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THE NEWSPAPER FOR THE CHEMICAL AND LIFE SCIENCES MARKETS

Markets and Companies

C3X Chemical Customer Connectivity Index Powered by ATKEARNEY

The results of the first C3X poll are in!

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Chemicals

Health and Beauty – Suppliers present innovations at CPhI and Sepawa Congress

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No Room For Complacency

Staying Ahead in the Dog-Eat-Dog Business of APIs

With increasing pressure from Asia and skyrocketing oil prices, fine chemical makers and their supporting industries have not had a smooth 2008. New strategies are needed, and the overused term "thinking outside the box" has never been more relevant. Ahead of this year's CPhI in Frankfurt, Brandi Schuster and Ana Wood asked several industry leaders about their companies' strategies for challenges on the road ahead. Read more expert opinions on pages 20 – 21.

Malik Aslam
President of AFC

*"**Increased competition** from Asian countries coupled with increased pricing pressure from customers is prompting fine chemical manufacturers to come up with new technological solutions to reduce cost and still be able to maintain margins."*

Peter Murin
CEO of Halocarbon

*"Look at some of the very real – and tragic – problems that have occurred over the past few years. I believe the **regulations** should be harmonized globally to something like we have here in the U.S."*

Lukas von Hippel
Vice president, marketing and sales, AllessaChemie

*"The **global economy** will have effects on all of us: The housing crisis in the U.S. is not only an issue for the bankers, but for all of us – if consumers for whatever reason do not consume, we will not be able to sell our products."*

David Hipkiss
CEO of Prosonix

*"Our customers are increasingly understanding the **importance and impact** of how right, first- time advanced particle engineering can play a major impact on formulation performance and clinical benefit."*

Frank Wicks
President of SAFC

*"…Pharmaceutical companies are placing greater importance on their **external partnerships** as the outsourcing trend continues to grow in the drug development business."*

Wolfgang Schmitz
CEO of Saltigo

*"In the west, consolidation of the fine chemicals sector is at an early stage and is long overdue after the **excessive increases** in capacity during the 1990s."*

Tom Hoshiba
General manager, TCI Europe

*"Ask anybody in our business and they will tell you that the challenge coming out of **India and China** is intense … there is absolutely no room for complacency."*

Roger Chantillon
Industry Business Director of Univar Europe

*"The pressure from generics and competition within the generics industry, with increasing Asian presence, is putting pressure on prices when the market is moving in the **opposite direction** because of oil and energy price rises."*

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CONTENT

BASF Makes Takeover Offer for Ciba

Dr. Armin Meyer
Ciba's board chairman

BASF said it plans to take over Swiss specialty chemicals company Ciba to strengthen its position in that speciality business. BASF said it would offer 50 Swiss francs ($44.05) in cash for each nominal share in Ciba, corresponding to a premium of 32 % over the closing price of Ciba shares on Sept. 12 and valuing the company at 6.1 billion Swiss francs ($5.37 billion), including debt.

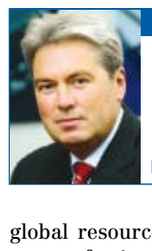
"Against the backdrop of increasingly challenging conditions within our industry, this is a transaction that combines a fair price with an industrially compelling solution for Ciba."

BASF said it had reached agreement with Ciba under which its board of directors supports the BASF offer and recommends its acceptance to its shareholders. The offer period is expected to begin on Oct. 1 and BASF expects to complete the deal in the first quarter of next year. The bid is subject to a number of conditions, such as the tendering of at least 66.67 % of all nominal shares, approval by the relevant authorities, and removal of various takeover defenses in Ciba's statutes, BASF said.

Dr. Armin Meyer, Ciba's board chairman said, "Against the backdrop of increasingly challenging conditions within our industry, this is a transaction that combines a fair price with an industrially compelling solution for Ciba." ■

Jan Secher Steps Down as Clariant CEO

Jan Secher



Hariolf Kottmann

Clariant has announced that CEO Jan Secher will be leaving the company at the end of September. The company's board has appointed Dr. Hariolf Kottmann as his replacement, effective from Oct. 1. Kottmann is a board member of Germany's graphite and carbon maker SGL Carbon AG.

"Dr. Hariolf Kottmann has broad leadership experience in the specialty chemicals industry and an outstanding track record in successfully improving the performance of existing businesses as well as building up new business opportunities," board chairman Dr. Juerg Witmer said. "Our objective is to substantially improve the performance of the Clariant group and to leverage Clariant's potential on the basis of a cohesive business portfolio, a global resource base as well as a professional team of business leaders."

Secher has been Clariant CEO since 2006 and carried out a series of restructuring measures. The company said he will pursue interests outside of Clariant. ■

Altana Acquires USBP Pigment Business

Altana has signed a contract to acquire the effect pigment business of the American company United States Bronze Powders (USBP). In 2007, USBP achieved sales of approximately $8 million in this business area. USBP retains its powder business as well as its aluminum pigments business. Within the Altana Group, the acquired business will be integrated into the Eckart Effect Pigments division. The acquisition is subject to approval by the antitrust authorities.

The acquired business mainly comprises the production of copper pigments, bronze pigments, stainless steel pigments, as well as press-ready metallic printing inks. USBP generates about 60 % of its sales of these pigments in the Nafta region, and about 15 % in each of Asia and Europe. No manufacturing site and no employees are included under the agreement with USBP; the production for this business will be transferred to Eckart's U.S. affiliate Eckart America in Painesville, Ohio, and to its main factory in the Bavarian town of Güntersthal in Germany. ■

Henkel CEO: China in Top 5 Markets

Kasper Rorsted
CEO, Henkel

Henkel's most recent acquisition will help the supplier of detergents and glues, make China one of its five biggest markets by sales in 2010, chief executive officer Kasper Rorsted told Capital Investor in an interview. The acquisition of National Starch's adhesives and electronic materials businesses for £2.7 billion has strengthened Henkel's Chinese business and helped it to become profitable, he told the magazine. "We would otherwise not be at this point," he said. Rorsted does not believe that a "bubble will burst in China," even though its economy is held back by the weakness in the U.S., he said. China's biggest problem is rising inflation, he added. Asked about rising raw-material costs, the CEO said costs are up 7 % to 9 % across all product types, more than the 4 % to 6 % expected until recently. The company has already lifted sales prices for adhesives and detergents but higher mark-ups are needed, Rorsted said. ■

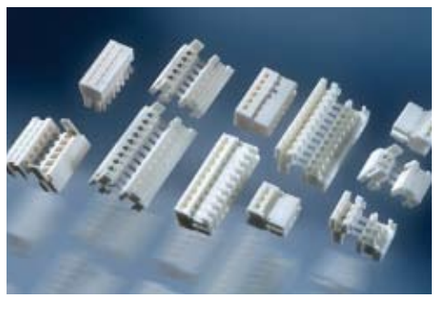
Evonik CEO Mueller to Step Down at Year-End

Werner Mueller

Klaus Engel

Evonik Industries chief executive Werner Mueller is stepping down from his post, effective at the end of this year, the company said. Mueller will be replaced by Klaus Engel, who currently oversees the chemicals division. The company was not immediately available for comment. Evonik is a conglomerate focusing on chemicals, energy and real estate. Owner RAG-Stiftung earlier this year sold 25.01% to CVC Capital Partners for €2.4 billion and said it plans to float the company in the medium term. ■

DSM Engineering Plastics Announces Acquisition



DSM Engineering Plastics announced that it has reached an agreement on the acquisition of the polymerization assets of Diolen Industrial Fibers. These include the facilities for polyester polymer production in Emmen (Netherlands), which will now be integrated with DSM's polyester compounding facility in Emmen. As part of the acquisition, DSM will offer employment to 45 Diolen employees.

