratory concept intends to combine chemical research and development activities, which belong to the company's Group Technology Services group; and application-oriented laboratories and technical marketing functions, which belong to several of Clariant's 10 business units. The new building will also become home to New Business Development, Intellectual Property Management and the company's Patent department. The company said that combining different disciplines will allow it to further expand its R&D pipeline and strengthen its innovation power.

Innovation Hub

"We have an enormous synergy potential within Clariant," said Martin Vollmer, chief technology officer and head of Group Technology Services. Vollmer said that by creating a centralized R&D hub, the business units can work better together on innovative projects and inadvertent competition between the 10 units can be avoided.

Clariant has developed what it calls an "Innovation Chain," which it says links the "technology push" with the "market pull." At the group level, chemical R&D; process R&D and pilot plants; and new business development will all be brought together within the new center in Frankfurt. Application development and technical service as well as production will still take place at the business unit level.

Innovation is big on the company's agenda. Following the conclusion of its Project GANO – Clariant's wide-reaching restructuring program that began in 2008 – CEO Hariolf Kottmann is clear on his vision for the company's future.

"Innovation in combination with an increased strategic focus on profitable growth will be a key cornerstone for our company," he said at the unveiling of the R&D center design in December. "The goal is to establish Clariant as an innovation leader in the field of specialty chemicals within the next few years."

The company invested about 130 million Swiss Francs (approx. €100 million) in R&D in 2010, or about 2 % of sales, which, while it is the industry average, could be considered low for a company with such high ambitions.

"We have clear targets in terms of profitable growth."

"This is merely our starting point coming out of restructuring," Vollmer said. "We are currently in the process of defining our future product portfolio. If we see sales potential in a particular area, we will of course selectively increase our R&D resources. However, we haven't yet defined a target for 2011; this will be clearly driven by our initiatives which are our technology platforms and new joint R&D projects with our customers."

Looking ahead to projected R&D spending in the years leading up to the completion of the R&D hub in Frankfurt and beyond, Vollmer said it was difficult to put an exact price tag on it.

"This is really a selective approach, looking at our new setup of our R&D centers and the projects we agree upon with our business units," he said.

The new Clariant Innovation Center's design was inspired by the key concepts of innovation, movement, energy, emotion, enthusiasm and courage. (Design by HPP Architekten)

Design

The new innovation center was designed by HPP Architekten of Düsseldorf, Germany. The company was chosen from a pool of competitors, which was overseen by Bäumle Architekten/Stadtplaner.

Sales of New Products and Role of Renewables

If the company's sales generated by products five years and younger are any indication, then it will be likely that R&D spending will increase over the coming years. Currently, the 22 % of the company's sales come from such new products, and Vollmer said he expects this percentage to increase through the company's definition of its future innovations programs.

"We have clear targets in terms of profitable growth, and this growth will be driven in part by new innovation projects," he said. "In the long run, we will not only see growth through the sales of existing products and regional expansion, rather also real innovation will also contribute to profitable growth."

Vollmer said he believes biggest challenge is to understand the market needs around the world and to turn these market needs into the right chemistry.

"We have to translate the needs into the right R&D projects," he said.

The company said it is looking toward megatrends to drive its product innovations. Renewable energies, energy efficiency and renewable resources are just three areas expected to open new business markets for Clariant beyond its current ones. However, Vollmer emphasized that these are not completely new areas for the company.

"Sustainability is part of our corporate strategy."

"Renewables already play a very important role in the current Clariant portfolio," he said. "In the business unit Industrial and Consumer Specialties, more than 20% of the product portfolio is based on renewables. Sustainability is part of our corporate strategy."

Brandi Schuster

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Chemicals

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Nourishing The World

DSM's Feike Sijbesma Named UN Humanitarian of the Year

Feed The World – When DSM's CEO Feike Sijbesma was awarded the UN's 2010 Humanitarian of the Year Award, it put the chemical industry in a new light. Sijbesma, who won the award for his commitment to corporate social responsibility and in particular for DSM's partnership with the United Nations World Food Programme, said: "Although some people think that our industry is part of the problem, in fact we are already a substantial part of the solution." Brandi Schuster asked him about the role the chemical industry plays when it comes to global problems.

CHEManager Europe: Mr. Sijbesma, what responsibility do chemical companies have when it comes to tackling to global problems?

F. Sijbesma: We all have a responsibility to do what we can, not only the (bio-)chemical industry. The private sector, and our industry in particular, has unique competencies that are key in addressing global issues, like combating climate change, developing alternative energies, addressing health and wellness for many, etc. This goes beyond the traditional corporate social responsibility, since the private sector can develop market-based solutions to tackle many global problems. For me, it is a combination between feeling the responsibility to contribute to the global issues as well as using the same issues as a business driver.

How would you say the international chemical industry is doing as a whole as far as helping counter global problems is concerned? Will the industry ever be able to shake off its oftentimes questionable public image?

F. Sijbesma: Today within the chemical industry, achieving a top ranking on the Dow Jones Sustainability Index has become very competitive, which I think shows that things have already changed substantially in the chemical industry. The savings of greenhouse gas emissions in end-products, at the level of our customers and the final users, are two to three times higher than the emissions during the production and transport of our products. In other words: Although some people think that our industry is part of the problem, in fact we are already a substantial part of the solution. We might need to communicate this better, indeed. On top of this, the industry will move more and more towards renewable inputs, such as bio-mass. This will also make that the industry will be seen more as a green industry. This shift has already started, and at DSM we are working on growing this bio-based economy from a niche market to the mainstream. I also like to add here the contribution our company is making in the combat against (hidden) hunger.

Do you think your winning this award will serve as a wake-up call for other major chemical companies to get involved in such global issues?

F. Sijbesma: That is my hope. There are already many private corporations involved in public-private partnerships aimed at addressing a variety of global issues, but more action is needed. The private sector has an enormous wealth of unique expertise that should be shared to help realize global aims such as the United Nations Millennium Development Goals. DSM has been active in helping to make progress towards achieving these goals: by partnering with the World Food Programme, we have made a commitment to fight hunger and malnutrition around the world. In addition to providing technical and scientific expertise and developing new products, we are raising awareness of this pressing issue of malnutrition – also known as hidden hunger.

How is it financially possible for a company to develop products for a consumer group that is essentially without means?

F. Sijbesma: As the world's largest supplier of vitamins and nutritional ingredients, DSM is committed to help the beneficiaries of the World Food Programme. Together we can improve the quality of the food basket that is provided to the world's neediest and most vulnerable people. We want to share our knowledge and expertise and create better, brighter lives for them and for generations to come. Almost two billion people in the world suffer directly from hunger or so-called hidden hunger. DSM has the ability to help these people. We decided to do so and not turn our back.

Dying people are no business model: They need our help. So, we offer our knowledge and patents for free for this purpose to this group of people. I often say: We cannot be, nor can we call ourselves, successful in a society that fails.

Next to the "poorest of the poor," there is a large group of low-income people who don't have the financial means to afford the variety of foods needed to meet their nutrition requirements but, in most cases, can afford the marginal costs associated with fortified foods. The cost to add these nutrients is so low (i.e. $3.00 per ton of flour) that it does not even have to result in a higher final market price. Here DSM is applying its "normal business models."

DSM started its strategic partnership with the World Food Programme in 2007; what initially sparked the relationship between your company and the UN program?

F. Sijbesma: Through the sponsorship of the non-profit humanitarian organization Sight And Life, DSM has strived since many years towards better scientific understanding of the impact of hidden hunger and addresses specific micronutrient deficiencies. People who have enough carbohydrates but a shortage of vitamins and minerals stay alive but become ill and develop diseases like blindness, fatigue, anemia, etc., and become a burden for already poor societies.

In addition, DSM had already been active in food fortification for many years prior to the partnership with the World Food Programme and had created DSM's Nutrition Improvement Program. One of the main goals of this program was to develop strategic partnerships to assist in the development, implementation and monitoring of successful food fortification programs.

Against this background and realizing we are the largest player in the world in the field of mirconutrients, I was triggered at the World Economic Forum in Davos listening to some African leaders being concerned about carbohydrate rich food aid without micronutrients and claiming they might become poorer due to this. Then we decided to offer our help and give the UN access to our knowledge and expertise.


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According to DSM, almost two billion people in the world suffer directly from hunger or so-called hidden hunger.

What are specifically the kinds of products your company has developed to help combat hidden hunger?

F. Sijbesma: DSM worked in close partnership with the World Food Programme to develop new nutritional solutions. For example, DSM developed a sachet of micronutrients called MixMe, which simply needs to be sprinkled over the food. It provides the full recommended daily nutrition intake and does not require people to change their diets.

We have also developed a rice product called NutriRice that is made from broken rice kernel, a by-product of normal rice, and vital vitamins and minerals (especially vitamin A). It is added to normal rice at a ratio of 1:100 and doesn't change the taste or the color of the rice but provides the necessary nutrients.

We are proud of the innovations that we have developed, which have helped more than two million people to date. Through our partnership with the World Food Programme we aim to provide improved nutrition to 80 % of WFP's beneficiaries.

What other global trends do you anticipate will shape the future of chemical R&D? More specifically, what other projects is DSM working on to this end? Does DSM have similar programs in operations in other business units, such as in pharma?

F. Sijbesma: Climate and energy, health and wellness, and global shifts are fundamental trends that will have a massive impact on our industry. Our strategy as a company is to focus all our R&D activities on meeting the unmatched needs in relation to these trends.

On climate and energy, the chemical industry is, for example, going to have to make the transition from fossil fuel dominated to more sustainable bio-mass based production. With our life sciences and materials sciences combination we are uniquely positioned to develop bio-based solutions and are leading the way in terms of the development of bio-based materials, and the development of sustainable second generation bio-fuel. The implications of the climate and energy trend are so profound it is already touching all areas of our business and its importance is set to increase dramatically over the coming years.


Feike Sijbesma, CEO of DSM

For example: we make products that make solar cells more efficient, that increases the blade size of windmills, that make cars lighter (so less fuel and CO_2), that make paints cleaner and greener, etc.

In 2009, DSM, having significant experience in sustainable production, was the first non- pharmaceutical company to join the Green Chemistry Institute Pharmaceutical Roundtable of the American Chemical Society (ACS), as an associate member. The Roundtable was founded in 2005 to promote green manufacturing of active pharmaceutical ingredients (APIs).

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International Year of CHEMISTRY 2011

Diversity Attracts Diversity

Recruiting Senior Female Managers Often Challenging in Chemistry Industry

The Right Chemistry – The quest for talent is one of the greatest challenges for companies across the globe and Univar is no exception; hiring the right mix of talented senior management is crucial in maintaining the long-term success of the business. However diversity is not always easy to achieve, particularly in an industry that is perceived by many to be male-dominated and unwelcoming to women.

Sheila Mowatt, director of Operations, Univar EMEA, has worked in the industry for more than 20 years and has seen a lot of progress since she started out, when a manager suggested it was preferable for women not to wear trousers.

Eveline de Wit, Human Resources director, organization and staffing, Univar EMEA

"As a female employee you were expected to wear a skirt," she says. "Another time, when I was recruiting an operator the candidate handed me his coat, assuming I was the secretary." These days, more and more women are entering the industry and rising through the ranks, though some feel that there is sometimes a bit of a "boys' club" at the higher levels of management, making it difficult for them to achieve the very top positions.

"Either you have very open-minded leaders who go for diversity or those who look for people that are the same," says Sonia Pires, director, SHE & Sustainability, Univar EMEA. While it can be more comfortable to recruit people who are unlikely to challenge you because they have a similar outlook to your own, there is a real danger that your company will be unable to evolve and innovate at the rate that your competitors do. As Pires points out, "If you do things the way you have always done, you will get the results you have always got."

Quotas Perhaps a 'Necessary Evil'

In recent years, significant legislation has been introduced to promote diversity in the workplace, though many have mixed feeling about this. Pires is uncomfortable with recruitment quotas as it forces people to hire women rather than encouraging them to do so of their own accord but concedes that it is perhaps a "necessary evil." Mowatt agrees, saying that for a company to make real progress, senior management must truly embrace diversity themselves.

David Jukes, president of Univar EMEA, understands the value of fostering a diverse leadership team and recognizes the role he and his staff have to play in achieving this.

"It's a mindset: You have to want to do it, and then you will. It needs to come from the top," he explains.

Univar does not enforce quotas for hiring women but instead tries to create an open and meritocratic environment that is attractive to female candidates.

'Diversity Attracts Diversity'

Introducing the option for staff to work flexibly, both in terms of times and location, has been very well received by both male and female employees and has led to increased output. In addition it enables Univar to attract talented female staff for whom the option to work from home is essential; women who would otherwise go to another employer.

Having women in senior positions also filters down through the rest of the company ensuring that the drive for diversity gathers momentum naturally.

"Diversity attracts diversity," asserts Jukes. "Once 30 % of your leadership team is comprised of women, you will naturally attract more women coming through."

Mowatt is one of four women in Univar EMEA's Leadership Team, which is made up of the 12 most senior managers in the region. She spends part of her time mentoring more junior women in the company and agrees that having women in top positions generates a pervasive culture that is very encouraging and attractive for other women.

Common Misconceptions

While companies like Univar have done much to make the chemical engineering sector more appealing to women, there is still a misconception in many schools that it is an industry where women are not welcome. This is particularly true in the UK, says Mowatt, where she feels companies should be more active in reaching out to female students who are considering their career choices. This year she will be conducting a series of seminars with male and female students in Scotland to educate them on the opportunities in chemical engineering and dispel some of the myths surrounding the sector.

Janet Wang, Finance and Administration manager, Univar China, echoes Mowatt, explaining that traditional views about work have been very influential in China, though this is beginning to change.

"Traditional parents will often prefer their daughters to do an arts degree and their sons to study science, but this is happening less and less; nowadays young people are making their own decisions about what they want for their future."

In Southern Europe and in the U.S. this seems to be less of a problem. In countries like Italy, Portugal and Greece it has long been common for women to work as chemical engineers while in the U.S., schools are much more active in promoting a wide variety of career options to their students, often working with companies to do so.

Taking The Initiative

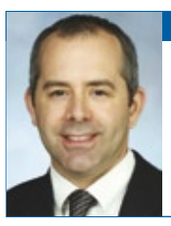
While much of the responsibility for promoting diversity lies with companies themselves, women must also take the initiative and be active in pursuing the top jobs.

Continues Page 8

On Risk Governance and Nanotechnology

Ensuring the Sustainable Application of Nanomaterials

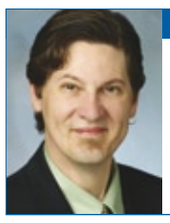
Responsibility – The benefits to humankind from the application of nanotechnologies are as varied as the different questions that need to be addressed to establish a reliable risk-based regulatory framework. Industry has critical continuing roles to ensure responsible, safe, and sustainable use of nanoscale materials and to work with regulators and the public to establish efficient and effective risk governance of manufactured nanoscale materials.



Eric Dubé, Steptoe & Johnson

Anna Gergely, Steptoe & Johnson

Seth Goldberg, Steptoe & Johnson



Erik Janus, Steptoe & Johnson

Nanotechnology: Promises And Challenges

The marketplace for manufactured nanomaterials (MNMs) will continue to see impressive growth well into the next decade. According to BCC Research, this market could be worth $25 billion to more than $2 trillion by 2015. Benefits resulting from application of nanotechnologies are vast and varied, with promises of cleaner soil and water, cheaper energy, improved and more effective consumer products, industrial equipment, and medical tools and devices. If regulatory complexities and public acceptance of these new applications of this emerging technology can be addressed, sustainable application of MNMs in products and devices stands to revolutionize life as we know it.

However, public acceptance of nanotechnology depends on many variables. Information is needed to establish an acceptable risk-based regulatory framework. Regulatory issues are also challenging, varied, and require a life-cycle approach, beginning with minimizing exposure during manufacturing, ensuring safe consumer use, and managing disposal of MNMs to protect the environment.

Based on this uncertainty, the largest challenge now is how to apply traditional regulatory approaches or develop novel risk-based decision frameworks. Other key challenges include understanding how critical physicochemical characteristics of individual MNMs, such as surface charge, composition, size, etc., influence biological reactivity and under what conditions. Previously published approaches to understanding the risks from MNMs have ranged from more qualitative, such as the use of expert elicitation to perform a relative risk ranking, to more quantitative, which can include "bridging" to toxicity data from existing materials, such as ultrafine particles. Applications of these approaches have ranged from more theoretical and descriptive to more practical and prescriptive, such as the use of engineering controls at manufacturing facilities.