Fredric Petit, Business Manager Arnitel & Arnite of DSM Engineering Plastics, said this acquisition gives DSM backward integration into polyester polymer production for its engineering plastic product lines Arnitel TPC, Arnite PBT and Arnite PET. ■

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Chemical Customer Connectivity Index (C3X)

Knowing What Matters to Your Customers

Serious Questions – Is the economic recession coming or not? This is the $1 million question that is increasingly stirring emotions in the European chemical industry. After years of uninterrupted growth, the industry had already lost some headway in 2007 and in early 2008, and production growth continued to drop. In view of the general conditions prevailing in the market, this is not surprising. The strong euro is still having a noticeable impact. Similarly, while it is true that the high prices of oil and other commodities have recently eased a little, it is not certain whether this signifies a turnaround or is merely temporary relief. It is no surprise that the European Chemical Industry Council (Cefic) lowered its growth forecast for the 2008 financial year to 2 % in July.

Thomas Rings
A.T. Kearney

Tobias Lewe
A.T. Kearney

"The situation is getting harder in the European chemical industry," said Thomas Rings, vice president and head of global process industries practice at A.T. Kearney. "This makes it all the more important for market players to remain focused on growth, and it is essential to continue with long-term activities such as innovation. Business strategies too need to be optimised, business portfolios revised and operational efficiency improved.

"We have often observed that there is no clear understanding of the requirements and specific characteristics of particular customers, so that improvement activities are not delivering the right results. Those who lose their customer focus now are missing an important opportunity to improve their competitive position during an economic downturn and to increase market share on a sustainable basis."

C3X: Customer-Supplier Relationship under the Microscope

What are the key requirements and issues in the customer-supplier relationship in the European chemical industry? To what extent are they recognized, understood and addressed by chemical companies? Answers to these important questions were provided by the first survey of the C3X (Chemical Customer Connectivity Index) panel, initiated by management consultants A.T. Kearney and CHEManager Europe. The panel is comprised of senior executives of leading European chemical companies and companies in customer industries, all of whom will be surveyed about customer-related matters at regular intervals. The first survey, which took place in the period from June to August, involved managers from 10 European countries, representing chemical firms and client companies in equal measure. The customer industries cover 10 different sectors, ranging from the automotive industry and food industry to the cosmetics industry.

Cyclical Growth Break

While growth in the industry has demonstrably lost momentum, the surveyed companies still appear optimistic about the industry development in the coming 12 months. Although neither chemical firms nor customer companies anticipate any significant volume growth, they do expect further short-term price rises as a consequence of the general rise in raw material costs. It remains to be seen whether these can be maintained over the medium term, given current recessionary pressures.

Questioned about expected future contract structures, the majority of the chemical industry executives interviewed indicate that they anticipate a change in their customers' contract structure in the next 12 months. The panel participants expect a drop in fixed-price agreements in the course of the year but a corresponding rise in formula-price agreements. This is a clear sign that customers are preparing for a possible downturn and are therefore making their contract structures more flexible.

Opportunities at the Interface to the Customer

A key finding of the C3X panel survey is that chemical companies address their customers' concerns best when they understand the requirements of their customers' customers. For approximately two thirds of the surveyed executives in the chemical sector, this is the fundamental driver when it comes to defining customers' needs. By comparison, a significantly smaller role is attributed to the technical department, the commercial department and the end consumer.

Smooth supply-chain management including delivery reliability and availability is simply taken as a given by almost all chemical customers surveyed, matching suppliers' own aspirations. By contrast, inventory management and packaging flexibility are perceived by customers as "nice to have."

"There is an expectation among the customers of chemical companies that by eliminating these 'non-differentiating' services they can realize cost savings," Rings said. Finally, criteria such as the relationship between the buyer and seller and the financial stability of the supplier are of secondary importance.

Furthermore, the C3X panel survey indicates that the significance to the customer of a sensible price-performance ratio is frequently misjudged by chemical companies.

"There is great potential to address this issue through more highly differentiated and carefully tailored pricing concepts," said Dr. Tobias Lewe, vice president in the Process Industries Practice at A.T. Kearney. "This will facilitate greater customer orientation."

The importance of environmental protection and sustainability to the chemical industry's customers is also clearly underestimated. Thirty-five percentage points more customers than chemical companies rate environmental protection as important or very important and for sustainability the difference accounts for 22 percentage points.

"In this respect chemical firms are wasting important opportunities to differentiate themselves from their competitors," Lewe said.

Customers credit their suppliers with a better overall understanding of customer requirements than chemical companies claim to have themselves. Three quarters of the surveyed customer representatives consider themselves to be excellently or well understood by their suppliers, whereas only approximately half of chemicals firms claimed such customer knowledge.

"Here, the chemical companies reveal themselves to be a little too self-critical, because their understanding of their customers' requirements is good. The focus should be on leveraging this know-how more effectively and trigger innovation activities, that deliver products and services that are more precisely matching customer needs and thereby achieve growth," Lewe said. "We often find that chemical companies are well aware of what their customers want but are not in a position to convert this knowledge into new offerings in a creative way."

What are the issues that are at the very top of the customers' agenda and should be given the highest priority by the chemical companies? For 88 % of the customers in the C3X panel survey, "pricing excellence" heads the list, followed by "process excellence" (73 %) and "new markets and customers" (67%). The chemical companies, however, perceive their customers' priorities differently and consider, for example, the topic of "value-added services" to be on of the most important ones.

"Chemical companies need to close the gap here to ensure that the focus of their efforts is in line with their customers' expectations," Lewe said. Surprisingly, the chemical regulation Reach did not feature highly in the list of internal issues of concern.

Great Expectations For Innovation

Customer expectations are similarly high when it comes to innovation; they expect both "incremental innovation" and genuine "game changes" from their suppliers. Entirely new chemical products are expected by 73 % of those customers surveyed, new applications by 71 % followed by new product features (69 %). Chemical companies, on the other hand, continue to prioritize step-by-step innovation based on changing or further developing existing products and applications. This is no surprise given that, in some cases, game changes are associated with decades of research and enormous up-front investments.

A further finding of the survey is that the understanding or definition of innovation is considerably broader on the customer side than it is on the part of chemical companies. Whereas the customers of the chemical industry also see new services, marketing techniques and business models as innovations, the chemical industry concentrates on conventional product and application innovations, in other words on continuing development of existing product lines.

"There is still very much a scientific focus in the chemical industry, and a lack of sales competence at the interface is often apparent. As a result, in many cases the industry still does not quite manage to make use of marketing and sales for its own purposes as an integral part of the innovation process," Lewe said.

A glance to the future suggests that over the next year, too, the broader forms of innovation will retain their importance. From the customer standpoint, however, "value-added services" will attain even greater significance and the chemical companies must develop those services whose added value is recognized by the customers – and which consequently are in demand.

"It is important that chemical firms offer the additional services that help them to distinguish themselves from the competition in their customers' eyes. Companies that want to score a hit with their customers must provide these services efficiently and at an attractive price," Lewe said. For instance, sustainability services of all kinds are already important today, and their importance will increase further over the next 12 months.

"Collaborative innovation" between chemical companies and their customers is "very important" or "important" for about two thirds of all C3X panel participants and chemical firms actually rank it even a little higher than their customers.

"After all, by involving the customer at an early stage allows chemical suppliers to better align expectations and therefore proactively manage the risks associated with innovation," Rings said. Chemical companies also try to share the burden of the high costs of research and development with the customer. That, though, is not always in the interest of the customers and a not inconsiderable proportion classified "collaborative innovation" as unimportant. The extent to which the customer is involved in the innovation process also varies from one customer industry to another with, for example, close collaboration being particularly widespread in the automotive industry.

A similarly differentiated picture emerges in the share of turnover annually invested in innovations. On average the share is around 2–4 %, while in innovation-oriented companies it is as much as 8 % or more. Finally, it is striking that the transparency on "innovation management efficiency" is still very poor in many cases. In well over a third of the companies surveyed, the proportion of the innovation budget that is assigned to defined projects is 40 % at most.

Sustainability Significantly Increases in Importance

The C3X panel survey also revealed that sustainability is becoming increasingly important both for chemical companies and their customer industries – even if the chemical firms do clearly underestimate the importance of this topic for their customers.

The survey answers make it clear that the customers of the chemical industry attach the greatest importance to being supported by their suppliers in helping their own customers to improve their sustainability.

"It is obvious that the issue of sustainability is one that the customers' customers have very much taken to heart," Rings said. "The chemical industry, which still largely views sustainability as a threat linked to plant efficiency, technology and raw materials, needs to better align with its customers. If sustainability is to be addressed fully and correctly, there is a need for a holistic understanding of the customer-industry value-added chain.

"We have also identified that chemical firms do not yet see sustainability as an opportunity to further expand their offerings, differentiate against competition and finally align their own portfolio with customer requirements."

Customers indicated that in the next 12 months, social responsibility and a positive environmental track record will be the key requirements that will gain importance. These, too, should be addressed by the chemical companies in the interest of aligning with their customers' sustainability priorities.

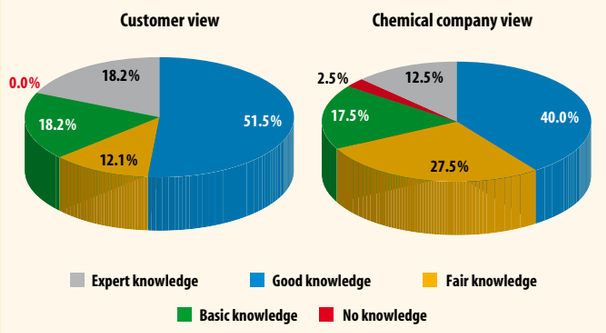
"It is important that chemical firms offer the additional services that help them to distinguish themselves from the competition in their customers' eyes."

Summary

No matter what the answer may be to the $1 million question: "Long-term thinking is a fundamental building block in a sustainable customer-supplier relationship. Those who understand the interface to their customers and address the relevant issues of today, tomorrow and beyond are well prepared and have a clear advantage," Rings said. "In reality, however, it is apparent that there are still significant opportunities that can be exploited by better fulfilling customer requirements. Offering real value-added services, for example in the area of sustainability present important opportunities for companies to raise their profile; many chemical companies are simply not yet exploiting these opportunities sufficiently."

Contact:
Meike Fuhlrott
AT Kearney
Düsseldorf, Germany
Tel.: +49 211 1377 2275
Fax: +49 211 1377 2990
meike.fuhlrott@atkearney.com
www.atkearney.com

How well do chemical suppliers know specific requirements of their customers? Figure 1
Understanding of chemical customers' buying requirements



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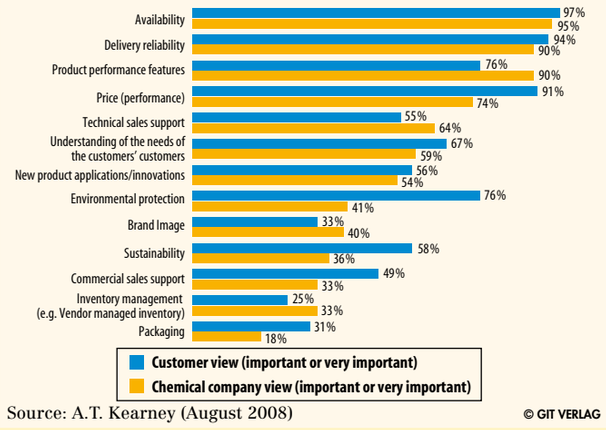
What are today's key buying criteria of chemical customers? Figure 2
Importance of chemical customers' buying requirements



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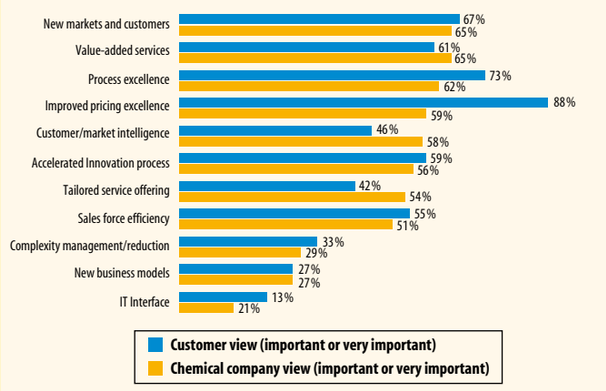
Which topics should be addressed by chemical supplier(s)? Figure 3
Key focus areas of chemical suppliers