Drive For Good Governance

Regulatory oversight of nanotechnologies requires good governance based on efficient and effective regulation responding to the needs and concerns of both industry and the public. Efficient regulation exists where total benefits to some exceed total costs to others, while effective regulation maximizes compliance with minimal resources and/or requirements. Data gaps associated with emerging nanotechnologies, however, make it difficult to propose and optimize efficient and effective regulation.

To fill the data gaps, good governance should strive toward internationally harmonized regulatory practices, with sufficient flexibility, to allow innovation and product development while maintaining the protection of human health and the environment and building public trust and confidence. This requires outreach and education to familiarize the public with the safe and responsible application of nanotechnologies and their benefits. Failure to engage with stakeholders and consumers early and often can yield to precautionary bans, such as recent decisions on acceptable organic standards in the U.S., Canada, UK, Australia, and Austria.

Principles comprising good governance of MNMs are not materially different for any other emerging technology. However, differences in existing laws, even within the same jurisdiction, can have an effect on how these products are regulated and if regulatory approval is even sought.

A good example is the U.S. standard, the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA), which was recently described as "comparatively well-suited for assessing and managing risks from pesticides, including those containing nanomaterials" and, thus offers a "greater level of oversight and a more precautionary approach than [the Toxic Substances Control Act, TSCA] and several other statues." FIFRA requires a very data-intensive registration process and, unlike TSCA, FIFRA has been used to justify an enforcement action on an unlabeled antimicrobial-treated product making a pesticidal claim. To date, only a handful of companies have even attempted to get an EPA registration for nanopesticide, the most notable was a recent decision to issue conditional approval to a nanosilver-based antimicrobial pesticide intended for textile preservation.

Fundamental Needs

Before efficient and effective regulation of nanotechnology can be actualized, universally accepted "generic" definitions for MNMs are needed.

Definitions need to be broadly applicable, practical (legally clear and unambiguous), and achievable (enforceable using existing methods or easily adapted methods) – based on international consent. This is not currently the case, and it is unclear whether the existing multitude of definitions can be harmonized on the international level. For example, the lower end of the size range for nanomaterials is usually 1 nanometer (nm), but the upper bound can vary considerably, with some as high as 1,000 nm in diameter. As testament to the difficulty of this process, it should be noted that International Standards Organization (ISO TC 229) initiated work in 2005 and only recently released "Nanotechnologies — Vocabulary — Part 1: Core Terms" in 2010 (see ISO/TS 80004-1:2010).

Another fundamental need is the establishment of "essential elements" of the MNM hazard and exposure databases for regulatory needs. Currently, such databases are not publicly available for any single MNM. Equally important are developing exposure data and validating standardized approaches to measurement, interpretation, and application of such data.

Present Policies and Governance Initiatives in Europe

In the European Union, the existing legal framework contains both horizontal and vertical legislative measures, which are also applicable to nanotechnology. The horizontal measures apply to all industries and cover general fields, such as the environment, waste, chemicals or general product safety and product liability, while the vertical measures address specific industry sectors.

One of the most relevant horizontal legislation for nanomaterials is Reach, which does not specifically mention nanomaterials but covers all substances under its scope, whether in "bulk" or nano-form. For registration purposes, Reach does not consider the nano-scale forms of existing bulk substances as "new" substances. Therefore it was expected that for the first registration deadline of the high production volume (above 1,000 MT) bulk substances, relevant toxicological data for the nano-forms, manufactured in much lower quantities, had to be submitted by the end of November 2010 as well. Discussions whether it is necessary to update Reach and specifically address MNMs is ongoing.

There are several existing vertical directives and regulations that cover potential nanotechnology applications without specifically addressing MNMs (i.e. cosmetics, food contact uses also in active and intelligent packaging applications), and these are now individually revised and amended to specifically address nanotechnology. These amendments include several proposed definitions of nanomaterials, which collectively may lead to difficulties of compliance and with enforcement without thoughtful consideration.

The Role Of Industry

If companies wish to sell products made with or including MNMs in the global marketplace it is imperative they perform due diligence regarding product stewardship, including use of safe manufacturing practices, product testing, and assessment of potential environmental releases when products are disposed.

To ensure full knowledge of how properties can be harnessed for maximum efficacy and minimum "contamination" across a product's life cycle, "up front" thinking is required about product need, use and composition. Data available from early product development and materials research may serve quite useful to the global knowledgebase. These could be contributed under some voluntary data provision initiative similar to the former EPA Nanomaterials Stewardship Program. While it is recognized that past voluntary efforts in both the U.S. and in some EU Member States might not have met the expectations of authorities, they can "play a constructive role in nanotechnology oversight as well" if managed properly with clear consequences and practical milestones for success.

There are other novel approaches that could be taken more globally, such as the "safe harbor" approach that U.S. Food and Drug Administration has taken with its regulated community. In this case, discussion of MNM data from early in the discovery process could be crucial to the success of later data submissions and help build the necessary minimal hazard and exposure datasets. In addition, such a forum would be ideal to discuss the utility of "bridging" to existing toxicological data to satisfy certain specific regulatory requirements.

Recommendations And Conclusions

With regard to MNMs, global regulatory oversight and international harmonization of definitions, reference materials, testing strategies and risk assessment methods are needed to secure consumer trust and prevent precautionary over-reactions. Possible reactions include blanket prohibitions that impede free market movement of goods and stifle innovation in ways that can lead to trade barriers.

Industry has a role in providing regulators the necessary data and in assisting in the implementation and application of these data through transparent, participatory and collaborative policy development. Effective and efficient governance requires a wealth of data yet should include all viable existing regulatory options and voluntary measures along with mandatory requirements, and should be based on international consensus. It should be in the interest of industry to contribute towards the development of hazard and exposure databases and place safe MNM products on the market. This can drive "good" cooperative governance and ensure MNMs can be sustainably applied in the global marketplace.

Erik Janus, Anna Gergely, Eric Dubé, Seth Goldberg

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No Dumping Ground

U.S. Policymaking on Chemicals Is Gaining Momentum

Legislation – Reach is just the tip of the iceberg. Albeit the European Union has set the pace for strengthening chemical legislation there is a lot of regulatory progress in the U.S., too. The agenda is driven by both politicians and public pressure groups determined to put UN's Strategic Approach to International Chemical Management (SAICM) into practice. While the far-reaching reform of the Toxic Substance Control Act (TSCA) is still pending, federal states have taken the lead: In the last eight years, 18 states have passed 71 chemical safety laws according to a report published in November by a Washington-based coalition of 250 environmental and health advocacy groups. The report also found that the pace of state policymaking on chemicals has more than tripled in eight years.

Berndt Stürznickel,
Global solution manager,
SAP

At the federal level, California's Green Chemistry Initiative is widely seen as the lighthouse project. Representing the eighth largest economy in the world, the Golden State is expected to provide the blueprint for collaborating with manufacturers, importers and retailers to increase the safety of use of chemicals.

"Our regulatory proposals are intended to prevent California from becoming a toxic dumping ground," said Maziar Movassaghi, Acting Director of the California Department of Toxic Substances Control, in a recent Bloomberg Businessweek article. Although the statement might sound somewhat harsh for European observers, his sentiments reflect the current situation in which the federal players see the need to act on their own, especially since Congress appears to take an indefinite amount of time to pass the reform of TSCA.

Pending TSCA reform

Even though the legislative procedure carries the name "TSCA Reform 2010," it was obvious that decisions would not be made before 2011. Despite growing public resentment over the delay, the outcome of the recently held mid-term elections is not likely to refuel the process. Political observers expect both houses to adjust the pending proposals to the new majorities. On top of this, a serious number of co-introducers of the bills have lost their mandate in the election. On the other hand, there still is broad consensus in both the Senate and the House of Representatives on the need of making the existing law fit for the requirements of the global market, particularly in light of Europe's Reach regulation. Furthermore, the regulatory developments on federal level, especially the commencement of the California Green Chemistry Initiative, will have a strong impact on Washington, too.

As the reform's passage is inevitable, global players should prepare both their enterprises and value chains for the upcoming changes. The U.S. Environmental Protection Agency (EPA) is determined to place a much harder workload on industries.

"More than 30 years after Congress enacted TSCA, it is clear that we are not doing an adequate job of assessing and managing the risks of chemicals in consumer products, the workplace and the environment," stated Lisa Jackson after taking over her new role as EPA Administrator in 2009. "It is now time to revise and strengthen EPA's chemicals management and risk assessment programs."

Following the example of the EU, the U.S. will shift the burden of demonstrating the safety of chemicals to importers, manufactures and processors. All market participants will have to provide the agency with sufficient information showing that new and existing chemicals are safe. In connection with these goals, TSCA will focus more strongly on the risks of sensitive subpopulations like children. For this purpose, the EPA will define a minimum data set that is to be submitted. The set will include data on chemical identity, substance characteristics, biological and environmental fate, transport, toxicological properties, volume manufactured, process or import status, intended uses and exposures from all stages of lifecycle. Any "failure" – a term which has not yet been defined by the EPA – to submit the required data might limit or even stop the market access of a substance.

Health And Consumer Protection

The overall goal of the reform is to establish a framework to ensure that all chemical substances to which people are exposed will be reviewed for safety and restricted where necessary to protect public health and the environment. Although TSCA will take into consideration already existing test data from regulations like Reach, enterprises have to be prepared to deliver additional data regarding the uses of a substance. As it stands, there are no plans for data sharing or establishing organizations similar to Substance Information Exchange Forums (SIEFs). However, it is likely that consortia structures will be revived, at least for funding the costs associated with testing.

TSCA has asked EPA to reduce the use of chemicals of highest concern. To promote the development of safer alternatives, the EPA will issue a priority list that comprises at least 300 new and existing substances and mixtures. The required data must be submitted 18 months after the publishing of the list. Risk management decisions should take into account sensitive subpopulations, cost and availability of substitutes, etc.

According to the pending Senate bill, all other substances have to be addressed within 30 months of addition to safety determination or within 14 years after enactment of TSCA 2010, whichever comes first. In contrast to this, the House bill encompasses three timelines – ranging from three to five years – depending on production volumes.

California Green Chemistry Initiative

As TSCA reform 2010 is still waiting to be passed, the California Green Chemistry Initiative is attracting increasing attention. The initiative is a broad public policy striving for safer products, the expansion of pollution prevention and product stewardship programs as well as the move toward a cradle-to-cradle economy. Due to its wide focus the initiative is expected to significantly increase the compliance management burden of any company whose products are sold in California.

The Initiative comprises of two laws coming into force early this year. One of them, AB 1879, will establish a safer alternatives regulatory regime for consumer products. At press time, the law was expected to concentrate until 2016 on children's products, including toys, personal care products and household cleaners, as well as on the associated components of these products. From 2016 on the law is going to cover the full range of consumer products. In contrast to European law there will be only a few exemptions like food, pesticides, prescription drugs and medical devices. Another law, AB 289, provides an important means for DTSC to obtain information regarding chemical manufacture, use, and fate in California.

While TCSA regulates the substance sector, the California Green Chemistry Initiative operates at product level. Because of, manufacturers, distributors and retailers will have to analyse the chemical composition of the products they deal with. In June, the Department of Toxic Substances Control (DTSC) will release a list of Chemicals under Concern, from which a list of Priority Products will be generated, later on. Apart from EPA defined chemicals, the list is expected to encompass substances according to Reach Annex XIV, Canada Schedule 1 and CA Prop 65. If companies use Priority Chemicals in their products, they are requested to show all effects that are connected with the uses of the product. Although details on the scope of examination have not yet been published, it is expected that DTSC is going to demand more data than the European Chemicals Agency (ECHA). Nonetheless the DTSC will also accept dossiers submitted under Reach. If the proportion of a Chemical of Concern is below 0.1 % w/w or below the thresholds established for hazardous waste companies only have to submit a corresponding notification.

On top of their reporting duties, companies will have to perform assessments for each Priority Chemical they are using in order to explore safer alternatives. After successfully replacing Chemicals of Concern, companies are obliged to report the corresponding product composition changes to DTSC.

Proactive R&D

In order to avoid regrettable substitutions, companies should not entirely concentrate on valid substance lists but also look for chemicals discussed by regulatory stakeholders and influencers. Regarding both listed and discussed chemicals, R&D, portfolio, sales and procurement managers have to find viable answers to questions like: In what way does a substance have a regulatory impact on which product? Does the substance add an essential value to this product? If not, how can a substitution process be organized? If the substance is indispensable, what is to be done to provide all required data on safe uses?

To minimize both the costs and the risks of compliance management, any R&D project should start with a comprehensive definition of target markets. Product stewards depend on this knowledge to find synergies from organizing the necessary compliance processes holistically. European companies, for instance, should structure the management of Reach regulation in a way that allows them to reuse the data in the U.S. and vice versa.

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Strong Investments, Stable Revenues

Tenants Invest €495 Million in Industriepark Höchst

ADVERTORIAL Milestone – Total investment in Industriepark Höchst hit another remarkable milestone in 2010. Tenants invested €495 million, bringing total capital expenditure to €4.8 billion since 2000, Jürgen Vormann and Roland Mohr, CEO and COO of Infraserv Höchst, the park's operator, announced recently.

The high level of investment is primarily the result of two major projects currently underway at Industriepark Höchst. Ticona's new production facility and the waste-to-energy plant, which will further optimize the park's energy supply, have kept investment strong after 2008 and 2009 saw investment reach €602 million and €644 million, respectively. These record-breaking years were partly due to the two projects. "Obviously, we don't expect total investment to remain so high, but we find that investment is staying healthy – above and beyond these large projects," Vormann explained.

Infraserv Höchst Optimizes Energy-Supply Capacity

The park's operator is currently commissioning the new gas-turbine plant, which consists of two 45 MW turbines and was erected near the combined-heat-and-power plant. As this advanced facility adds production capacity and boosts the efficiency of the energy infrastructure, it will help keep energy prices competitive for tenants. However, it benefits the environment, too. Efficient technology and eco-friendly natural gas will slash CO_2 emissions. The waste-to-energy plant, scheduled to go online in the first half of 2011, also makes ecological sense. It reduces the need for fossil fuels and consequently cuts CO_2 emissions. Infraserv Höchst currently produces enough power to serve 60% of the park's needs. Once the two plants have come on stream, its output will go up to 100%. The park will then be largely self-reliant and independent of external supplies or price fluctuations in the electricity market.

Sewage-sludge incinerator at Industriespark Höchst

The biomethane-upgrading plant currently under construction in Industriepark Höchst will also expand the supply of clean energy. Beginning in mid-2011, biogas – which Infraserv Höchst has been producing from sewage sludge and organic waste since 2007 – will be upgraded to pipeline-quality methane in the new plant and then injected into the public grid. Infraserv Höchst and Mainova, a utility, set up Infranova Bioerdgas GmbH as a joint venture specifically for this purpose.

An Efficient Energy Supply Is Climate Protection In Action

With efficient power plants, widespread use of co-generation and the recovery of waste heat from production and incineration plants, Industriepark Höchst is already contributing to climate protection. These measures eliminate 400,000 metric tons of CO_2 emissions each year. Mohr said, "Energy efficiency is part of our day-to-day business as a park operator and industrial-service provider. Between these efforts and our considerable investments, Infraserv Höchst and the park's tenants are helping to cut CO_2 emissions significantly."

Infraserv Revenues: €1.2 Billion

The year 2010 turned out to be a strong year overall for the Infraserv Höchst Group. Infraserv Höchst KG and its wholly-owned subsidiaries – Infraserv Logistics, Provadis, Partner für Bildung und Beratung, Technion and Infrasite Griesheim – generated around €1.2 billion in revenue, on par with the previous year.

"We succeeded in stabilizing our business at a healthy level after the economic crisis," Vormann said. The positive trend is mostly apparent in production-related infrastructure services, where demand has rebounded to near pre-crisis levels as tenants ramp up production. The project business and services, by contrast, remain relatively subdued. However, manufacturers have shown strong interest in consulting, management and operation services for industrial parks.

"Manufacturers are taking a hard look at their costs in light of the economic crisis and growing cost pressures," Mohr said. "They are asking themselves if it would make more sense to outsource non-core processes to specialized providers of infrastructure services. In most cases, the answer is 'yes'."

Successful Start Of Infrasite Griesheim

The first year of operating Industriepark Griesheim, an Infraserv Höchst subsidiary, has been successful. The site offers services that range from information technology to utilities and waste management to environment, health and safety. It also provides plant security and fire-department services. Synergies and cost reductions have been achieved in many areas; the operator has already attracted a new tenant, R.A.T.H.. "Infrasite Griesheim got off to a very good start. This experience will help us in optimizing other industrial parks," Mohr said. ■

Catalyzing A Sustainable Future

How Biocatalysis Can Pave the Way to Greener Manufacturing

Going Green – One of the great challenges that the pharmaceutical, chemical and allied industries face in the 21st century is the transition to greener and more sustainable manufacturing processes that minimize, or preferably avoid, the generation of waste and the use of toxic and/or hazardous materials. Biocatalysis has many benefits to offer in this respect. Reactions can be performed in conventional reactors (no specialized equipment is needed) under mild conditions (ambient temperature and pressure, physiological pH) in an environmentally acceptable solvent (water) using a biocompatible and biodegradable catalyst (an enzyme) that is itself derived from renewable resources.