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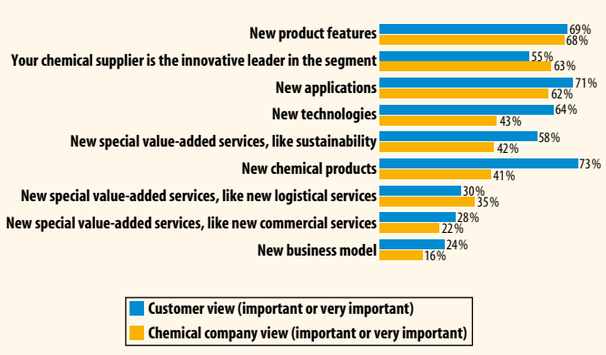
How important are different types of innovations? Figure 4
Importance of innovation routes



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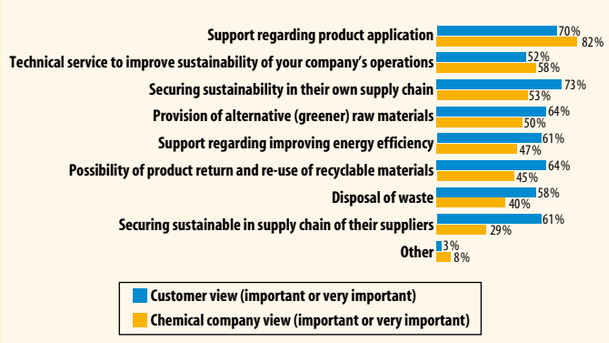
How can chemical suppliers help their customers to become more sustainable? Figure 5
Importance of sustainability related services



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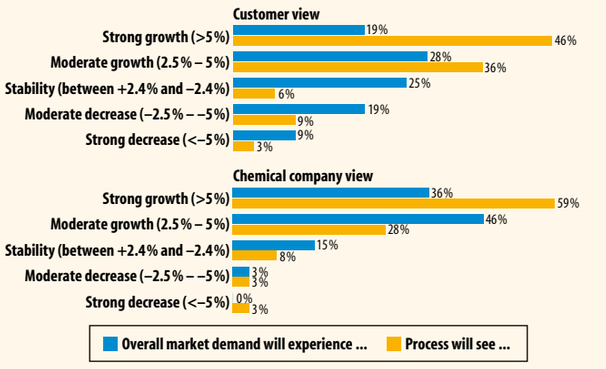
How will the chemical industry develop over the next 12 months? Figure 6
Chemical cycle outlook



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Capacity Utilization

A Pragmatic Approach to Determine Workforce Demands in Operations

Making Adjustments – The economic situation of companies has improved significantly after years of stagnation, and plant capacity utilization is on a clearly higher level at the moment than a couple of years ago. At the same time, requirements rose regarding documentation and quality issues caused by legislation or customer demands.

The current workforce capacity determined during the years of stagnation is no longer sufficient to manage the daily business effectively and efficiently. An intelligent adjustment of the workforce capacity is necessary in order to meet the increased workload, to increase flexibility and to reduce business risks. In the following case study, focusing on the role of a senior supervisor in a refinery, a pragmatic approach is presented how the partly contradictory requirements can be successfully met.

Company

Shell is a global group of energy and petrochemical companies in more than 110 countries. Shell Germany achieved a turnover of €36.7 billion in 2006 in the business areas mineral oil, gas and chemicals. In addition to an extensive network of service stations, Shell Germany operates three refineries and participates in two additional ones.

The refinery in Heide, Germany, is a plant of Shell Deutschland Oil with about 490 employees and is one of the most modern in Europe. The capacity amounts to 4.5 mt/y. The product portfolio includes the classical mineral oil products like petrol and diesel as well as raw material for companies in the chemical industry.

Initial Situation

Operations have been organized in area teams already for many years. An area team is a group of employees responsible for a specific asset area. In total seven area teams are installed in the refinery. An area team comprises the roles shift supervisor, senior supervisor, production manager, maintenance coordinator and process engineer.

Characteristic for the area teams is the close cooperation and direct coordination of day-to-day business issues. Typical tasks that are handled by the team refer to the main processes operation, maintenance and projects (fig. 1). The level of contribution varies for the different area team roles depending on the main process.

The area team concept has already been adapted in several steps to changes in the objectives or the general framework since its introduction in 2001. Due to the latest changes regarding changes of responsibilities within the area teams and new tasks resulting from internal standards, it was necessary to re-assess the workforce demand for the role senior supervisor.

Scope of the project was to determine the necessary workforce demand of senior supervisors. Thus, it was important that the workforce demand is determined free of discretionary decision and that the manpower situation can be described in a transparent, comprehensible and controllable way. On the other hand a reasonable workload of the employees should be guaranteed in order to avoid gaps in the workforce capacity.

Method Selection

Objective of the quantitative workforce planning is to determine the workforce capacity per position or work area which has to be made available at or for a certain period of time in order to handle the planned scope of work including all preparatory work and additional supporting work tasks.

Several different approaches are available in order to determine the workforce demand:

- Analytical
- Best guess
- Mathematical

In case of an analytical approach, all activities of a work area/function are evaluated regarding amount of time spent and are extrapolated to the annual demand. The gross demand can then be calculated by dividing the evaluated annual demand by the net annual hours of work. To determine the amount of time spent per activity different ergonomic assessment tools like MTM or REFA can be used.

Best-guess approaches include estimation methods, functional diagrams or the critical path method. When using these methods the respective tasks are estimated by the employees regarding the needed time. The quality of each of the methods depends solely on the experience of the evaluator and is therefore often replaced by group evaluations. These approaches are often used in practice.

Mathematical methods can be sub-classified into trend, regression and correlation analysis as well as simulation. These methods are strongly data driven. On the basis of selected headcount predictors the necessary workforce demand is derived from. Benchmarking is one of the tools that are often used in this connection.

Under consideration of the available data basis, the necessary accuracy, the acceptance of the results and the limited time, a combination of different methods was used in order to derive the workforce demand.

In this case study the determination of the current and future workforce demand was based on estimation methods and if possible by using ergonomic methods. The results were verified by benchmarking and correlation analysis.

Project Approach

The determination of the to-be workforce demand was carried out in the three project phases: data collection, analysis and workforce determination.

Phase Data Collection: At first the tasks of senior supervisor s within each of the relevant processes were further detailed and specific characteristics for each senior supervisor were determined. On the basis of the already determined job profile for the approximate time expenditure was estimated for each task by the senior supervisors. The estimation was not only restricted to the current demand but also included an estimation of the future needs.

The workforce demand was either derived from the quantity structure of a task and its known duration (e.g. number of meetings x duration of meeting) or by a general estimation of the duration of an activity.

In order to find out more about the estimations of the senior supervisor and the specific characteristics of the respective area team, in-depth interviews were undertaken. The following aspects were covered during these interviews:

- What are the objectives of the department?
- Are there any specific characteristics in the department that influence the workforce demand for senior supervisors?
- Which of the tasks have a seasonal characteristic?
- Which further tasks could be outsourced in a relative short period of time?

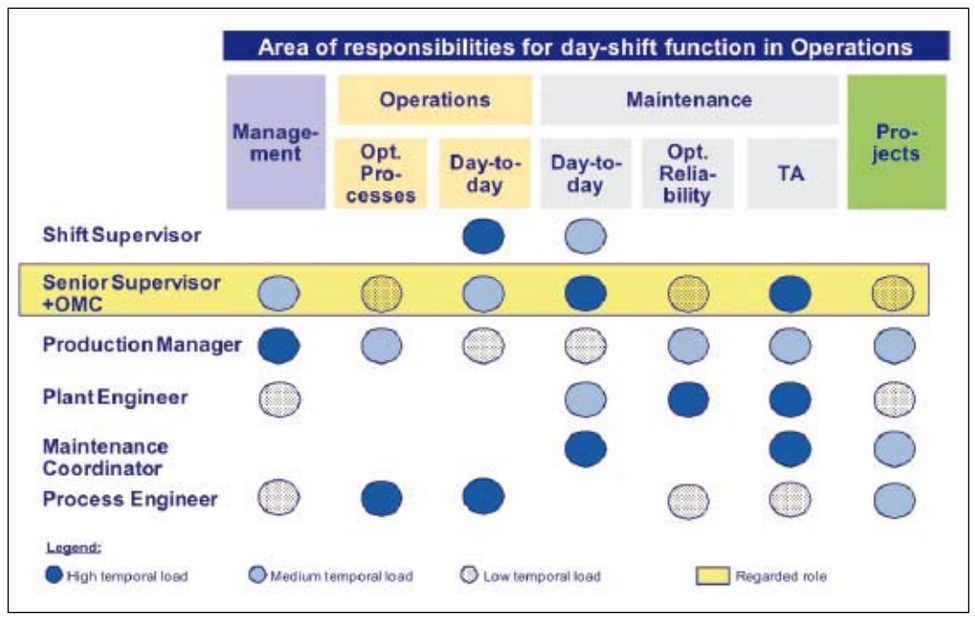

Fig. 1: Distribution of roles and responsibilities within an area team

But information about the absolute duration of a task is not sufficient as a database to derive the resource demand. Equally important is also the process quality. Therefore a thorough evaluation of the process quality was undertaken focusing on the following aspects:

- How is the process quality ranked?
- Which tasks offer improvement potential?
- Which improvements (qualitative/quantitative) can be generated when implementing all improvement measures?
- What are the most important criteria per task that influence the quantity of structure?
- Which key performance indicators can be used?

Hence, a qualitative and quantitative assessment of the tasks of senior supervisors was available from an internal view. As a supplement the external view, meaning the evaluation of process quality by peers and superiors and subordinates, was also analyzed.

In parallel, calculation rules were agreed upon that are necessary to calculate the workforce demands. Of high importance was the determination of the current and the to-be annual working times as well as the level of employment.

Phase Analysis: The analysis phase comprises on the one hand the consolidation, harmonization and analysis of the collected data and on the other hand a plausibility check.

Essential for the plausibility check was the determination of the headcount predictors per process and the determination of the specific characteristics of the area teams that lead to higher or lower resource demands (e.g. process quality, infrastructure, etc.). By assessing all area teams sufficient information was available to use scatter diagrams for visualization of identified predictors and duration. As an example fig. 2 shows the scatter diagram with regression line for the criteria "Number of Maintenance Orders."

In cases of high variability (fig. 2) a cause-effect analysis was conducted, necessary improvement measures were implemented promptly and the sustainability of the initiated actions was checked using performance indicators. Hence the variability of the resource demand was reduced.

Phase Workforce Determination: The determination of the workforce demand was based on benchmarks for each group of tasks which were derived from the scatter diagrams with regression line. In a first approach the benchmark target value was set as the average of the specific benchmark over all area teams.

The net workforce demand for senior supervisors was then calculated on the basis of the benchmark and the average quantity structure. To calculate the gross demand, detailed calculation rules had to be agreed upon including rules how to consider peak time demand or inactive periods.

A complete coverage of peak demands with own staff that might occur due to the saisonality of some tasks, is mostly very cost intensive. In such cases, it was assumed that the seasonal fluctuations can be covered by flexible working time regulation or by contractors. The use of a correction factor was therefore obsolete.

Inactive periods like vacation, illness or training are more or less constant factors that can be partly planed, were considered in the determination of the future workforce demand by using a correction factor.

Not to be neglected has to be the consideration of trends and/or developments, which have influence on the headcount predictors and thus on the workforce demand. Possible indicators for trends are here among other things enterprise-internal mid-term planning respectively external studies regarding industry trends.

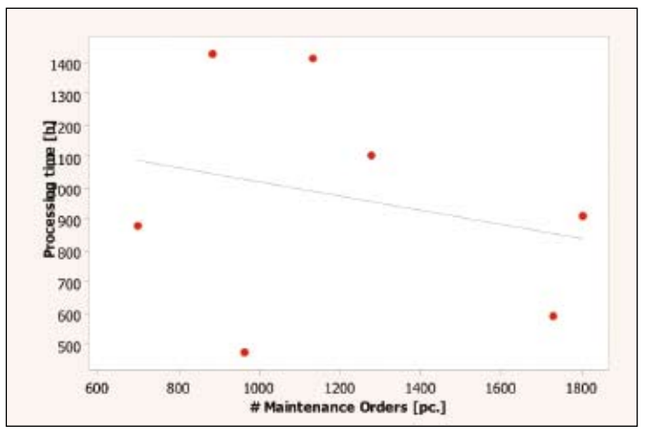

Fig. 2: Scatter diagram with regression line

Conclusion and Key Success Factors

A periodical assessment of the workforce demand is a necessity in order to cope with the changing general framework, the adapted requirements and to prevent overwork for employees. There are different methods available to determine the workforce demand. The decision which method to use, mainly depends on the specific enterprise situation.

As the most important key success factors during the whole process the following aspects have proven:

- Involvement of all process participants from operations, maintenance and engineering
- A precise differentiation of roles and responsibilities between the process participants
- Periodic and target orientated communication within the company
- Validation of the estimated future workforce demand
- Intensive analysis of variability and derivation of countermeasures.