Roger Sheldon,
CEO, CLEA Technologies

By using enzymes, reactions involving multifunctional molecules can proceed with high regio- and stereoselectivity and generally without the need for functional group activation and protection and deprotection steps required in traditional syntheses. Hence, generally speaking, enzymatic processes generate less waste than conventional synthetic routes, are more energy efficient and provide products in higher purity. The use of enzymes also circumvents product contamination with traces of metal catalysts, which often necessitates expensive purification steps in pharmaceutical manufacture.

The time is ripe for the widespread application of enzymes in chemicals manufacture. Thanks to the sequencing of numerous bacterial and fungal genomes, many new enzymes have been identified in recent years. The application of modern protein engineering techniques, mostly developed in the last two decades, such as directed-evolution by gene shuffling, has enabled the optimization of their properties to fit pre-defined process parameters. Advances in recombinant DNA technology have paved the way for their economically viable large-scale production. In short, more enzymes are available; they can be "tailor made" and can be produced on a large scale for an attractive price.

Enzyme Immobilization

Nothing is perfect, however, and enzymes do have some limitations. For example, they often lack operational and storage stability. Enzymes are complex, highly sensitive molecules with unique three-dimensional structures that are essential for their activities. Exposure to certain conditions, such as elevated temperatures or organic solvents, can lead to denaturation (unfolding) and concomitant loss of activity. Furthermore, enzymes are generally used as aqueous solutions, which makes recovery and re-use problematical and can also result in contamination of the product. These obstacles can generally be overcome by immobilization of the enzyme, affording improved storage and operational stability and providing for its facile separation and re-use. Moreover, immobilized enzymes, in contrast to free enzymes, which can penetrate the skin, do not cause allergic reactions.

Immobilization is an enabling technology that typically involves binding the enzyme to a support, such as an ion exchange resin or silica, or encapsulation in an inert matrix. Such strategies can be costly and afford carrier-bound enzymes with low productivities (kilograms of product per kilograms of enzyme) owing to the large amount of non-catalytic ballast (often more than 95% of the total mass). In contrast, immobilization by cross linking of enzyme molecules affords carrier-free immobilized enzymes with high productivities. Cross-linked enzymes, produced by mixing an aqueous solution of the enzyme with an aqueous solution of glutaraldehyde, were already known in the 1960s but generally had low activity, poor reproducibility, low stability and shelf life, and were difficult to handle and gelatinous materials. Consequently, carrier-bound enzymes became the method of choice for the next three decades. In the early 1990s, Altus Biologics introduced the use of cross-linked enzyme crystals (CLECs) as industrial biocatalysts. The methodology was applicable to a wide variety of enzymes and CLECs exhibited excellent operational stability, controllable particle size coupled with high productivity and facile recovery and re-use, making them ideally suited to industrial biocatalysis. However, they had one inherent limitation: the need to crystallize the enzyme, a laborious procedure requiring enzyme of high purity. In practice this translates to relatively high costs.

Protease-CLEA (a free-flowing powder)

Enter Cross-Linked Enzyme Aggregates (CLEAs)

Several years ago, we reasoned that crystallization could perhaps be replaced by precipitation of the enzyme from aqueous buffer, a simpler and less expensive method not requiring highly pure enzymes. This led us to develop a new class of immobilized enzymes, which we called cross-linked enzyme aggregates (CLEAs). The CLEA methodology essentially combines two unit processes, purification and immobilization, into a single operation. In principle, one can even take the crude enzyme extract from fermentation broth and produce the immobilized enzyme in one simple operation. A variation on this theme involves performing the cross-linking in the presence of a monomer that undergoes polymerization under these conditions. This results in the formation of CLEA-polymer composites with tunable physical properties. For example, if the cross-linking is performed in the presence of a siloxane the latter undergoes polymerization to afford a CLEA-silica composite. The hydrophobic/hydrophilic properties and particle size of the latter can be tailored by manipulating the structure of the siloxane used. More recently, we have made "smart" magnetic CLEAs by conducting the cross-linking in the presence of functionalized magnetic nanoparticles. These mCLEAs can be separated by magnetic decantation or can be used in a magnetically stabilized fluidized bed and we envisage that this will lead to novel combinations of bioconversions and downstream processing. A further elaboration of the CLEA methodology is the preparation of combi-CLEAs, from mixtures of two or more enzymes, for use in multi-enzyme cascade processes.

CLEAs have many economic and environmental benefits in the context of industrial biocatalysis. They are easily prepared from crude enzyme extracts and the costs of (often expensive) carriers are circumvented. They generally exhibit improved storage and operational stability towards denaturation by heat, organic solvents and autoproteolysis and are stable towards leaching in aqueous media. Furthermore, they have high catalyst productivities (kilograms of product per kilograms of biocatalyst) and are easy to recover and re-use. CLEAs are highly porous materials and diffusional limitations are generally not observed in typical bioconversions. Diffusional limitations have been observed in colorimetric assays which are usually very fast reactions. Obviously, the rate of diffusion is also influenced by the particle size which is amenable to tuning. Optimum rates are observed with smaller particles but practical considerations, e.g. ease of filtration, often dictate the use of larger particles.

The proprietary CLEA methodology has been commercialized by CLEA Technologies, which produces CLEAs from commercially available enzymes for sale on the open market as well as custom CLEAs from enzymes provided by clients on an exclusive basis. CLEAs are currently being developed for application in a wide variety of industrial settings, from peptide synthesis and chiral resolutions to cosmetic ingredients, oils and fats conversions, carbon capture and biofuels.

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Diversity Attracts Diversity

Continued Page 6

"If you go back over the last 20 or 30 years, there have been plenty of women in the pipeline, but we have to ask ourselves why they are leaving, why are they not achieving," says Shirley Schumacher, vice president - Sales & Marketing, Univar USA. She agrees that in some cases the industry can still be a challenging environment for women but says that they should still take responsibility for their own career progression.

Women often prefer to be shoulder-tapped, which means have to reach out, which might mean missing out on some great candidates who are not putting themselves forward.

Jane Wells, vice president - Marketing, Univar USA, also sees networking as an important asset when it comes to career progression and notes that there are now many more opportunities for women to network professionally than in the past. Pires agrees, though feels that many women are still not making the most of these opportunities.

"Sometimes women are not as comfortable with networking as their male counterparts," she says, "but you just have to get out there and do it – don't be shy!"

Diverse Experiences and Insights

The benefits of having a mixed team at the top tier of your business are clear. "Bringing people from different backgrounds into the most senior levels of management ensures that when developing strategy you are discussing different viewpoints based on diverse experiences and insights," says Wells. "This can only be a good thing," she adds. As well as improving strategic decision-making by providing different perspectives, there is also a growing awareness that women typically possess certain "softer" skills that can give them an advantage in certain situations.

Wang says that women are often a little more cautious and think more about how they are communicating, a view echoed by Schumacher. "Men often see things in black and white whereas women look for the nuances. We are more in touch with body language, emotions and feelings which can be a real asset during negotiations, particularly when it comes to diffusing tense situations."

It is clear that the ability to recruit and retain talented women into senior roles can provide companies with significant advantages over those which do not. Creating a supportive and encouraging environment will help to foster young female talent, encouraging them into more senior roles, as well as attracting top women from other companies who will bring valuable experience, contacts and skills with them.

The chemicals industry has made a great deal of progress in recent years, and while there is still much to do, right now it is already a very positive environment for young women looking to build a successful career. As Schumacher points out, "There is no glass ceiling anymore; making it to a top position in the industry is not easy and requires sacrifice, but now women have the choice over their future. I am incredibly proud of the workplace that women of my generation and I are leaving behind for our daughters who already realize they have the power to be anything they want to be."

Eveline de Wit, Human Resources director, organization and staffing, Univar EMEA

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EU Presses Pharma Companies for More Info on Patent Deals EU regulators are pressing pharmaceutical companies for more information on their patent deals with generic companies to make sure there is no delay in cheaper drugs coming to market. The move is the latest in a series of EU crackdowns on possible anti-competitive practices in the pharmaceutical sector after a 2009 patents enquiry pointed to significant risks for European consumers, the Commission said. It did not mention any company it requested information from, but Britain's AstraZeneca and GlaxoSmithKline, France's Sanofi-Aventis and Novartis and Roche of Switzerland said last year the Commission had contacted them about drug patent settlements. The European Commission said it had asked firms to submit copies of their patent settlement agreements concluded in the bloc last year. Patent settlements are generally fees paid by pharmaceutical companies to generic drug makers to persuade them to delay selling the generic version of their medicines. "Patent settlements are an area of particular concern because they may delay the market entry of generic medicines," Competition Commissioner Joaquin Almunia said in a statement.

Merck & Co, Parexel to Develop Biotech Medicines Merck & Co struck an alliance with contract researcher Parexel International to develop copies of biotech medicines, deepening the U.S. drugmaker's investment in so-called biosimilar medicines. The agreement, for which financial terms were not disclosed, is the latest sign that pharmaceutical and biotech companies, rather than just generic drugmakers, are interested in the burgeoning market for similar versions of pricey biotech medicines. Merck has previously said it was interested in biosimilars. Under the deal, Parexel will provide access to a range of regulatory strategy and clinical development capabilities for certain broad classes of biosimilars. A dedicated Merck BioVentures unit will be established within Parexel. Merck selected Parexel based on the contract organization's expertise in certain product areas "that are going to be very important to us in biosimilars," said Michael Kamarck, president of Merck BioVentures, although he declined to specify the products.

DSM and Codexis Sign Enzyme Supply Agreement DSM Pharmaceutical Products and Codexis have signed an enzyme supply agreement, the companies announced. The agreement grants DSM rights to use Codexis' custom biocatalysts and services, and secures supply of Codexis enzymes for commercialization of sustainable enzyme-based pharmaceutical manufacturing routes developed by DSM's InnoSyn route scouting services. Codexis technology enables development of new efficient manufacturing processes for active pharmaceutical ingredients and intermediates which reduce cost and environmental waste. Codexis technology is used at major pharmaceutical and chemical companies worldwide including Merck, Pfizer and Teva. The DSM InnoSyn route scouting team integrates cutting edge enzyme technology with the full range of advances in synthetic methods such as homogeneous catalysis, modern organic synthesis and continuous chemistry, using for example micro reactors. The new routes result in increased efficiency of the manufacturing processes while reducing cost and environmental impact.

J&J Blames Cleaning Procedures in Massive Recalls Johnson & Johnson faulted lax cleaning procedures and other problems at a manufacturing plant behind massive recalls of medicines like Tylenol, and said it was recalling nearly 50 million more bottles and packages of consumer medicines. The healthcare company's reputation has been tarnished by repeated recalls totaling nearly 200 million bottles in the last year and it could face criminal charges from the U.S. Department of Justice. Johnson & Johnson is now recalling bottles and packages of various kinds of Tylenol, Benadryl, Rolaids and other consumer products. J&J said the new recall followed a review of records dating back to 2007 of products made by its McNeil consumer healthcare unit, which produces most of the recalled medicines sold in the U.S. The company investigation found insufficient equipment cleaning procedures and instances where people failed to adequately document cleaning at McNeil's Fort Washington, Pa. plant, the company said. J&J suspended production there last April to address quality control lapses. The latest recall involved products affected by those issues, the company said, adding that it was "very unlikely" that this harmed product quality.

Eli Lilly, Boehringer Ingelheim in Drug-Development Alliance Eli Lilly struck a drug-development alliance with Germany's Boehringer Ingelheim as the U.S drugmaker tries to revive its diabetes business after setbacks and help it maneuver past generic competition. Lilly will initially pay €300 million ($388.5 million) plus potentially up to €625 million depending on future development progress for the right to co-develop two of Boehringer's experimental diabetes pills, linagliptin and BI10773, the two companies said. Unlisted Boehringer, in turn, has agreed to pay as much as $650 million depending on development milestones for the right to co-develop Lilly's two injectable basal insulin analogues. For the fifth drug covered by the pact, Lilly's anti-TGF-beta monoclonal antibody, the U.S. company is eligible to receive up to $525 million, comprising an opt-in fee and success-based payments. The move follows regulatory and development setbacks in Lilly's diabetes drugs business. U.S. health regulators in October declined to approve diabetes drug Bydureon, co-developed by Amylin Pharmaceuticals, citing the need for further studies.

Pharma On The Move

Lessons to be Learned from the Chemical Industry

Shifting Priorities – Our world is faced with a growing and aging population. In developed countries, people search for wellness, while in emerging economies, populations seek better conditions of life. All this is triggering growth in the health and nutrition sector.

Dr. Uwe Nickel,
Arthur D. Little

Edouard Croufer
Arthur D. Little

Nevertheless, the industry seems to envisage the opposite. The $780 billion global market is on the move and so are their key players – and they are suffering.

In the last half of 2010, several announcements were made by Roche, Novartis and Bayer. They all send the same message: cutting manpower, costs and searching for higher efficiency. But this is only the tip of the iceberg. In the last years, Pfizer has laid off more than 30,000 employees, GlaxoSmithKline more than 10,000, Merck around 23,000, while AstraZeneca is close to 20,000 less employees due to restructuring and optimization programs. So what is happening to an industry that still enjoys high margins?

The growth engine has slowed down from 9% per year in the last decade to slightly above gross domestic product (GDP) levels. This provokes a deterioration of top line growth that will have an increasing impact on margins if costs and services are not adapted. At the same time, a number of patent-protected blockbusters are set to expire in nearly every global pharmaceutical company. Moreover, R&D has doubled since 2000, while the number of new drugs remains at a constant level over the last few years.

Patent expiries in attractive blockbusters have triggered the strong, double digit annual growth of generics. Today, the highest growth of Drug Master File (DMF) submissions – as an indicator of changing markets – already comes from India. It is followed by the U.S. for DMFs of generic APIs – in other words, a commoditization is taking place in traditional markets, and competition is rising in developing countries. Furthermore, the market is rapidly changing from a supplier to a buyer market. The pharmaceutical industry does not seem to be prepared for this: A plant utilization rate of 50–60% is a true indicator for the current effectiveness of this industry.

Learning From the Specialty Chemicals Industry

All these threats have been seen in another industry: specialty chemicals, often considered the historic root of the pharma industry. It was during the first oil crisis in the 1970s that the petrochemical industry awoke and started a long journey to efficiency. History repeated itself with slightly different mechanisms when specialty and fine chemicals were threatened by cheap imports from China and India in the late 1990s. The industry has learned its lessons, but over a long and suffering journey paved with mistakes.

For years, companies in the specialty chemicals industry believed that all solutions to globalization and rising competition in the East, especially from China, could be answered with better technology, new products and a stronger focus on more services to win the battle.

It took time for the industry to understand that the problems could only be solved by changing the business model towards a more market-centric model. This went hand-in-hand with the experience that, in many markets, it was sufficient to provide offerings of "good-enough quality." Many companies had to learn the hard way that some specialties have been commoditized, that services do not pay off a premium and that the cost structures have to consequently be adapted significantly.

Furthermore, the number of true specialties that can afford high costs has not increased since the mid 1990s. The industry needed to learn to live with decreased top- and even bottom lines between 1998 and 2006 – for which the whole process chain had to be adapted.

The cost optimization cycle started by improving the production processes, followed by site closures and a shift of production to other regions. Much time and money was wasted by incremental optimizations in one part of the process chain (e.g. production). However, in 2004 it became obvious that a more comprehensive approach, covering many parts of the process chain with measures from different areas that tie into each other, was needed to produce a step change in costs.

A perfect indicator for sustainable improvements is SG&A costs: They will only drop and remain at a lower level if many parts of the process chain are optimized simultaneously. A recent study by Arthur D. Little shows that this process is not finalized, and many chemical companies are still struggling with a multi-step approach for operational improvements.

A key element of success is the focus on core competencies that fit to well-understood markets and customers, and the reduction of complexity of products and processes at all levels. Iterative improvements have only lead to partial optimizations in the profit and loss, which have not been sustainable over more than two to three years.

It took roughly a decade for the industry to change its way. A lot of approaches have been tried and tested but capital efficiency – a clear indicator of success – remained below average for a long time.

Challenges Going Forward

Today, the pharmaceutical industry is confronted with most of the challenges the specialty chemicals industry has dealt with in the last decade – namely, a business active in different markets, with many different products. It is looking for answers in a changing environment. And the business models that proved to be right for many years seem incapable of tackling the challenges of the future.

There are several key challenge areas for the pharmaceutical industry through 2020, including slow overall market growth and an increased market share going to generics.

Each challenge offers opportunities, but also presents multiple issues to be tackled. Some pharmaceutical companies have already started to optimize certain areas. What is often missing is a holistic approach, which might end up in new business models and different ways to operate.

First of all, the business model has to be revised. Five key recommendations will change the landscape of approaching the market: getting back to the core science; focusing on patients; integrating technology; rethinking core activities in light of changing demographics; and increasing collaborations.

This will lead to a change from the historic product centric approach to a market centric approach. This also implies that companies have to rethink the location of their core activities, because changing demographics are forcing globalization.

For the pharma industry, it will not be sufficient to use a step-by-step approach or to optimize parts of the process chain. A holistic approach, with multiple measures starting in R&D and ending with different skills and approaches, will be needed in order to maintain market share and profitability.

It is of interest to learn how the specialty chemicals industry discovered the answers: Changing business models required well-elaborated and realistic change concepts and a carefully designed holistic implementation in order to reach new horizons.

Why would the pharmaceutical industry repeat mistakes and waste resources when the answers can be found just across the fence?

Dr. Uwe Nickel and Edouard Croufer, Arthur D. Little

The pharma industry has to make some serious changes if it wants to keep its clout.

Infobox

Key Drivers in Evolution Towards a Global Pharmaceutical Industry 2020

Market

- Growth in the global pharmaceutical market is expected to slow down to 3% a year
- Pharmaceutical companies struggle to maintain both growth and profitability as margins decrease
- Pharma growth is now driven by emerging countries, reorganizing geographic priorities for the industry
- As blockbuster products come to an end, niche marketing becomes ever more important

Regulation

- The global debate on patents fuels political pressures and incentives which pave the way for generics
- Limitation of available funds leads to price pressure
- Attention in healthcare is shifting towards prevention
- New regulations limit access to and interaction with prescribers

Technological

- Innovation becomes more complex; despite continuing R&D spend, new drug approvals are lagging
- A global wave of partnership formation is taking place
- Rapid growth of biotech leads to increasing share and value of biologics
- Increased technology integration

Science

- Prescriber access is more and more challenged as focus on patient centrism is growing
- Key target patient groups are changing with demographic evolutions (e.g. aging population)
- Higher pandemic risks lead to an increased importance of vaccines

Source: Trends in pharma and prioritization (outlook 2020), Arthur D. Little analysis

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Pharma Sourcing from India and China

Asia Continues to Develop Business to Cater to New Opportunities

Go East – India and China continue to be the chosen destinations for a pharmaceutical industry hungry to lower research, development and manufacturing costs without sacrificing quality. While the growth of clinical research and other contract development services in India and China has tended to occupy the news headlines, the most significant part of this growing industry involves the manufacturing of active pharmaceutical ingredients (API) and finished drugs (FD).

How have Indian and Chinese companies developed their businesses to cater to these new opportunities, what are their capacities to continue to expand services offered to highly regulated markets and what is likely to happen in the future?

The Current World Pharmaceutical Climate

According to IMS Health, the future growth expectations for world pharmaceutical markets vary widely from modestly growing to small declines in the highly regulated markets of the U.S., Europe and Japan to in excess of 10 % in less regulated, emerging markets like India, China, Russia and Brazil. Big Pharma continues to consolidate and produce few new product launches while at the same time having to prepare for a large number of "blockbuster" patent expiries over the next few years. The business environment is equally challenging for generic pharmaceutical companies who face increasing competition from producers in lower cost countries like India, extreme price pressures in the major markets of the U.S. and Europe, and for whom the promise of biosimilars is still some years from coming to fruition.

Despite these pressures, at around $66 billion at the end of 2010, the global pharmaceutical manufacturing market is growing strongly at around 13 to 14 % according to CIBC. Of that spending, nearly 70 %, occurs in-house, with the remainder coming from outsourced FD ($7 billion) and outsourced API ($11.5 billion) manufacturing. In a recent report by consultants Frost & Sullivan, global API market revenues are expected to grow by a steady 5 % to reach $100 billion by 2013. In terms of API consumption, some 60 % is still for captive use, with roughly 20 % each going to the generic merchant and brand merchant markets according to the Italian industry organization Chemical Pharmaceutical Generic Association (CPA).

The Global API Manufacturing Landscape

During the past decade, Thomson Reuters has rated the capabilities of API manufacturers worldwide according to a series of objective measures that indicate their relative skill and experience in supplying highly regulated markets of North America, Europe and Japan. Measures contributing to the rating include regulatory filings made by companies in major markets, plant inspections made by regulatory agencies and demonstrated ability to support patent challenges, in addition to additional information gleaned from primary research activities. These ratings range from Established (much experience over a long period of time), though Less Established (a good deal of experience over time) to Potential Future (little experience, or some gained only recently). A final rating of Local applies to companies with no demonstrated experience in working with highly regulated markets. It's also important to bear in mind that these ratings are not a pronouncement on the quality of the material produced by the companies, merely a gauge of their experience and ability to work in highly regulated markets.

Figure 1 (page 11) shows that the vast majority of the world's manufacturers are at Local or Potential Future rating, which leaves 422 companies or less than 25 % of the global industry with a demonstrable capability to supply highly regulated markets. Of those 422 companies, almost half are vertically integrated, meaning that they also produce finished products, and more than 60 % of those companies are located in India, China, Italy or the U.S. Access to such a concentrated and relatively small segment of highly experienced API manufacturers has been one of the major drivers for consolidation in the generic industry over the past decade where today 9 out of the top 10 companies are vertically integrated and where many major acquisitions have been focused on acquiring API plants.

The Indian Industry in Detail

Now the 13th largest pharmaceutical market in the world according to IMS Health, India is home to many API manufacturers, contract services providers and finished dose producers. According to some estimates from the Indian government, India produces between 20 and 25 % of the world's generic drug supplies and exported more than $8.5 billion of pharmaceutical products in 2009, $1.7 billion of which was API.

The significant cost advantages, concentration and proximity of raw materials, and manufacturing capacity coupled with better capital efficiencies and a rich pool of chemists and pharmacists have made India a natural destination for outsourced pharmaceutical research and manufacturing in recent years. It's useful to reflect on the development of this industry and capability that has been in progress for at least a decade.

Figure 2 (page 11) shows the typical strategic path traversed by most Indian producers who have expanded quickly from domestic API production to supplying finished drugs on a worldwide basis. From there, many have been able to develop and offer contract research and manufacturing services (CRAMS), and a few have progressed as far as being able to develop their own novel drug delivery systems (NDDS) and innovative new chemical entities (NCE). As an example of just this transition kind of transition can been seen with Jubilant Organosys, which went from a base of producing pyridine chemicals and derivatives in the 1990s to a fully fledged pharmaceutical organization offering API production, finished dose form manufacturing and diverse contract services.

Much of the Indian API industry remains focused on domestic production or works with unregulated markets. Of the nearly 600 Indian API manufacturing groups tracked by Thomson Reuters, 442 of them are rated Local while only 67 have demonstrated long-term experience in working with more highly regulated markets (Established or Less Established). India has 89 companies with a Potential Future rating, indicating that there is a large class of companies that will continue to develop their capabilities and join the ranks of the Less Established and Established companies in the coming years.

The strength of the outwardly focused segment of the Indian industry can be seen through the lens of many regulatory measures. Filings of U.S. Drug Master Files (DMF) by Indian companies have risen almost exponentially from just 20 in 1999 to more than 285 in 2009, and the number of Abbreviated New Drug Applications approved by the U.S. Food and Drug Administration (FDA) that were submitted by Indian companies rose from a handful in 1999 to 142 in 2009. The Indian industry makes an equally strong showing in similar measures in Europe and other major regulated markets.

Not surprisingly, the development of this powerful industry has lead to a steady growth of its ability to offer contract services to companies elsewhere. According to the Indian Pharma Alliance, the Indian CRAMS industry is projected to grow to more than $2.5 billion in 2010,

Continues Page 11

The Biosimilar Revolution

Overcoming the Challenges of Monoclonals

Embracing Monoclonals – Modern manufacturing methods and analytical tools have developed to a level that enables assured production of highly similar monoclonal antibodies. In Europe, the biosimilar revolution has begun to embrace monoclonals, and to date, the Committee for Medicinal Products for Human Use (CHMP) has provided scientific advice on the development of a number of biosimilar monoclonals, and draft guidelines are imminent.

Cecil Nick,
Vice president Technical,
Parexel Consulting

Less Complex Structure

Monoclonals are in some ways structurally less complex than some of the initial biosimilars approved in Europe. In particular epoetins, which are not as large as monoclonals, display a complex array of added sugar molecules in short branching chains. In fact, about one third of the mass of an epoetin is contributed by sugar residues. Monoclonals also possess added sugar molecules but to a lesser extent. Nevertheless, the pattern of added sugar molecules on the monoclonal can heavily impact important biological effects, such as potency and clearance from the blood.

It follows that like all proteins, monoclonals exist as a heterogeneous mixture of molecules; these include different patterns of added sugars and also other differences, such as modifications of some amino acid side chains. Aggregates or fragments which may form during manufacture or on storage add to the heterogeneity.

Biological Testing Important

Biological testing plays an important role in distinguishing changes that are inconsequential from those that are not. In view of this heterogeneity, each batch of originator product will differ from the last and, therefore, there is a need for the biosimilar manufacturer to understand the acceptable range of variability of the originator product. This cannot be done by studying just one batch. The primary challenge is not so much whether differences can be detected but to understand the impact of the differences that certainly will be found. In fact, many differences in structure may have no clinical impact on activity, while slight differences can have a major effect. Biological testing using a range of different methods that assess the ability of the monoclonal to bind target receptors, interact with immune system and exert an effect on cellular and animal models can play an important role in distinguishing changes that are inconsequential from those that are not.

Animal Data of No Value?

Monoclonals present special challenges in the design of immunogenicity studies; such studies may prove of little value or even not feasible for some monoclonals because of immunogenicity and/or species specificity. The key demand for in vivo safety data will be to give some degree of comfort that it is safe to enter clinical trials with similar monoclonal. However, even this will present a challenge when no suitable species for toxicity testing exists at all. What is clear is that there is the need to maximize whatever data can be gleaned from using in vitro based techniques and a minimum of animals.

Phase 1 Studies Require Novel Thinking

As for any product, monoclonal development needs to start with Phase I, which the CHMP guidelines state should be finished before advancing to Phase III, Phase II generally not being required for biosimilar programs. Phase I studies are frequently conducted in healthy volunteers, but with monoclonals this may not be possible due to potential toxicity. To make matters more difficult, single-dose studies in patients might not be possible, either. This could mean that it may only be possible to study comparative pharmacokinetics in patients at steady state, perhaps as part of the Phase III program.

Demonstrating Comparative Efficacy Presents Major Challenges

If a monoclonal product displays comparable physico-chemical and biological properties as well as similar biological effects to the originator product, this provides convincing evidence for a similar clinical efficacy profile. The clinical comparability program is, therefore, confirmatory not exploratory and the magnitude and complexity of the plan should be reduced accordingly. It is not a question of demonstrating efficacy all over again but understanding the science and providing just sufficient evidence to demonstrate expected therapeutic equivalence. Thus a limited program ought to be acceptable although in effect the test population needs to be representative of the complete target population and sensitive to differences that might impact the efficacy, safety, and immunogenicity profile.

The current CHMP non-clinical and clinical comparability guideline requires that "efficacy and safety has to be justified, or if necessary, demonstrated separately for each of the claimed indications." (CPMP/437/04) If two monoclonals prove to have comparable physicochemical and biological properties and display a similar pharmacokinetic and pharmacodynamic profile, then it seems reasonable to deduce that if comparable efficacy and safety are demonstrated in suitable and sensitive populations, similar effects would occur in other populations and situations.

One also needs to bear in mind that the trials on the original biological entity could be designed to demonstrate efficacy against placebo. However, placebo trials will not generally be ethical, at least for serious and life-threatening diseases, once an effective therapy has been established. This requires demonstration of non-inferiority or equivalence which is more difficult to prove and will require trial sizes far greater than the initial placebo studies.

Selection of end point, particularly in the oncology arena, may invoke debate. An overall survival endpoint will require many years to complete, and it may not even be possible to interpret survival data as patients will often be transferred to new next line therapies at the time of progression. Progression-free survival might be the best end-point that can be achieved, but even this may require many years to demonstrate equivalence. Another more feasible possibility would be to use a response rate to assess equivalent therapeutic effect with survival secondary endpoints. It should be remembered that for biosimilars, the objective is not to prove efficacy all over again, but to show comparability between two products and use of response rates endpoints in these circumstances is supported by regulatory precedence.

Safety Needs to Be Demonstrated in Most Sensitive Population

As for efficacy, safety is best demonstrated in the most sensitive populations, for example patients most prone to develop an immune response and/or patient groups receiving the highest doses and this population may prove to be different to the most suitable efficacy population. The nature and extent of safety data will differ depending on the profile for the originator product. However, generally six month's data from a minimum of 300 subjects would meet current The International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) requirements for chronic therapies and this number of patients will likely be required to demonstrate equivalence with respect to efficacy (ICH S6). Nevertheless, in theory, serious adverse reactions may only emerge after extensive exposure and there is therefore a requirement to follow safety post-marketing.

Immunogenicity a Critical Part of Biosimilar Program

The potential for immunogenicity is highly influenced by the patient population and is generally less of an issue in immuno-compromised patients. The route of administration will also affect immunogenicity with the sub-cutaneous route being reported to be associated with the greatest immunogenicity. Comparative immunogenicity testing against originator product should be integrated into the safety program.

While there are challenges with the application of state-of-the-art methodology, novel approaches and novel thinking biosimilar monoclonals will certainly soon be a reality.

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The Perfect Storm

U.S. Patent Expiration Wave to Intensify in 2011

Set of Challenges – Pressures on the U.S. pharmaceutical industry has built over the past few years, stemming from an increasingly stringent drug regulatory environment and the global economic downturn. Drug developers have also contended with expanding government efforts to contain healthcare cost burdens during the past year. While attention has been focused toward overcoming these challenges, a building wave of key drug patent expiry that began in 2010 is anticipated to crest over the next two years, which is the final element to an unprecedented set of challenges that lay ahead for the industry.

Patent Expirations to Impact Specific Drug Makers

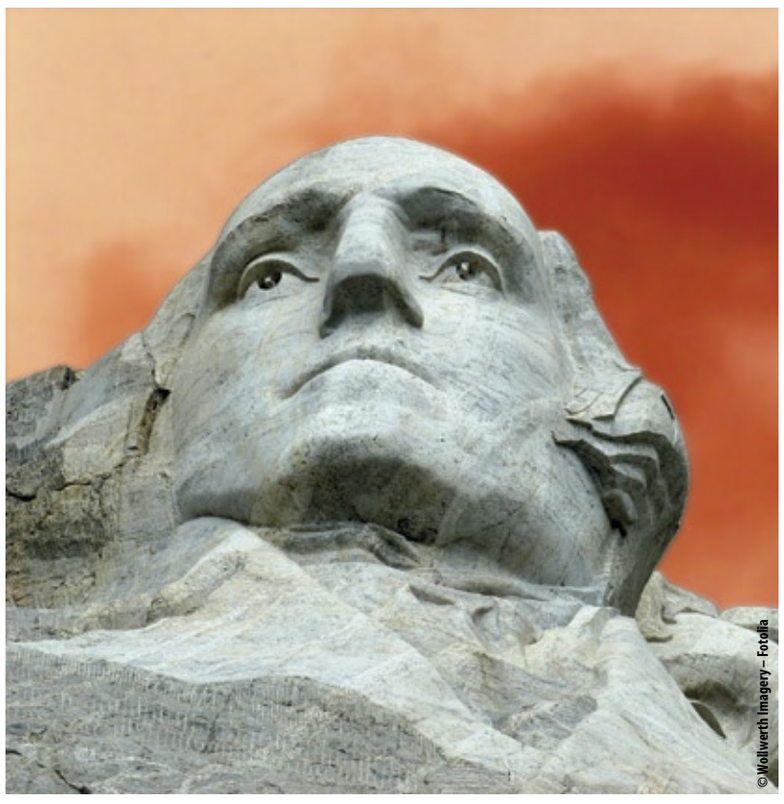
A period of significant drug patent losses is upon the industry that is expected to accelerate erosion of revenues to record levels in 2011 and 2012. The patent cliff encompasses the loss of patent protection for seven of the world's 10 best-selling pharmaceuticals by the end of 2014. This year, three major drug patents potentially expiring are Pfizer's cholesterol-lowering medicine, Lipitor, in November; Eli Lilly's schizophrenia treatment, Zyprexa , in October; and Bristol-Myers Squibb's anti-clotting medication Plavix – in November. Not surprising, U.S.-based drug developers with the highest risk of patent losses over the next three years are Pfizer, Eli Lilly and Bristol-Myers Squibb, as each faces the potential expiration of their top-selling drug products.