Contact:
Bernd M. Vollmüller
Dr. Kalaitzis & Partner GmbH
Dortmund, Germany
Tel.: +49 231 430057
Fax: +49 231 432493
bernd.vollmueller@kalaitzis.de
www.kalaitzis.de

Henkel Q2 Adjusted Ebit Up 7.8% at €372 Million

Henkel said second-quarter adjusted Ebit rose 7.8% to €372 million on strong demand for its industrial glues, but the figure fell short of what analysts had expected. The German maker of shampoos, detergents and industrial adhesives said in a statement that surging raw-material prices weighed on results and it lowered its full-year earnings guidance slightly. The quarterly Ebit figure – excluding costs from an ongoing round of job cuts and from the integration of newly acquired adhesives businesses – fell short of the average forecast of €388.6 million in a Thomson Financial News survey of nine analysts. The company also posted a net profit of €38 million, down from €234 million a year earlier, on integration and restructuring costs.

Total restructuring and integration charges amounted to €256 million in the second quarter, almost a third of the €770 million to €780 million in one-off charges Henkel plans to incur in the full year. Henkel has said it will slash up to 3,000 jobs to counter a surge in raw-material prices and fierce competition. About 1,000 German jobs will be affected, the company specified. Quarterly sales rose 11.4% to €3.668 billion, boosted by the April acquisition of National Starch's adhesives and electronic materials businesses, but less than the €3.743 billion expected by analysts. Excluding acquisitions and currency effects, revenue increased by 6.1%.

"We achieved highly encouraging second quarter organic sales growth, despite a difficult economic environment still characterized by significantly increasing raw material costs and a weak U.S. dollar," said Chief Executive Officer Kasper Rorsted. Looking ahead, Henkel said it now aims for an increase in operating profit "at the lower end of the mid-teenspercentage range" when adjusted for restructuring charges and one-time effects but including cost savings from an ongoing overhaul. It previously cited a mid-teens percentage range. The company earlier this year started a restructuring program that will result in about 3,000 job cuts. It had a staff of about 53,000 at the end of 2007. ■

Positives Despite Economic Outlook

Jean-Pierre Clamadieu
CEO

French chemical group Rhodia hopes to benefit from the lower euro exchange rate and softer oil prices, despite the uncertain economic outlook, Chief Executive Jean-Pierre Clamadieu said.

"I think a couple of things have changed in the past few weeks," he said. "During this period, we've seen the exchange rate changing quite significantly ... euro weakening, which is clearly good news for European-based companies," he said. The euro, which climbed as high as $1.60 in July, has fallen to below $1.50, offering relief to European companies. "The second important element is raw materials," he said, pointing especially at crude oil prices, which have come off their high at around $148 a barrel to about $107. "We've seen a very significant reduction in the price of oil, although this has not yet translated in the price of the petrochemical raw materials that we buy," he said. He said there were solid growth opportunities in many world markets despite some slowdown in areas like the U.S. and European construction sectors. "We're looking very carefully at the current situation, because people are much more worried than they were a couple of months ago," he said. "But when I look at my order book today, I don't see actual changes. My order book is very similar to what it was in the first or second quarter of the year." ■

3M Completes Acquisition of Ligacon

3M announced it has completed its acquisition of Ligacon, a Swiss-based manufacturer and supplier of filtration systems and filter elements for the pharmaceutical, biotech and general industrial markets. Terms of the transaction were not disclosed. As part of 3M CUNO Filtration, Ligacon will gain access to 3M technologies and developments, which will allow improved offerings to the market and provide an excellent base for attractive growth and opening up new market segments. ■

Umicore Says Right Time to Acquire

Thomas Leysen
CEO, Umicore

Belgian speciality materials maker Umicore said that now was probably the right moment for it to make acquisitions as the valuation of some of its peers becomes more attractive.

"Certain valuations become more attractive, so the scope for doing something is there," Chief Executive Thomas Leysen told an analyst conference call. "Certainly in the field of broadening our scope in advanced materials, broadening our scope in catalysts, moving into consolidation of the precious metals products business is one of the areas where we certainly would have scope for consolidation, for buying direct competitors." ■

Altana Q2 Ebita €69.7 Million, Up 10%

Altana said second-quarter operating profit rose 10% to €69.7 million, coming in below expectations as demand for its specialty chemicals products was tempered by slowing economic growth. It also revised its guidance lower. Analysts had predicted an operating profit or Ebita of €70.64 million, based on the average of 12 estimates collected by Thomson Financial News partner dpa-AFX. The German maker of pigments and coating additives said net profit dropped 11% to €33.9 million. Net income still exceeded the €33.09 million expected by analysts. Quarterly sales advanced 1% to €359.2 million, below consensus of €364.97 million. The company hived off its pharmaceuticals business in 2006 to focus on speciality chemicals. Altana also lowered its full-year sales target for the second time, saying the economic slump in the U.S. has started to seep over to Europe. It now expects 2008 sales to reach €1.41 billion to €1.45 billion, below its previous target range of €1.42 billion to €1.47 billion. The 2008 Ebita figure is set to increase to between €260 million and €280 million, Altana added. While the lower limit of Altana's Ebita guidance range remained unchanged, the upper limit is lower than the previous €290 million. The outlook is based on an average exchange rate of $1.55 per euro in 2008, above previous expectations of $1.50, Altana said. Pretax earnings are likely to fall below year-earlier levels because Altana no longer receives income from the financial investment of proceeds from the sale of its drug unit, according to the statement. ■

Commerzbank to Sell Linde Stake

Commerzbank is seeking to sell its stake of almost 10% in German industrial-gases specialist Linde., manager magazin reported, citing unspecified sources. The proceeds from the stake, which has a market value of about €1.4 billion, could help Commerzbank fund its takeover its rival Dresdner Bank from Allianz. Commerzbank announced its €9.8 billion takeover of Dresdner bank at the end of August. ■

Kemira and Rockwood Close JV

The formation of joint venture between Kemira and Rockwood Holdings has been completed. Creation of the new company is part of the implementation of Kemira's new strategy. The deal will create one of the world's leading producers of specialty titanium dioxide pigments, according to the company.

The joint venture combines Kemira's titanium dioxide business and Rockwood's titanium dioxide pigments and functional additives business. The joint venture, which had pro forma revenues of approximately €560 million for 2007, is headquartered in Duisburg, Germany. Wolf-Dieter Griebler, who has been president of Rockwood's titanium dioxide business, will head the new joint venture. It is 61% owned by Rockwood and 39% owned by Kemira. The new company, which operates as Sachtleben, is a producer of specialty titanium dioxide pigments for the synthetic fiber industry, specialty titanium dioxide pigments for packaging inks and specialty titanium dioxide grades for the cosmetics, pharmaceutical and food industries. ■

Borealis And MCC Agreement

Borealis and its U.S. subsidiary, Borealis Compounds, have entered into manufacturing and supply agreements with affiliates of Mitsubishi Chemical Corporation (MCC) to improve the supply of polypropylene compounds (PP/CP) to the automotive industry in Europe and the U.S. The agreements are intended to aid all companies in meeting demand and enhancing the competitiveness of their automotive customers, through localized production and supply of high quality, high-performance PP/CP materials. ■

Perstorp Aquires Isocyanate

Rhodia and Lyondell Chimie, a subsidiary of Lyondellbasell Industries, announced that they completed the sale of their Isocyanates businesses to the Perstorp Group. This divestment includes Rhodia's aliphatic Isocyanates activity and Lyondell's aromatic Isocyanates business. These activities are essentially based in Pont-de-Claix, France, and Freeport, USA, and together employ around 680 people. ■

Bayer CropScience to Invest €3.4 Billion in R&D

Friedrich Berschauer
CEO, Bayer CropScience

Bayer CropScience said it plans to invest €3.4 billion in research and development through 2012 to strengthen its grip on the near €50 billion euros agrochemicals and seeds industry.