While the patent wave looms over the entire industry, in reality, it is specific to the companies that are tasked to mitigate the negative affects to profitability resulting from aggressive generic drug competition subsequent to key patent lapses. Drug manufacturers employ various strategies to counter the market exclusivity losses, notably by bolstering research productivity, implementing restructuring programs and cost efficiencies and deploying diversification measures including mergers and acquisitions.

Pharmaceutical Innovation Not Pacing Patent Expiration

New medicines arising out of R&D programs are not likely to solely supplement revenue losses due to the more limited nature of maturing drug portfolios over the next two years. This is especially evident for those drug manufacturers with the weakest intellectual property positions. On the bright side, a positive trend of the U.S. Food and Drug Administration (FDA) approvals – one proxy for innovation of the pharmaceutical industry – has been sustained since 2008. Examining the current late-stage pipelines of major industry participants in the U.S. and Europe indicates the continued upswing in marketing clearances that may be granted during 2011, including the promising metastatic melanoma treatment ipilimumab from Bristol-Myers Squibb and the novel anti-coagulant Xarelto developed in partnership between Johnson & Johnson and Bayer.

Historically, large pharmaceutical companies focused on successful commercialization of novel medicines arising from internal research and development efforts in order to replace lost revenues from expired drug products. However, drug manufacturers have eased the stress on once-sacrosanct research programs through risk sharing agreements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with external researchers. Development and marketing partnerships afford a reduction of the risk and cost of advancing experimental drugs through the drug regulatory approval process while still reaping the benefits upon market introduction. For example, Bristol-Myers Squibb and Pfizer established such an agreement pertaining to the potential anti-coagulant medicine, apixaban, whereby the research investment is divided, thus easing the cost burden on both companies. Business development activities directed to filling R&D and product portfolio gaps are expected to be favored over major industry consolidation.

Reimbursement and Demand Challenges Ramp Up

Across the globe, governments are taking steps to control federal budgets including measures aimed at minimizing the rise in healthcare spending, most notably U.S. healthcare reform efforts legislated in March 2010 and European austerity measures. The drug industry typically sees a modest gross impact to revenues on an annual basis due to various government cost containment policies instituted throughout Europe. However, focus on incremental cost control arose in 2010 as certain European countries faced ballooning deficits, which led to reimbursement cuts for brand name pharmaceuticals, specifically in Greece, Spain and France. The new policies are expected to double the historical impact on revenues.

Much uncertainty pertaining to the outlook for the industry was alleviated early last year with the passage of the Patient Protection and Affordable Care Act (PPACA) in the U.S., whose impact has proven to be relatively innocuous to the industry given the exclusion of direct price negotiations between the government and pharmaceutical manufacturers. Pharmaceutical companies will bear the brunt of the cost of implementing provisions of the new law prior to expansion of healthcare coverage in 2014 to approximately 34 million presently uninsured patients. Net sales have been dampened by increased rebates under Medicaid in 2010 and will be further influenced by partial filling of the coverage gap under Medicare Part D starting this year. Also, this year a fee of $2.5 billion will be levied on the industry split by market share. Collectively, the influence of the healthcare reform will essentially double in 2011 from the low single digit growth impact in 2010.

Further demand pressure on brand name pharmaceuticals comes from greater use of generic drugs. Managed care organizations and third-party payers use generic drug substitution as a primary means to contain pharmaceutical spending, effectively shifting prescription drug volumes from brand name medications to generic copies. The generic substitution rate in the U.S. already approaches 75% of total prescriptions and is expected to expand in the midst of the current period of record drug patent challenges.

Weak Macroeconomic Conditions Lead to Treatment Avoidance

Exacerbating the pricing and demand effects of reimbursement cuts by various governments and drug spending control by third-party payers, the lagging effects of the U.S. recession will hamper branded prescription drug demand throughout the coming year as people focus on containing disposable income including reducing healthcare expenses and delaying non-essential care. Despite the end of the recession in the U.S. in the third quarter of 2009, unemployment will continue to weigh on the prospect for the industry. Fitch Ratings forecasts U.S. GDP growth of 3.2% in 2011, yielding a somewhat improved unemployment picture at 9.1% in 2011, still far above historical levels.

Treatment avoidance is only partially eased through another potential extension of unemployment benefits in the U.S. and patient-assistance programs offered by drug manufacturers. Moreover, greater cost burdens are placed on patients from increasing drug co-payments for prescription drugs and expanded use of co-insurance for specialty medicines. Resultant demand reduction is expected to pressure top-line growth for large pharmaceutical firms.

Profitability Supported by Cost Containment

Most large brand-name pharmaceutical manufacturers in the U.S. have reduced operating costs over the past few years as the industry faces prospects of lower top-line growth from near-term patent challenges, government reimbursement changes, and patient treatment avoidance. Restructuring actions have gone beyond headcount elimination and facility consolidation to remaking entire organizations into smaller, more nimble business units and to refocus corporate R&D programs toward specific disease states or therapeutic areas. While some drug manufacturers have redefined their organizational structures, others have chosen to consolidate in order to confront the many industry challenges. The benefits gained from merger and acquisition activities may bear out through incremental margin support attained from integration synergies, notably Pfizer's estimated annual synergies of $4 billion by 2012 from the Wyeth acquisition, and Merck & Co's annual savings of $3.5 billion to be achieved beyond 2011 arising from the merger with Schering-Plough.

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Pharma Sourcing from India and China

Continued Page 10

50% of which will come from the contract manufacturing of APIs, 25% from drug discovery services and 25% from contract clinical trials work. Together CRAMS is likely to represent some 10% of all Indian pharmaceutical revenues very soon.

The Indian CRAMS business is dominated by Jubilant, Dr. Reddy's and Piramal but there are many other smaller and mid-size companies that now see significant revenues from this part of their business. The development of this contracting business has also spawned nearly 50 M&A deals totaling nearly $900 million of investment over the past few years and today, Indian CRAMS providers are working with partners as diverse as Amgen, Pfizer, Novo Nordisk and Nycomed on major long-term projects.

The Chinese Industry in Detail

China has also received considerable attention from Western companies looking to offshore pharmaceutical research and manufacturing. China is currently the 9th largest pharmaceutical market in the world at $12 billion according to IMS Health, and is projected to grow at between 12 and 15% during the next few years, a figure that is likely to make China the 3rd largest market by 2011–12. The China Pharma Review reported that the domestic API market is worth some $31 billion and Chinese manufacturers exported nearly $17 billion of APIs and $2 billion of finished dose forms in 2009.

Like India, the low costs, large capacity and talented base of scientists and engineers has been a major attraction, and improved protections for intellectual property have also helped drive the growth of the Chinese industry considerably in recent years.

Of the nearly 950 Chinese API manufacturing groups being tracked by Thomson Reuters, almost two thirds (603) are rated as Local. 143 are in the Potential Future tier and a mere 37 are either Established or Less Established, or about half that of India. The contrast between the capability and experience of the Indian and Chinese industries to serve highly regulated markets is further shown by Figure 5 where Chinese companies best their Indian rivals in Japanese DMF filings only. Like India, the large number of companies at Potential Future rating also suggests that their industry still has plenty of room to develop and expand its capability to supply highly regulated markets.

While China boasts nearly 1,300 finished dose manufacturers, there are only three companies holding U.S. Abbreviated New Drug Application (ANDAs) in comparison to nearly 30 Indian companies. On closer examination, it's also interesting to note that these Chinese-held ANDAs were in fact all acquired from US manufacturers, are therefore not Chinese-developed generic products, and a number of those products are discontinued in the U.S. However, as Figure 6 shows, there are now many Chinese companies working on contract with both major innovators and generics and it is very likely that new ANDAs will soon be approved for more Chinese companies.

The Future Outlook for Pharma Sourcing from India and China

Many Indian companies continue to shift their attentions away from API supply and towards more lucrative finished products and value-added CRAMS business. While this will certainly fuel continued healthy growth in outsource work for Indian companies, it is also likely to create an opportunity for more capable Chinese API manufacturers to fill the increased demand. Chinese companies are also likely to gain from the increased sourcing of advanced intermediates by Indian companies no longer able to, or interested in, producing these complex chemicals as their businesses move away from API production altogether or focus on performing final synthesis steps only.

While today, most discussion of API sourcing is usually focused on small (chemical) molecules, it's important to note that Indian and Chinese companies are also very active in manufacturing biologic drugs. While the quality and testing of these drugs may not yet meet the needs of major market biosimilar regulations, certainly for supply to their domestic, in addition to less regulated and unregulated markets, China and India are likely to be major destinations for supply of copy-biologic drugs too.

As regards the development of the Chinese outsource business, the effects of strengthened State Food and Drugs Administration (SFDA) oversight, more stringent EHS regulations and enforcement, coupled with increasing labor costs is raising costs. Smaller and less capable companies will fall by the wayside or be acquired by stronger firms who will then have the financial muscle to compete to supply more regulated markets. However, the extent to which Chinese companies enter highly regulated markets in significant numbers is likely to be strongly influenced by the growth of their domestic market. For many companies, it may be a far less costly and less risky proposition to compete in a strongly growing domestic market rather than to acquire the skills, knowledge and experience to compete with established players in highly regulated markets.

But whatever the outcomes, simply for reasons of cost containment, sourcing from China and India will continue to be a dominant theme of the pharmaceutical industry throughout this decade and there is plenty to suggest that there is a strong and capable industry in both countries that are eager to address this growing demand.

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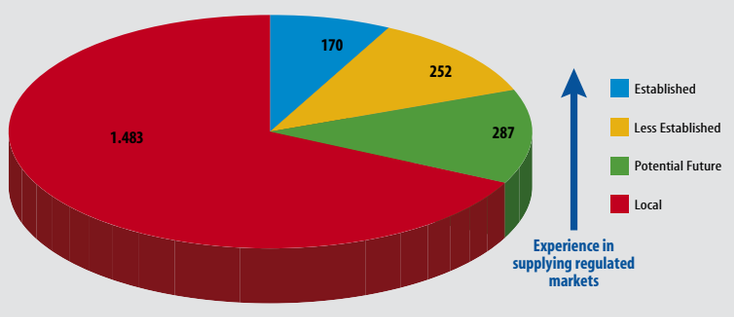
World generic API manufacturer landscape Fig. 1



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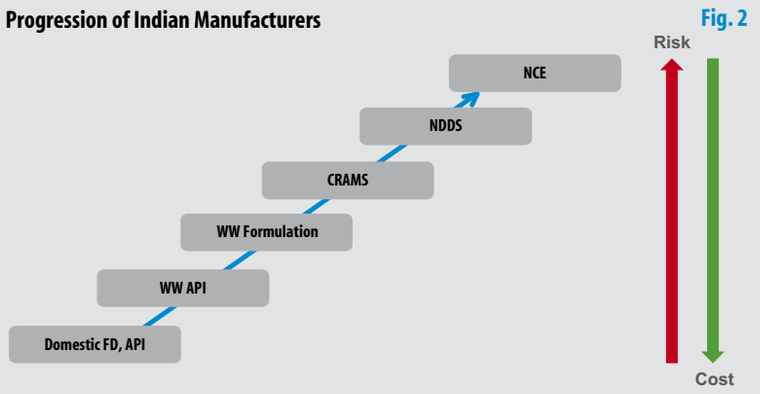
Progression of Indian Manufacturers Fig. 2



Source: Piramal Investor Presentation 2008 © GIT VERLAG

Supplier Controls In Healthcare

How Clariant and LyondellBasell Have Responded to the Challenge

Poor Controls – In the past five years, several contaminated products have led to patient and end-user injuries and death globally. In 2007, there was diethylene-glycol contaminated toothpaste, and millions of toys were recalled due to lead contamination. In 2008, contaminated heparin was recalled by the U.S. Food and Drug Administration (FDA) and melamine-contaminated milk caused thousands of adverse events and several infant deaths. Investigations into the causes of these adverse events found that, among other reasons, inadequate or poor supplier controls were a factor.

These incidents have triggered U.S. and European regulatory bodies to increase their vigilance on supplier controls for the medical device and pharmaceutical industries. In December 2008, the Global Harmonization Task Force (GHTF) issued a guidance document that outlines the steps medical device manufacturers should include in their supplier control process. A second document issued in November 2009 (in draft form) describes the techniques for inspecting a medical device manufacturer's supplier controls.

The level and extent of controls should be based on the criticality and risk of the products or services that could affect the safety, effectiveness and quality of the final product. It is the responsibility of the manufacturers of the finished product or device to determine and communicate those requirements to their suppliers. The benefits of good supplier controls translates to effective quality management systems and risk management processes, high quality and consistent products, lower scrap, improved productivity, and fewer adverse events, complaints and recalls.

More Rigor And Control

Component, part and material suppliers to medical device manufacturers and the healthcare industry must be prepared to expect much more rigor and control from their customers. The level and extent of controls on suppliers will not only depend on the criticality and risk of the product they supply, but also on their position in the supply chain. Tier 1 suppliers will see more controls versus Tier 2 and Tier 3 suppliers (fig. 1). Wherever material suppliers fall in the value chain, they must still ensure that their products meet all the performance and regulatory requirements needed for the specific application.

Understanding The Risks

Many companies in the supply chain do not fully understand where risks and changes to their products can come from. In some cases they see the medical device and pharmaceutical market as high risk and of low business interest. A few suppliers have developed a dedicated approach to supplying their products and services to this market. Clariant and LyondellBasell work closely with each part of their supply chains to mitigate risks posed not only to themselves and their direct customers, but ultimately to the pharmaceutical and medical device companies. Clariant is a supplier of masterbatches and compounds, and LyondellBasell is a supplier of polyolefin resins to a diverse industrial base including the healthcare industry. Each company has served the industry for decades, and has adopted similar approaches to ensure that their business processes and healthcare products are well positioned to meet the challenges associated with more stringent controls.

The medical device and pharmaceutical industries continue to use plastics with high-performance properties and aesthetics in ever-increasing amounts. These materials must meet specific properties such as sterilization resistance, chemical and lipid resistance, and biocompatibility. Slight differences in impurities, extractables or leachables could potentially affect the biocompatibility and toxicity of the final formulated product. The U.S. Pharmacopoeia (USP) and the European Pharmacopoeia (Eur.Ph) require detailed information on the material components and formulation, manufacturing processes, and extensive supporting data with respect to physical and mechanical properties, chemical resistance, biocompatibility and toxicity tests. The results must be maintained in specific files, or the material must meet required properties set in standards. The advantage of this system is that manufacturers of finished products could use these materials in their designs and products with the confidence that they would meet regulatory and application requirements. The disadvantage however, is that this file or record is a point-of-time submission and is material-specific and formulation-specific. Managing any material or formulation change over time is thus not easy and becomes a formidable task both from regulatory and business perspectives.

Clariant And LyondellBasell

In order to meet the ever changing requirements and needs of both the healthcare industry and their customers, Clariant and LyondellBasell have implemented strategic business processes that involve working with their customers (developers and manufacturers of finished healthcare products, converters and processors, trade associations, etc.) and their suppliers (resins, pigments, additives, catalysts, etc.) to manage, control and mitigate the risks associated with the products they supply to the healthcare industry.

Clariant has several business units (BU) that supply the medical device and pharmaceutical industry with products such as intermediates, excipients and masterbatches. BU Masterbatches is a leading player in color and additive concentrates and compounds for the plastics processing industry across diverse applications from consumer electronics, toys, food, personal care packaging, textiles and automotive parts. The business unit is concentrating the know-how at three dedicated centers of competence across the globe with offering the possibility of complete manufacturing line-segregation capabilities for medical grade materials. These centers have a global quality management system that is based on current good manufacturing practices and that uses the ISO 13485 standard for medical devices.

Processes and procedures instituted for medical products include fully traceable production lots, an "open to audit" policy (a policy that encourages both direct customers and the brand owner to carry out audits) and rigorous change control processes. The result has been introduction of two new internal classifications of manufacturing for products used in medical and pharmaceutical applications referred to as MedCat 1 and MedCat 2 and the introduction of a new brand to distinguish products and services from the conventional products. The levels of controls with respect to material change notification, process controls, risk management, quality management systems and documentation, are different from the normal processes used in standard compound and masterbatch production sites.

LyondellBasell's Purell is a brand of polypropylene and polyethylene developed for use in the healthcare industry. The value of Purell products includes consistency of formulation, continuity of supply, single sourcing, backup plants and pharmacopoeia compliance. LyondellBasell was the first polyolefin company to launch a dedicated group of products used in healthcare applications, with dedicated internal quality systems and procedures that exemplify the spirit of pharmaceutical and medical device good manufacturing practices. Risk management procedures are also an integral part of this process.

Using Risk Management

Clariant and LyondellBasell work cooperatively to educate medical and pharmaceutical suppliers. They are building awareness of the importance and significance of change controls as they are applied to polymers, masterbatches and compounds. Using risk management to control products used in the healthcare industry is also part of their strategy. Both companies recognize that risk increases with the complexity of the supply chain, and have developed strategies to mitigate such risks and manage raw material changes, consistency and quality. Clariant has been working with their suppliers to provide pigments and additives with consistent quality and purity. The less the variation in these chemicals, the better the confidence that the masterbatches will not change their biocompatibility and toxicity properties from lot to lot or batch to batch.

CoA Based on Macroscopic Properties

The macroscopic properties of polymers and resins such as viscosity, flow, and physical and mechanical characteristics are well understood, and can be controlled and measured. These physical properties are used in the evaluation and selection of materials used by customers in healthcare applications. Certificates of analysis (CoA) and quality metrics are also based on these macroscopic properties. LyondellBasell recognizes that properties specific and critical for healthcare applications such as leachables and extractables, biocompatibility and toxicity are highly dependent on the resin's microscopic properties such as impurities, molecular weight distribution and low molecular weight oligomers.

The Importance of Supplier Controls

Supplier controls are becoming an important aspect of the quality systems for finished product manufacturers in the healthcare industry. Inspections by regulatory bodies will be placing an increased emphasis on purchasing controls to ensure that these manufacturers exert the appropriate extent and level of controls on their suppliers based on product risk and criticality.

Clariant and LyondellBasell have taken a proactive approach to building awareness among their customers and suppliers of the importance of mitigating risk, minimizing change and maintaining compliance and consistency of their products supplied to the healthcare industry. In so doing, these companies are well-positioned to serve customers who require preferred suppliers that have understood and implemented risk-based quality systems for the healthcare industry.

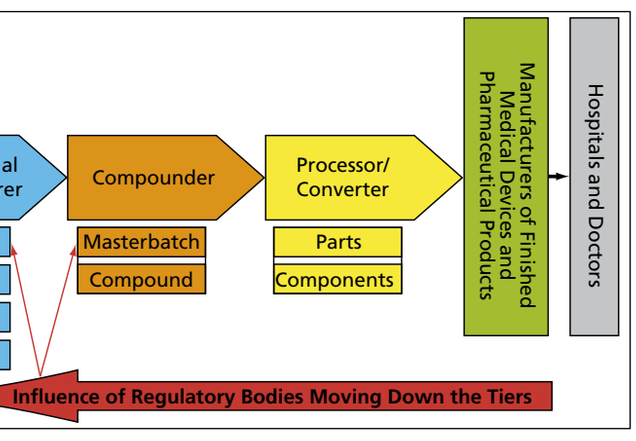


Fig. 1: Supplier Value Chain in the Medical Industry

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Alan Hippe

Alan Hippe to Leave ThyssenKrupp, Will Join Roche as CFO in April Outgoing ThyssenKrupp finance chief Alan Hippe will take up the same position at Roche Holding, replacing Erich Hunziker as the Swiss drugmaker implements cost cuts after a series of pipeline setbacks.

Hippe will join Roche as a member of the corporate executive committee in April, Roche said in a statement, as the group brings in another expert familiar with a hard business environment.

The pharmaceutical sector is facing tough times as companies struggle with price pressures, patent expiries on top-selling drugs, more competition from biosimilars – copycat versions of complex biotech medicines – and difficulties in getting new drugs to the market.

Roche, the world's largest maker of cancer drugs, is seeking to hack 2.4 billion Swiss francs ($2.5 billion) from annual costs from 2012 onwards with 1.8 billion francs of savings expected from this year after a spate of product disappointments.

Hippe's appointment comes after Roche said industry heavyweights Royal Dutch Shell CEO Peter Voser and Lufthansa head Christoph Franz would stand for election to its board.

Scott A. Tozier Elected CFO of Albemarle Albemarle has elected Scott A. Tozier as senior vice president and chief financial officer. Tozier assumed responsibility for all financial and fiscal management aspects of the company's operations on Feb. 1.

Tozier has over 20 years of diversified international financial management experience. Following four years of assurance services with the international firm Ernst & Young, Tozier joined Honeywell International, where his 16-year career spanned senior financial positions in the United States, Asia Pacific and Europe. His increasingly progressive roles included management of financial planning, analysis and reporting; global credit and treasury services and chief financial officer of Honeywell's Transportation Systems, Turbo Technologies, Building Solutions and Process Solutions divisions. Most recently, Tozier served as vice president of Finance, Transformation and Operations of Honeywell International.

Tim Stevenson Appointed as Johnson Matthey Chairman Johnson Matthey has appointed Tim Stevenson as its chairman, succeeding current chair Sir John Banham. Stevenson will join the board as chairman designate effective from March 29 and will be appointed as chairman in July, which is when Banham is set to retire.

Stevenson has been chairman of The Morgan Crucible Company since December 2006. He was chairman of Travis Perkins from November 2001 to May 2010. He was a non-executive director of Tribal Group from 2004 to 2008 and was latterly the senior independent director. From 2001 to 2005 Tim was Senior Independent Director and Chair of the Audit Committee at National Express. From 2000 to 2004 he was non-executive director of Partnerships UK. From 1975 to 2000 Tim held a variety of senior management positions at Burmah Castrol, including chief executive from 1998 to 2000.

Dominique Baly

Dominique Baly Appointed to Sartorius Top Management Team Former Millipore executive Dominique Baly, has assumed cross-divisional management of marketing, sales and service for the Sartorius laboratory business as president of Sartorius group Laboratory Business.

In this newly created position, he reports to the CEO and is a member of the group executive committee. Sartorius Group highest-level management team is now composed of six individuals, including the executives of both Sartorius AG and the subgroup Sartorius Stedim Biotech.

The company said the new management appointment is a key component in the further strategic and operational development of its laboratory business. The major goals of this initiative are the expansion into strategic, fast growing market segments, the targeted extension of the product portfolio and the reinforcement of direct sales organizations in key markets, the company said in a press release.

Alexander R. Wessels

Alexander R. Wessels Named President and CEO of DSM Pharmaceutical Products Alexander Wessels, previously president and CEO of DSM Food Specialties, has officially assumed responsibility for DSM Pharmaceutical Products, the pharmaceutical ingredients and contract manufacturing organization of Royal DSM NV. He reports to Stephan Tanda, member of the DSM managing board, and will oversee the implementation of DSM's "driving focused growth" global strategy, as announced in September 2010, within the pharmaceutical products business group. The strategy includes sales from high growth economies, innovation and sustainability solutions as well as from partnerships.

Wessels has worked in the life sciences, nutrition and pharmaceutical industries for 20 years, including four years at DSM, most recently as business group president of DSM Food Specialties, strongly improving theperformance of this global business and market leader. Headquartered in Parsippany, NJ, the DSM Pharmaceutical Products business group serves the global pharmaceutical and biopharmaceutical markets offering manufacturing services, R&D/formulation and technologies for biologics, active pharmaceutical ingredients and intermediates, as well as finished dosage manufacturing. The business group works closely with all DSM pharma interests including DSM Anti-Infectives.

Knut Schwalenberg Appointed Managing Director of Akzo Nobel Industrial Chemicals Knut Schwalenberg has been appointed Managing Director of Akzo Nobel Industrial Chemicals. Schwalenberg succeeds Werner Fuhrmann, who has been appointed to Akzo Nobel's new executive committee, with responsibility for Integrated Supply Chain.

Schwalenberg studied business economics at Essen University, Germany. He joined Akzo Nobel more than 25 years ago and has held a number of management functions in human resources, control and general management, including that of general manager of Akzo Nobel's Chlor-Alkali business.

Lanxess Invests €40 Million in 2 Projects in Germany Lanxess has announced a €40 million investment in two projects at its Krefeld-Uerdingen, Germany site.The company is building a production plant for the formalin needed to make trimethylolpropane (TMP). The applications of this trivalent alcohol include numerous products used in the furniture, construction and automotive industries. In addition to the plant itself, new formalin and methanol tanks will also be built on a total area of 1,000m² and is due to start up at the end of 2011.
In addition, the company said it is responding to strong global demand for menthol by investing in the expansion of its existing menthol production facilities. Synthetic menthol is a key component of numerous aromas and pharmaceutical products. Lanxess – in collaboration with Symrise – is the world's leading manufacturer of synthetic menthol and thymol. Initial planning work on the expansion of the hydrogenation facility is already under way, and the project is due to be completed during the first half of 2012.

Shell Wants 30% of CNOOC Refinery Shell is in talks with Chinese oil company CNOOC on a 30% stake in a $7.5 billion refining project, the China Daily newspaper reported, citing CNOOC officials.
The project, expected to become operational in 2014 with an annual refining capacity of 10 million tons and ethylene production of 1 million tons, is the second phase of CNOOC's Huizhou refinery at Daya Bay in Guangdong province. The Chinese government was expected to give the CNOOC refinery project the green light in the first half of this year, Dong Xiaoli, general manager of the Huizhou refinery, told China Daily.
The paper quoted Zhu Mingcai, deputy chief executive of CSPC, a 50/50 joint venture between the two firms, as saying Shell had shown strong interest in participating in the second phase plant, as had several other international petrochemical companies.
Shell is offering to give up 20% of its stake in CSPC to get a refinery deal, the paper said.

Petrovietnam Awards $5 Billion Refinery Deal to Technip, Others Vietnam has picked France's Technip, Japanese engineering firm JGC Corp and Spain's oil engineer Tecnicas Reunidas for a $5 billion deal to build Nghi Son oil refinery, the country's largest, a state-run newspaper reported. Petrovietnam Construction Corp, a subsidiary of state oil group Petrovietnam, will join the three foreign firms in the engineering, procurement and construction contract for the 200,000-bpd refinery, the Vietnam Economic Times newspaper quoted Petrovietnam Chairman Dinh La Thang as saying. He said the selection of partners in the EPC contract would enable construction of the refinery, which has a total investment of $7 billion, to start in March.
Nghi Son's operation is scheduled in 2014, and together with Dung Quat oil refinery, the country's first refinery, the two will meet half of domestic oil product consumption, the newspaper reported, without giving any figures for consumption in 2014. In early 2010 state media said output of the two refineries could meet 80% of domestic need.
Petrovietnam has also picked JGC Corp as adviser for a plan to raise Dung Quat refinery's capacity to 200,000 barrels per day from 130,000 bpd now, and the project is expected to be completed in 2016.

Saudi SABIC Unit Awards Deals To CTCI, Sinopec Arabian Industrial Fibers Co (Ibn Rushd), an affiliate of Saudi Basic Industries Corp (SABIC), signed contracts with Taiwan's CTCI and China's Sinopec Engineering to expand its capacity, SABIC said. The contract with CTCI would double Ibn Rushd's aromatics production capacity to 1.2 million tons per year from 560,000 tons and more than double its terephthalic acid capacity to 750,000 tons per year, SABIC said in an emailed statement. It did not give the value of the deals. The contract with Sinopec Engineering will see the creation of a new polyethylene terephthalate (PET) plant and increase capacity to 750,000 tons per year from 330,000 tons, it said. The company said the projects will take between 24 and 27 months.

Octal Secures $296 Million for Next Phase of Expansion Octal is on track to complete the second phase of its operational expansion this year following a new round of funding from six Middle Eastern banks. The privately owned, Oman-based manufacturer opened a 400,000 metric tonPET resins and sheet packaging facility in the southeast port city of Salalah in January 2009.
Phase two of the complex, which will be commissioned from June 2012, will add an additional 527,000m/t of production, making Octal the world's largest producer of PET resins on one site and the largest PET manufacturer in the world. Octal has secured a RO 114 million ($296 million) senior term loan from a group comprising Bank Muscat, Bank Dhofar, National Bank of Oman, Bank Sohar, Ahli Bank and Qatar National Bank. Existing shareholders Muscat Overseas and Oman & Emirates Investment Holding Company have also agreed a junior debt facility of $15 million.

Lanxess Continues Jhagadia Expansion Lanxess is continuing the expansion of its Indian production site in Jhagadia, Gujarat state. The specialty chemicals group broke ground for new compounding facilities with an initial capacity of 20,000 metric tons per year. These facilities will start producing the high-tech plastics Durethan (polyamide) and Pocan (polybutylene terephthalate) at the beginning of 2012. The investment of more than €10 million will create 60 new jobs.
India is on course to become the third largest consumer market for high-tech plastics after the United States and China, driven by the automotive industry that is set to grow by more than 6% per year.

Through The Firewall

Why Cyber Security Is So Important

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Computer Attacks – Every month, security researchers discover hundreds of new worms and viruses attacking the world's computer systems, but usually few in supervisory control and data acquisition (SCADA) and process control take notice. In early July 2010, however, a new type of computer worm was discovered that shocked experts in the industrial automation community. Called Stuxnet, this worm had been designed specifically to attack the Siemens WinCC, PCS7 and STEP7 control systems. Suddenly industrial control systems had moved from an accidental target to the center of the bullseye.

Of course, in one sense this should be no surprise. Security personnel in the U.S. have been warning of the potential for a cyber attack to be its next Pearl Harbor for years. Richard Clarke, the chief counter-terrorism adviser to President Bill Clinton at the time, raised the prospect over a decade ago, and the comparison has proved enduring; this year alone CIA Director Leon Panetta and Admiral Dennis Blair, the former Director of National Intelligence, have echoed him, and Clarke himself has also been back with his book "Cyber Wars: The Next Threat to National Security."

He paints a catastrophic scenario. The "electronic Pearl Harbor" would start with the collapse of the Pentagon's computer network, followed by a meltdown of Internet service providers. Blows to the power grid, refinery fires and toxic releases at chemical plants would all follow.

Many have rejected this scenario as fanciful, but Stuxnet shows there is cause for concern. Even without a cyber-war, we can estimate that there are 400 to 500 cyber security incidents in Fortune500 companies in the U.S. alone each year, and in Europe it is probably worse. In the processing industries and infrastructure, the Repository of Industrial Security Incidents (RISI), which records cyber security incidents directly affecting SCADA and process control systems, shows the number of incidents increasing by about 20% a year over the last decade.

For all that, though, the truth is probably that the next cyber security incident we see is more likely to call to mind the Titanic than World War II.

In that case, an unforeseen accident sunk the vessel, in part because its bulkheads only extended 10 feet above the waterline and failed to make compartments fully watertight. Water from damaged compartments was able to flood undamaged ones, dragging the "unsinkable" ship down.

It is an apt illustration for most cyber security failures. Consider some examples: the Zotob worm that shutdown 13 assembly lines at Daimler Chrysler in 2005; Browns Ferry nuclear plant in 2006, where redundant drives controlling the recirculating water system failed, probably due to excessive traffic between two different vendors' products on the control system network; or the Hatch Nuclear power plant near Baxley, Georgia, which was forced into an emergency shutdown after a software update to a computer on the plant's business network.

They provide some important lessons for cyber security:

- Hackers are not the biggest risk. There are numerous other examples of intentional attacks like Stuxnet. In Queensland, Australia, for example, the Maroochy Shire sewage spill in 2000 was the result of a deliberate attack on the SCADA system by a disgruntled applicant turned down for a job with local government. However, such cases remain the minority. RISI figures show that less than a quarter are intentional attacks. Instead, almost 50% of incidents reported have been caused by malware, including viruses, worms and Trojans, not specifically targeted at the facility affected. Many of the remainder are pure accidents. The most common security incident remains the unintended consequence.
- Internet security is not enough. Daimler Chrysler had professionally installed firewalls between the Internet and the company's network, but the worm still made its way into the control system, probably from a laptop. From there it was able to travel from plant to plant in seconds. Or consider the 2008 attack on the Lodz city tram network in Poland. A 14-year-old boy used a modified television remote control to change track points, derailing four trams. Any protection of the central control system against untrusted networks was rendered entirely redundant. The hacker was not even using a computer, much less the Internet.
- Poor systems design and, in particular, a failure to contain communications in appropriate areas or sub-systems is a key problem. This is perhaps most obvious in the Hatch nuclear example. The safety system there was well designed, right down in the nuclear reactor. Understandably, it included a database to monitor cooling water levels, among other variables. However, it also included a direct link to a similar database in the business network, and, unfortunately the data flowed both ways. The result was that when software in the business system was upgraded, zeroing the database there, it did the same to the database in the reactor. The automated safety system interpreted this as a drop in water cooling levels and triggered a shutdown. The plant was offline for two days.