"We want to secure an above-average share of this market growth," Bayer CropScience Chief Executive Friedrich Berschauer said in a statement.

The company, the world's biggest supplier of insect killers, said it has also set a new goal to bring 10 new compounds with combined peak sales potential in excess of €1 billion to the market between 2008-2012. Bayer CropScience tops industry spending for research and development. New compounds often bring more lucrative margins than older products.

In addition, Bayer CropScience said its initial sales target of €2 billion from new compounds – set in 2000 – could now be reached in 2009 instead of 2011. Bayer CropScience, like its top agrochemicals rivals, is thriving on strong commodity prices that have led farmers to use more crop-protection chemicals to boost output. Bayer CropScience, which is also a top player in fungicides and herbicides, also said it plans to raise its prices again in the second half due to rising energy and raw material costs. ■

Akzo Nobel's Outlook Cut to Negative On Weakening Demand Standard & Poor's Ratings Services said it cut its outlook on Netherlands-based coatings and chemicals producer Akzo Nobel to negative from stable and affirmed the 'A-' long-term and 'A-2' shortterm corporate credit ratings on the company. The outlook revision reflects S&P's concerns over the softening demand the company is facing in the U.S. and Europe and the company's ability to pass on rising input costs and the resultant impact on credit protection ratios, the ratings agency said. S&P also said Akzo continues to benefit from its dominant position in many of its markets and a portfolio of key brands. However, it added that executing both volume and price increases, given the current macroeconomic conditions, will prove challenging and a dilution of profitability is likely in the coming quarters. The negative outlook reflects the expectation that operating performance and funds from operations (FFO) generation will continue to be under pressure due to weakening demand combined with ongoing raw material pressures, the ratings agency noted. ■

Chemtura's Outlook Negative, Ratings Affirmed Standard & Poor's Ratings Services removed Chemtura Corp.'s ratings from negative watch and assigned them a negative outlook. It also affirmed the company's 'BB' corporate credit and senior unsecured debt ratings. "The rating actions incorporate the company's improved earnings performance for the second quarter of 2008 compared to the similar period of the prior year and our expectation that credit measures should maintain an improving trend," S&P said. The ratings on Chemtura incorporate some vulnerability of its operating results to competitive pricing pressures, raw material costs and cyclical markets. They also reflect weak cash flow protection measures as a result of poor profitability in certain businesses, the ratings agency added. ■

France's Air Liquide Short-Term Rating Outlook Raised to Stable Moody's Investors Service changed its outlook for the 'Prime-1' short-term rating of Air Liquide to stable from negative. "Air Liquide's interim report shows that the company is well on track achieving the targets of its Alma-program which strives for increased capital productivity, cost efficiency and enhanced growth. Against this background and considering Moody's positive outlook for the industrial gases industry combined with the company's excellent liquidity, Moody's has moved the outlook to stable," the agency said. ■

Umicore H1 Rebit Rises 8.2% Umicore said its first-half recurring Ebit rose 8.2% to €215.4 million from €199 million last year, driven by precious metal services and advanced materials. Revenues excluding metal rose to €1.13 billion from 965.2 million. Turnover rose to €4.95 billion from 4.18 billion. The group said it expects full-year recurring Ebit to be between €385 million and €405 million. ■

Ciba Downgraded to 'BBB-' On Lower Profitability; Outlook Negative Standard & Poor's Ratings Services lowered its long-term corporate credit rating on Switzerland-based specialty chemicals producer Ciba Holding to 'BBB-' with a negative outlook from 'BBB' due to the "significant" deterioration in the company's profitability and cash flow generation and its continuously shareholder-friendly dividend policy. S&P said Ciba's announcement of significant strategic portfolio changes and a focus on growth, including acquisitions, which could lead to a further deterioration in credit quality, were also factors behind the downgrade. "The negative outlook reflects the risk that Ciba's operating performance will continue to be weak and the new strategic plan could further weaken the company's balance sheet and credit protection ratios so that it fails to achieve adequate levels for the 'BBB-' rating," the agency added. S&P however affirmed the company's 'A-3' short-term rating. ■

Merck KGaA Eyes Takeovers

Merck KGaA is "intensively" considering acquisitions to add to either its pharmaceuticals or its chemicals division, Chief Executive Karl-Ludwig Kley told Handelsblatt in an interview. "But we won't run around panting, just to produce headlines," he said. Kley said the chemicals division, which makes liquid crystals and specialty chemicals, is "part of our DNA," indicating he rules out a sale of the business. "The combination of pharmaceuticals and chemicals at Merck is not up for discussion," he said. Bernd Reckmann, the head of Merck's chemicals division, said the unit could benefit from takeovers in order to achieve targeted sales growth of above 5%. ■

Eastman Licenses Reduced Sulfur Start-Up Technology

Hydrogen Energy International (HEI) and Eastman Chemical Company announced they have signed a definitive agreement for Eastman to license to HEI its proprietary Reduced Sulfur Start-Up Technology. This patented technology allows for the operational startup of gasification reactors using a sulfur-free fuel to mitigate a source of sulfur emission during startup events.

The licensing agreement is part of Hydrogen Energy's plan to develop a commercial project in California that generates low carbon hydrogen power from an integrated gasification combined cycle (IGCC) system with carbon capture and storage. Terms of the agreements were not disclosed. ■

Dow Launches University Partnerships

Dow Water Solutions, a business unit of the Dow Chemical Company, has reached a multi-year joint development partnership with Virginia Polytechnic Institute and State University (Virginia Tech) and University of Texas at Austin (UT). Under the agreement, Dow Water Solutions will collaborate with Virginia Tech and UT on the research and development of oxidation-resistant reverse osmosis membranes.

This joint partnership will tackle a technical challenge in the water desalination industry, developing oxidation-resistant, or chlorine-resistant, reverse osmosis membranes that will simplify the water treatment process and convert highly-contaminated waters into potable water sources. ■

Stepan And Nalco JV

Stepan and Nalco Holding have announced the formation of a joint venture to globally market custom engineered chemical solutions for increased production of crude oil and gas from existing fields. The rapid increase in the price of crude oil has created renewed interest in enhanced oil recovery (EOR) technologies.