Defining Zones

Behind all of this, of course, is the move away from proprietary networks in process control and SCADA systems to standard platforms, such as Windows and Linux, and open standards such as Ethernet, TCP/IP and web technologies. The benefit this has brought to process control systems is significant: integrating different vendors' technology used to be a significant project, both financially and in terms of time. It can now be a morning's work. Similarly, few would now forego the business benefits of integration with enterprise and third party networks.

However, it has also introduced vulnerabilities. Control systems can no longer rely on security through obscurity. Instead, they need the same protection against network attacks and vulnerabilities that have long plagued enterprise IT systems.

Unfortunately, as the examples demonstrate, perfect security is unachievable and, even if it were, would be unaffordable. What is required therefore is network security that protects against external threats, while preventing problems that do materialize in one part of the system spreading to critical control systems. The solution is security zones.

Based on the ANSI/ISA 99 and IEC 62443 standards, key automation and control devices should be grouped into zones that share common security level requirements. Any communication between these zones must then pass through a conduit, a path that regulates the flow of data between zones to allow them to communicate securely.

Making A Start

The most obvious objection to implementing security zones is the upfront work involved, particularly when it comes to existing plant networks, and that is just one reason that the process should start with a thorough risk analysis. This will clarify, and where possible quantify, the business consequences should the threats identified materialize. These may be in terms of lost production, repair costs, clean-up costs or fines, not to mention environmental damage and loss of life. Identifying the potential to incur these costs will be key to defining the business rationale for implementing a robust cyber security system and gaining management support for it.

Furthermore, a risk analysis focused on the operational zone will help clarify the distinction between the threats facing the control system against those more commonly considered in the IT environment. This is vital because much of the knowledge needed for the exercise will come from the company's IT department, which will have the expertise in server and fire wall management, disaster recovery, backup and restore procedures, and so on. It makes sense to make use of this. Control systems are, after all, similar to mission critical servers in the IT space.

However, the priorities in the control room are not the same. IT personnel are primarily focused on protecting the company's intellectual property; process control security is about protecting the physical assets, the plant, its people and the surrounding environment. Similarly, patch management, firewalls, antivirus software and encryption must all be handled radically differently in a control environment. The analysis will help highlight these differences.

Finally, a risk assessment should help reveal the vulnerabilities that are actually in the system. It will, for instance, necessarily involve an inventory of the networks that will reveal where design drawings may no longer be up to date, and should help to determine where the risks actually lie. This will prevent any security strategy focusing just on high profile, but low probability events, such as a terrorist attack. Instead, the whole range of everyday threats can be identified, revealing the close interconnection between security, safety and reliability. The plant can then priorities dealing with the high probability, high impact vulnerabilities. That, in turn, should leave it as well placed as possible even if Clarke's worst fears do turn out to be true.

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Bridging Competencies

From Lab to Launch, Oracle's Agile PLM Reorganizes Pharma

Becoming Nimble – It's no secret that Big Pharma is facing some of the biggest changes in the history of the industry. The looming patent cliff is now forcing companies to reexamine the way they do business from the ground up: According to IDC Health Insights, between now and 2012, 19 of the industry's blockbuster drugs will come off patent, for approximately $60 billion in annual industry revenue. A "one size fits all" approach to drug development is outdated; the companies that are coming out on top in the pharma industry are the ones who can react quickly and with agility to their customers' needs.

The multinational technology company Oracle works "up front" with its customers when developing software, and within their close work with pharma companies, they learned that the top management do indeed realize that there is a significant need for them to completely change the way they are developing, said Denis Senpere, vice president of Product Lifecycle Management Solutions EMEA at Oracle. The company said the pharma industry needs to improve its paradigm for innovation in three different ways: by forming orchestrated drug-development networks; by supporting a more integrated R&D and regulatory process; and doing all of this within the framework of a globalized, scalable and secure supply chain.

"Ironically," Senpere said, "we saw this same situation 20 years ago in the automobile industry."

So why is the pharma industry lagging behind? Senpere said its due in part to the huge amounts of money that pharma companies were able to bring in through their blockbuster drugs over the last decades. However, he said the trends should have been visible back then, but in light of the profits that were being made, pharma companies placed more priority on acquisitions.

"The wake-up call came about three years ago," he said. And while companies are ready to "clean house," they are struggling to find the root cause of their woes and how to go about transforming their businesses. Senpere said many pharma companies wrongly believe they have departmental issues.

"They don't have department issues," he said. "They have enterprise issues."

'Siloization'

Senpere said the most common structure that can be found within pharma companies can be likened to silos, meaning every department works independently for themselves without much consultation or contact with other units.

"If you have different silos for clinical trials, R&D, commercialization, this leads to a proliferation of new processes that have never been consolidated within an enterprise management system," he said.

This leads to gaps throughout the entire process chain. The formation of the products and processes that go into developing drugs are exploding, as well as the knowledge capture that goes into behind these products and processes.

"But when you explode and have no infrastructure to control information, you have a massive proliferation of problems," Senpere said.

"That means the situation today has become absolutely abysmal in many companies," he said, citing a myriad pharma companies who have been fined for compliance issues. "These companies would've been better served by investing the money into internal process optimization systems."

From Lab to Launch

This is where Oracle comes in with its product lifecycle management system Oracle Agile PLM for Pharma that can help all players in the industry – large, small and all those in between – to more effectively develop products; eliminate waste; create a secure ecosystem of networked partners; and enable Quality by Design (QbD) practices. The software system, which can be tailored to fit the specific needs of a company, helps to eliminate the siloization and makes communication possible across all parts of the production chain – from lab to launch. The software touches many different functions across the chain, too: R&D; quality; production; clinical trials; packaging; regulatory affairs; and marketing.

In order to develop software to assist with this transition within the pharma industry, Oracle worked together with 15 leading industry players – members of the Oracle Pharmaceutical Strategic Council – to identify the seven common enabling elements needed for change. The Agile PLM is based on these elements:

- 1. Drug development portfolio management: This enables the user to enforce critical program deliverables and regulatory requirements by improving drug development execution, program management and cross function collaboration.
- 2. Comprehensive drug development records: Structured drug development records facilitate the re-use of Common Technical Documents (CTD) by capturing complex multi-dimensional data from material, equipment, process/recipes and analytical methods in one system.
- 3. Efficient clinical supply management: This enables faster clinical trials by allowing users to easily allocate materials and make equipment reservations as well as the efficient and effective management of recipe variations during the all clinical trials phases.
- 4. Faster technology transfer: The software facilitates the scale-up to commercial drug production volumes simplifying the analysis of the entire drug product development value chain, from suppliers to materials, equipment and processes.
- 5. Integrated quality and risk management: This assists the user in building quality into the development from the beginning and offers a comprehensive enterprise quality management solution that supports QbD and other quality programs. This results in faster and more efficient regulatory submissions.
- 6. Integrated packaging and label management: This is to improve the regulatory integrityof commercial content by providing a global repository for all packaging components, digitalassets and marketing collateral that are linked back to development evidence.
- 7. Global product registration: This makes it possible to create a single product registry to maintain thecontent required to support regulatory submissions and product rollout.

Satisfied Customers

Oracle boasts over 170 customers in life sciences, making it the enterprise PLM leader in that market. Companies such as Eli Lilly, Bayer, GlaxoSmithKline and Abbott have already implemented parts of the Agile PLM – part of the flexibility of the software is that not all seven elements need to be put into place at the same time, giving users the possibility to start with the area of their business where the need is most dire.

Wolfram von Ehren likes to use Bayer as an example of a successful user of the Agile PLM for Pharmaceutical. Von Ehren is a strategy and operations consultant at Deloitte, a professional services organization who is working together with Oracle.

"In our work with Bayer over the last 10-15 years, they have always been the first to try out new technologies and approaches. Part of their success is that they are willing to take the risk to be one of the first, but then they are also one of the first to reap the benefits."

After implementing several elements of the Agile PLM, Bayer HealthCare was able to reduce cycle times for packaging by one third; saw a 50% reduction in packaging/labeling errors and a 50% reduction in rework costs; is able to consistently track ingredient data per country; has seen improvement in quality and compliance; and has won overall global viability of data.

Senpere, however, stresses that Oracle's Agile PLM is not something companies can just download in order to make their enterprise problems disappear.

"If someone wants to change their whole company, then they will apply all seven initiatives over time of five to 10 years, depending on their size," Senpere said. "Transformation is a journey."

Brandi Schuster

Infobox

Members of Oracle's Agile Pharma PLM Strategy Council

Bayer
Eli Lilly
Glaxosmithkline
Novartis
Boehringer Ingelheim
Invitrogen
Merck & Co
Abbott Diabetes Care
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Ranbaxy
Dr. Reddy's
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Euticals to Acquire Archimica Group

The Italian pharma fine chemicals company Euticals will buy Archimica from TowerBrook Capital Parners for an undisclosed sum. Completion of the transaction is expected in early February.

TowerBrook acquired Archimica, a player in the pharmaceutical fine chemicals industry, in June 2006. The company has approximately 550 employees at six production sites in Italy, France, Germany, US and UK and achieved strong sales of €131 million in 2009, a 16% increase from 2008. Euticals Group is a successful pharmaceuticals fine chemicals company with sales in 2010 of €93 million and five production sites near Milan, Italy. Euticals and Archimica said they expect the combination to be strategic, creating new opportunities to further develop business activities in the fine chemicals sector. ■

Azelis Acquires Finkochem

Specialty chemicals distributor Azelis has acquired acquisition of Finkochem, a Serbian company specializing in the sales and distribution of a wide range of raw material for the food, chemical industries (detergents and homecare), plastics additives, metallurgy and rubber. With this strategic acquisition in Serbia, Azelis said it has gained the capacity to accelerate growth within their Food & Health, Personal Care and Chemical Industries business lines in the region. In particular, the combination with its existing operations in Croatia, will allow Azelis far greater access to markets in the region and will improve service levels for suppliers and customers of the group. ■

Süd Chemie to Provide Yara with Catalysts for Fertilizer Production

Süd-Chemie and Yara International have concluded a five-year framework agreement on catalysts for fertilizer production. The companies announced that the long-term supply agreement will cover more than 50% of the requirements of Qatar Fertiliser Company), a JV of which Yara owns 25%. Under the agreement, Süd-Chemie will develop, produce and deliver all front-end catalysts involved in the production of ammonia as well as applied technical support. Süd-Chemie expects to generate significant revenue of more than $40 million from the agreement during the next five years. ■

Going Green Using Real-Time Analytics

Proper Integration of PAT and Process Automation Vital

Facing Challenges – In today's world, the pharmaceutical and chemical industries face major challenges including globalization, environmental regulation, and shortening product life cycle. Meeting these challenges has required the development of innovative technologies and alternative approaches geared towards reducing costs and improving the environmental and economical profile of chemical processes. Breakthroughs in process operations and modeling have been necessary for achieving energy and material efficiency gains.

Proper integration of Process Analytical Technologies (PAT) and process automation together with the use of multivariate tools for design, data acquisition and analysis is critical and listed in U.S. Food and Drug Administration (FDA) guidance of PAT. The latest FDA Guidance for Industry released in November 2009 also defines Quality by Design (QbD) as "A systematic approach to development that begins with predefined objectives and emphasizes product and process understanding and process control, based on sound science and quality risk management." Although they began on different paths, the principles of green chemistry and engineering share plenty of common ground with the QbD and PAT initiatives. The use of PAT within a QbD framework promotes information-rich experiments that respond to the need for increased process development throughput, downstream consistency and reliability.

Fig. 1: Example of set up interfacing PAT (FTIR spectroscopy and FBRM) and process control instrumentation (EasyMax)

The Right Instruments

In situ particle system characterization, such as Mettler Toledo FBRM and Particle Vision Microscope (PVM), Attenuated Total Reflectance-Fourier Transform Infrared Spectroscopy (ATR-FTIR) reaction analysis with ReactIR, and automated laboratory calorimeters (RC1e, EasyMax) are easy to use, innovative technologies that responds to the need for increased process development throughput, consistency, and reliability. Case studies from major pharmaceutical companies (Bristol-Myers Squibb, Pfizer, Sepracor) illustrate how these instruments are used in chemical reaction and crystallization design to minimize waste, improve reaction output, increase energy efficiency, decrease the formation of by-products, as well as minimize the potential for accidents.

ATR-FTIR for Continuous Processing and Micro-Reaction Technology

Continuous processing is now becoming widely accepted in the pharmaceutical industry thanks to the many benefits it provides in drug discovery, chemical development and manufacturing. On a small scale, microflow and small scale flow reactors are better alternatives to the traditional round bottom flask. For instance, they are used to safely prepare grams to kilograms of material involving the use of highly energetic transformations (diazotation, hydrogenation, nitration) typically considered too hazardous to be practiced in non-specialized labs. On a larger scale, in chemical development and beyond, continuousprocessing bypasses some scale-up issues usually faced in batch mode (mixing, heat transfer), and often gives a better yield, better selectivity, and safer manufacturing operations.

The availability of convenient, specific, inline monitoring techniques is to count among the hurdles preventing a faster and earlier adoption of flow chemistry in the pharmaceutical industry. Indeed, what would be the point of being able to produce material continuously if quality control and analyses have to be performed in batch, in other words, by relying on occasional sampling for offline analysis?

Over the past few years, ATR-based FTIR spectroscopy has become one of the preferred inline techniques thanks to its structural specificity, fast data collection rate, and convenient software control. As a result, real-time measurement of product quality and concentration leads to a faster reach of steady state, more time efficient screening of process conditions, and overall reduction of material waste.

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Calorimetry for the Greening of Batch Processing

The fast adoption rate of continuous processing should not mislead us into believing that batch processing is no more the primary method for producing chemical intermediates and biologically active molecules. Batch processing has indeed major limitations: heat transfer, associated safety issues, mass transfer, and problems faced with solvent extraction and crystallization. However, batch production, from lab through plant scale, is and will remain the predominant technology thanks to its simplicity, flexibility, and the abundance of existing equipment (round bottom flasks, jacketed vessels, pilot plant and full scale plant manufacturing vessels).

Researchers at Pfizer recently gave us an excellent example of risk management using reaction calorimetry for the scale-up of an exothermic reaction. Although the chemists developed a greener alternative to CP-865,569, a CCR1 antagonist, that, unlike the old chlorine displacement route, does not generate a large amount of sodium salt, it involves a performic acid oxidation step that has the potential to release large amounts of energy and gas. A fully fledged calorimetry assessment was necessary to ensure thermal stability of performic acid and the associated heat of reaction could be safely controlled. Only under these conditions could the atom efficient, low cost, performic acid route be considered "greener." The oxidation displayed a formidable –975 kJ/mol heat of reaction, as measured in an RC1e calorimeter. The resulting adiabatic temperature rise (ATR) is significant at 172 °C. Finally, the maximum heat output was –44 W/kg, likely to exceed the maximum cooling capacity of the scale-up equipment. Despite these major safety warnings, calorimetry data showed that the reaction was fast and dosing controlled, meaning that simple slow down of dosing rate to match plant cooling capacity would ensure safe operating conditions. The oxidation process was eventually implemented at the 300-gal scale in the pilot plant under dose-controlled conditions. Five batches of 30–35 kg final product CP-865,569 were safely and successfully manufactured.

Applying the Principles of Green Chemistry to Crystallization and Downstream Processing

Designing an atom-efficient truly catalytic process as per some of the 12 principles of green chemistry would not fully make sense if a significant portion of the final product is to be wasted because of a poorly designed crystallization phase. Crystallization is indeed critical for the purification and isolation of organic compounds although often difficult to optimize unless good particle engineering practices are implemented. An inefficient crystallization phase can lead to poor product quality, low yield, often resulting in product reprocessing, which consumes time, material, and resources. Also, dry milling, often necessary when a crystallization step has not been engineered to produce the desired particle size, results in losses due to holdup in the milling equipment. The generation of fine particles in the milling equipment presents a risk of exposure to hazardous compounds and explosion hazard. In summary, one needs to take a holistic approach to the process required to manufacture the final product, and include the isolation phase when evaluating how "green" a chemical synthesis is.

A case study published by researchers at Sepracor demonstrates how real time monitoring of particle changes can help troubleshoot an existing crystallization process. Production campaigns at a contract manufacturing site would regularly fail optical purity specifications. It was observed that those failed batches would also take longer to filter and dry. More time was deemed necessary to investigate the seeded cooling crystallization process at lab scale using in situ particle system characterization (FBRM). This technology showed that although the batch was seeded at 46 °C, no significant crystal growth was observed for another hour or two at which time a sudden, poorly controlled, secondary nucleation would occur. This would be the cause for batch to batch variability. It was also found that when the nucleation occurred earlier, at a higher temperature, the batch would exhibit shorter filtration time and better product quality. Mixing efficiency and seed surface area were found to be key parameters to force nucleation and crystal growth to occur earlier, under less supersaturated conditions, leading to larger particles, a faster filtration, and better product quality. An improved procedure was tested at 50 l and 400 l in Sepracor's pilot plant, and then successfully transferred to full-scale manufacturing at the contract manufacturing site. This example illustrates how the use of PAT, in situ particle system characterization with FBRM in this case, helped identify the cause for variability in Sepracor's initial crystallization process, and design an improved, greener, procedure offering a much shorter cycle time, high optical purity, and consistency from batch to batch.

Conclusion

Over the past 15 years, in situ particle system characterizations with FBRM and PVM, real time ATR-FTIR reaction analysis, and reaction calorimetry have become ubiquitous in academic and industry laboratories. They are now to research and process development what laptop computers, smart phones, and GPS devices are to our everyday life: They help improve productivity, save time, energy and resources, in addition to simplifying our life.

Today, those analytical technologies have a small footprint, are intuitive to use, to the point where it is hard to imagine how much more miniaturization and user-friendliness could be built into those systems. It appears that current and future areas for improvement are on the side of software modules helping synthetic chemists and process engineers evaluate data more efficiently and more rapidly. Indeed, up to now, existing PAT have merely generated mass amount of data that scientists need to spend too much time analyzing.

I suspect that within just a few years, personal workstations integrating automated reaction platform and in situ characterization probes, especially designed for chemists and engineers, will fully replace the traditional chemist's setup made out of a round bottom flask and a temperature sensor (fig. 1). Then will it become possible to achieve the necessary energy and material efficiency gains that will allow us to achieve the ambitious goals of sustainability, green chemistry, and QbD set for the pharmaceutical and fine chemicals industries.

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Sumika Styron Polycarbonate: Styron, Sumitomo JV Gets New Name

The 50/50 joint venture between Styron and Sumitomo Chemical is being renamed Sumika Styron Polycarbonate Limited (SSPC). Company name change activities are underway and are expected to be fully effective as of April 1. Styron announced in October that it assumed ownership of the 50% share that was formerly owned by The Dow Chemical Company, following Dow's divestiture of Styron to Bain Capital Partners in June 2010. The joint venture will continue to be headquartered in Tokyo, and will continue to serve its customers and market polycarbonate products in Asia Pacific. ■

Norway's Oil and Energy Ministry Offers 50 Licenses in Mature Areas

Norway's oil and energy ministry said it would offer 50 production licenses in its Awards in Pre-defined Areas (APA) 2010 licensing round for mature areas on the Norwegian shelf. The ministry said it would offer 22 companies operatorships, and that 39 companies were offered stakes in licenses. "There has been great interest for this APA round," said Oil and Energy Minister Terje Riis-Johansen. Norway's Statoil was offered eight operatorships while Sweden's Lundin Petroleum and Wintershall, a unit of BASF, were offered six each. Of the 50 production licenses awarded, 31 were in the North Sea, 17 in the Norwegian Sea and two in the Barents Sea. Eighteen were additional acreage for existing production licenses.

The 2010 APA round was announced on Feb. 19, 2010. ■

Uralkali, Silvinit Merger Recommended by ISS

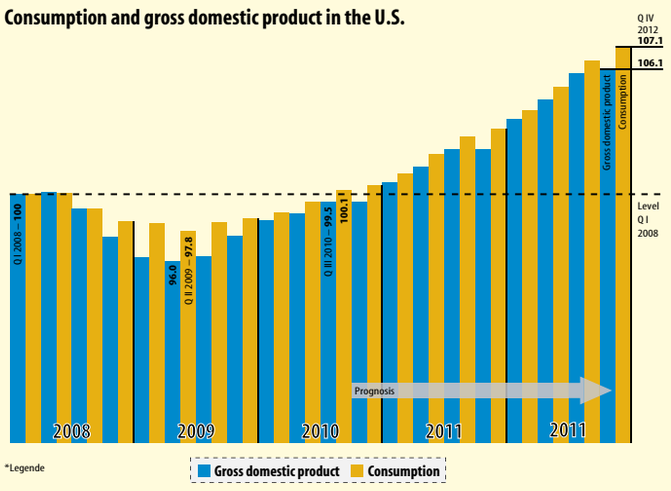
Russian potash miner Uralkali said on Thursday that the ISS proxy advisory service recommended shareholders vote in favor of its planned merger with domestic rival Silvinit. "This merger is certainly compelling based on the strategic rationale alone," the ISS said in a report sent to Uralkali. "The two companies are similar in many respects, including in terms of production and strategy. The expected gains from cost savings and scale can be substantial." The recommendation comes after minority shareholders in Silvinit last month demanded a revision of the merger terms, which they said favored Uralkali as it will receive a larger portion of the combined business. Fellow listed fertilizer group Acron, which owns 8% of Silvinit shares, voted against the deal at a board of directors' meeting and is expected to do so again at the shareholders' vote on February 4. Both companies are controlled by Russian billionaire tycoon Suleiman Kerimov and associates, who are aiming to consolidate their potash empire into a single Russian champion and the world's second-biggest producer. ■

BASF Acquires CRI/Criterion's Styrene Catalysts Business

BASF has announced that it has successfully completed its acquisition of CRI/Criterion's global styrene catalysts business. As part of this agreement, BASF has acquired CRI/Criterion's customer list, contracts and exclusive and non-exclusive licenses for intellectual property, including applicable patents and know-how in the field of styrene catalysts, as well as CRI/Criterion's styrene catalysts inventory. There were no plant assets associated with the deal. ■

The Highs and Lows of the U.S. Economic Upswing

Consumption and gross domestic product in the U.S.



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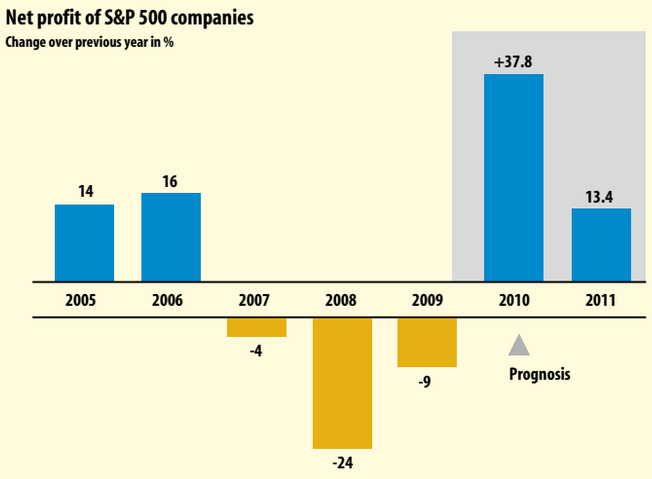
Net profit of S&P 500 companies
Change over previous year in %



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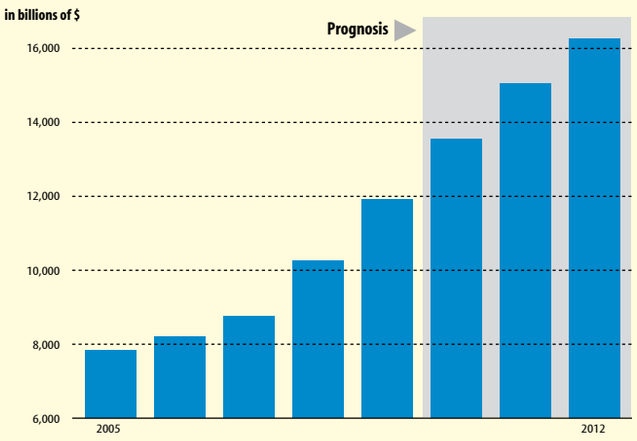
U.S. Debt
in billions of $



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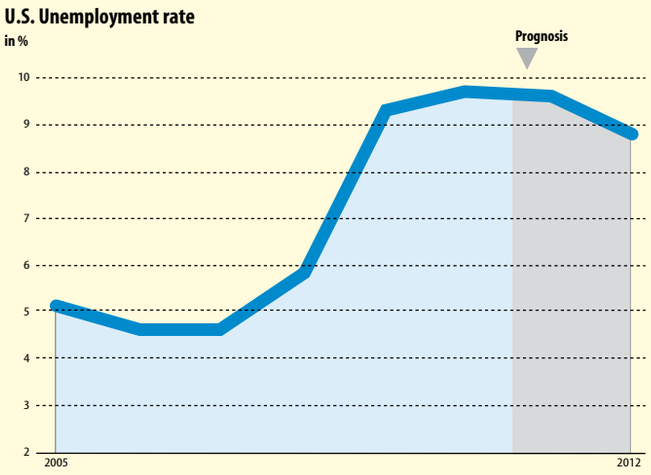
U.S. Unemployment rate
in %

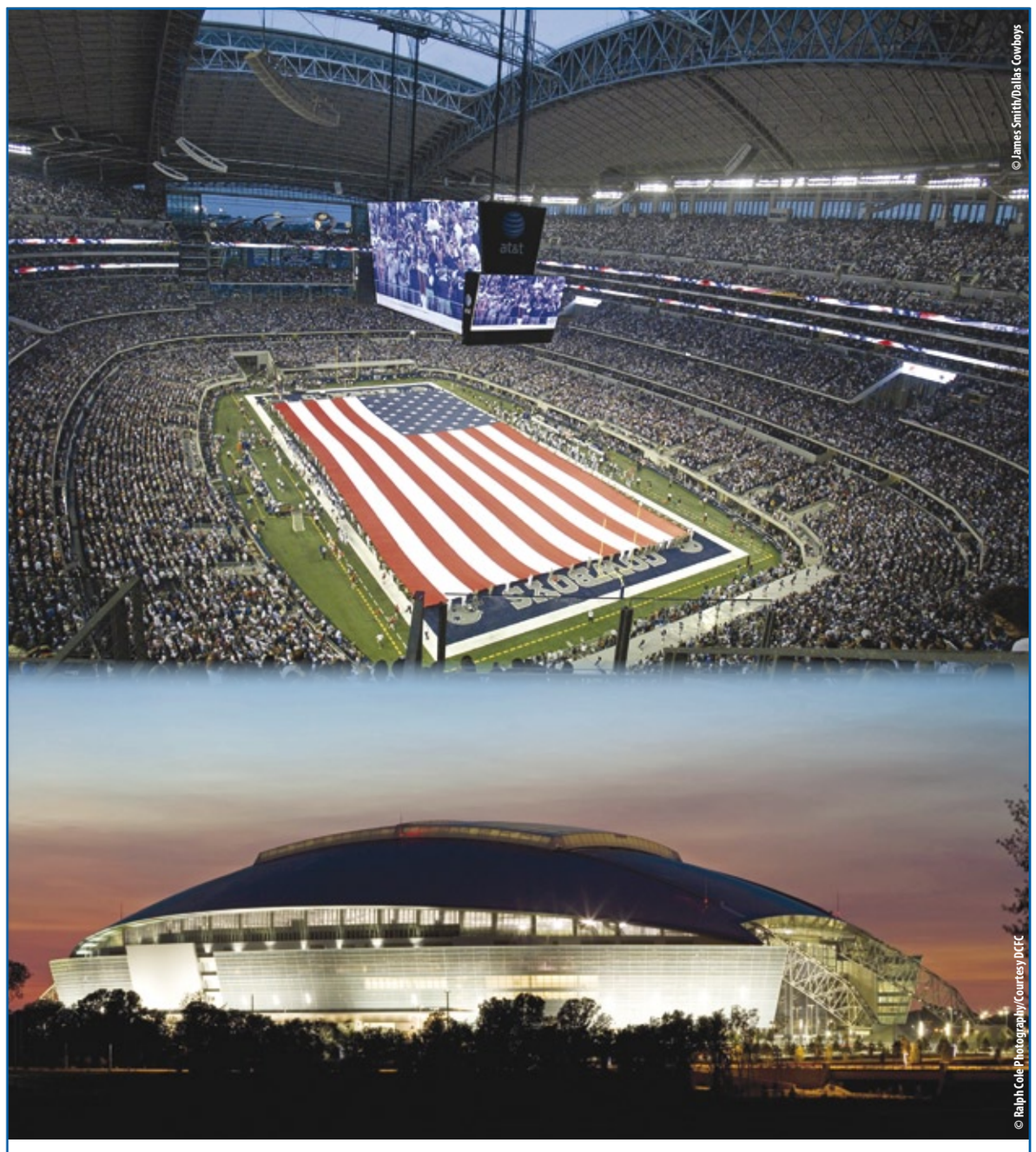


Source: Handelsblatt © GIT VERLAG

After two long years of the worldwide financial crisis, many U.S. companies are finally enjoying a comeback of the typical American optimism. Many companies have begun publishing their 2010 reports, experts expect to see impressive proof of the country's reclaimed earning power within the private industry. According to Thompson Reuters, the largest American companies were able to achieve 37% more profit than in 2009. Not only did public finance rank at the top, but also classic industrial companies, such as aluminum giant Alcoa. According to the U.S. Department of Commerce, such companies can also look forward to rising domestic earnings instead of just relying on stable foreign profits. Compared to Q3 2009, companies' domestic earnings went up one third in Q3 2010, and in light of the general upturn in demand, analysts expect equally strong results for Q4 2010.

One thing that's noticeable is companies are now less willing to use their profits for new investments or as dividend payments to their shareholders than they were before the crisis. The result is that cash holdings in 419 of the 500 companies represented on the S&P 500 grew by 49%. It could be concluded that this cash hording comes out of the fear that the upswing won't last long. However, more important are the intentions of America's top managers in 2011. For example, the CEO of U.S. engine maker Cummings said he wants to raise investments 50% to 600 million and wants to create 2,500 new jobs in the U.S. Companies such as General Electric and 3M have similar plans. However, something that could bode less well for the U.S. economy is the fact that most investments will be going into factories to be built in China and India; therefore it is unclear just how much the U.S. labor market – and the domestic consumption – stands to benefit from the newfound strength of American companies.

Of course, the upswing was made possible in part by a stimulus package and a recent extension of a George W. Bush-era bill, which just adds to the country's ever-growing deficit. U.S. Secretary of Treasury Timothy Geithner recently wrote an impassioned letter to Congress members, imploring them to raise the debt limit from its current level of $14.3 billion – the country already has $13.9 billion in total liabilities. While prognoses expect the U.S. economy to grow by 3.4% (thanks mostly to the $858 billion tax bill extension), the upturn is not reaching the masses, and unemployment is stagnating at over 9%. Chief economists warn that the U.S. could lose its AAA credit rating by 2015 if it doesn't take immediate steps to reduce its deficit and increase its income. (Source: Handelsblatt)



Are You Ready For Some Football? The new Cowboys Stadium in Arlington, Texas, is the world's largest indoor arena and will play host to the Super Bowl XLV on Feb. 6, where the Pittsburgh Steelers and the Green Bay Packers will face off. The stadium utilizes a variety of automation solutions to operate much of the "moving architecture" that makes the venue remarkable. The new home of the NFL's Dallas Cowboys features enough seating room for 100,000-plus fans, a roof with two retractable sections that each measure acres in length and width, and giant retractable end-zone doors. The face of each side of the video board, suspended on retractable cables at the center of the field, is larger than 5,000 52-inch screens placed side to side.
ABB plays a pivotal role in making many of these features work. 40 ABB regenerative drives are used to provide very strict control of the hoist system for the 600-ton video board. The retractable end-zone, glass doors are 180' wide by 120' tall; the "glass wall" is comprised of five, 38-inch panels, with each door taking 18 minutes to open fully and simultaneously. An ABB ACS350 drive, in conjunction with ABB motor starters, miniature circuit breakers, disconnect switch, contactors, and wire duct, control each panel. Each roof panel weighs 1.68 million pounds and travels 215 feet to close; it takes 12 minutes to open/close the roof. And a total of 128 7.5 HP gear motors are used to move them. ABB drives, featuring Direct Torque Control, allow each motor to share the load equally – and there is no need for encoders (from the motors to the drive). Because these drives deliver optimum torque at zero speed, the panels can be held and kept in the open position, until they are closed again.

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Bank Account
Commerzbank AG Darmstadt, Germany
Account No. 01715501/00,
Routing No. 50880050

Seventh year 2011
The current price list is valid from 1st October 2010

CHEManager Europe appears 10 times in 2010.

Print run: 15,000
(IVW Report Q3 2010: 14499 tvA)

Subscriptions
10 issues €100
incl. postage
single copy €13.50
plus postage

Students receive a discount of 50% upon presentation of a valid certificate. Subscription orders can be canceled within 1 week in writing. Dispatch complaints are possible only within 4 weeks after publishing date. Subscription cancellations are accepted 6 weeks before end of year.

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Printed by
Echo Druck und Service GmbH
Holzhofallee 25–31
64295 Darmstadt

GIT VERLAG
A Wiley Company

Printed in Germany
ISSN 1861-0404