Operating under the Tiorco brand, the joint venture provides an integrated sales and service channel that benefits from Nalco's extensive reach in global upstream energy markets, its recently acquired EOR polymer and reservoir expertise and Stepan's global surfactant technology and manufacturing capabilities. Tiorco will also serve as a primary sales and engineering service channel for Nalco's BrightWater Reservoir Efficiency Technology. The joint venture will be equally owned and controlled by Nalco and Stepan. Most of the value generation will be captured directly by the two partners. ■

chemanager-europe@gitverlag.com

EU Calls UK Biofuel Report 'One-Sided'

The British government said it would slow the expansion of biofuels following a report, which found they could increase greenhouse gas emissions and contribute to food price rises. Transport Secretary Ruth Kelly said a review had not recommended a temporary halt to the use of biofuels, which are sourced from organic materials such as palm oil and sugar beet. She said that while biofuels had the potential to cut carbon emissions there were "increasing questions" about them and she agreed with the report's recommendations to "amend not abandon" the government's policy. The review examined the indirect effects of biofuel production such as land use change and the effect on food prices. It called for biofuels to be introduced more slowly than first planned until controls are in place to prevent higher food prices and land being cleared of forest or agriculture in order to grow fuels. The study into the indirect effects of biofuels warned current policies may cause greenhouse gas emissions rather than savings and also found biodiversity could be reduced.

The European Commission slammed the report, calling it "one-sided." Energy commissioner Andris Piebalg's spokesman, Ferran Tarradellas Espuny, told reporters the report seemed to ignore a general consensus there is enough land for bioenergy and to meet growing demands for food. He said less than 10% of biofuels production comes from new land, with more than 90% coming from using existing land. The spokesman said the EU executive's target of 10% biofuels' use by 2020 requires an increase in commodities for biofuels consumption of 4 million t/y. The current global consumption of cereals is 2,200 million t/y, he said.

"We do not understand how an increase of 4 million t/y could drive the price of the market of 2,200 million tons," he said. "Only 2% of arable land in the EU is devoted to biofuels. (Our) future policy can hardly have any impact on food prices as it was only adopted on Jan. 23 and has not (yet) been approved," he added. The report warned current biofuels policy could push up grain prices in the EU by 15%, sugar by 7% and oil seed by 50%, while millions more people elsewhere in the world could be pushed into poverty. The review estimates that an extra 10.7 million people in India could be plunged into poverty, while hundreds of thousands of people in countries such as Kenya, Malawi and Bangladesh could be affected by food price rises caused by biofuels. Gallagher said the figures did not take into account the impact of climate change on poor people if biofuels were not introduced. The Gallagher report recommends biofuel production should target idle and marginal land, and the use of second generation biofuels, which use waste parts of plants for energy to avoid land use change and reduce competition with food production. Marginal and idle land could include set-aside land in Britain and Eastern Europe where farmland has fallen into disuse, the report's co-author Greg Archer said. Oxfam welcomed the caution expressed in the report, but said it should have gone further and recommended a complete moratorium on mandatory targets because biofuels were not a "magic bullet" for climate change.

European Business Lobby Group Calls for Review of EU Biofuels Policy

The European business lobby group Business Europe has called for a review of the European Commission's biofuels policy.

"Business Europe considers that the current high food prices give additional weight to its call for the EU to reconsider the 10% target for biofuels in transport," Business Europe President Ernest-Antoine Seilliere said in a letter to Slovenian prime minister Janez Jansa, whose country holds the rotating EU presidency. The commission has set a target that biofuels will account for 10% of all vehicle fuel by 2020, as part of a wider package of measures to combat climate change. The first generation of biofuels has been criticised for using up crop land needed to grow food for humans and animals, and for deforestation. The commission has defended its policy, however, reiterating that it will not change the target. Business Europe also said the commission's "ambitious but so far unilateral climate change strategy" risks increasing competitive disadvantages in Europe. It calls for energy-intensive industries exposed to international competition to receive 100% free allocations under the European Emissions Trading Scheme.

E.on Ruhrgas to Close Deal on Gazprom Gas Field

E.on Ruhrgas unit management board chairman Bernhard Reutersberg said his company hopes to conclude talks with OAO Gazprom over the acquisition of a 25% stake in the Yuzhno-Russkoye gas field by the end of this year, Russia's Vedomosti daily reported. Separately, sources at both companies also told the newspaper that E.on has discussed exchanging part of its 6.4% stake in Gazprom for the minority share of the Siberian gas field. However, Reutersberg told the newspaper that no such discussions were underway. Gazprom deputy chairman Alexander Medvedev also said he was not aware of this version of an asset swap. E.on in 2006 agreed to acquire the minority stake in the gas field, but the two sides have been unable to close the deal because of ongoing disagreements over which assets Gazprom will acquire from the German utility in exchange for the stake. Germany's BASF already agreed in October 2007 to exchange a stake in its Wingas gas distribution company for 25% minus one share of Yuzhno-Russkoye. The field has reserves of more than 700 billion m^3, and annual output is expected to reach up to 25 billion m^3. The companies plan to ship Yuzhno-Russkoye's gas to western Europe via the Nord Stream pipeline which is currently being built by Gazprom, E.on, BASF and Gasunie.

Dupont and Danisco's JV Cleared by EU

The European Commission said it has cleared Dupont and Danisco unit Genencor's proposed ethanol joint venture. The joint venture will develop and commercialize cellulosic ethanol, or fuel derived from non-food sources. The companies plan to invest $140 million in the U.S.-based venture over the next three years and hope to have a commercial-scale demonstration facility operating by 2012. The venture, to be called DuPont Danisco Cellulosic Ethanol, will focus initially on making fuel from the leaves and stalks of corn and from sugar cane bagasse, the remnants of sugar cane stalks after they are crushed for juice. The company plans to eventually explore fuel derived from wheat straw, as well as a variety of energy crops and other biomass sources.

Shell and Iogen Accelerate Biofuel Project

Anglo-Dutch oil group Royal Dutch Shell and Canadian biotech firm Iogen Corp have agreed to extend their commercial alliance to accelerate their biofuel project involving cellulose ethanol. The agreement will allow Shell to make a significant investment in the technology development with Iogen Energy Corp and increase its 26.3% stake in the company to 50%. Shell bought a stake in Iogen Energy in 2002. Cellulose ethanol is made from the non-food portion of renewable feedstocks such as cereal straws and corn stover and can be used as a fuel for cars.

New Kids on the Block

Future of the Chemical and Petrochemical Industry in the CEE Region

Industry Dynamics – What role do the 12 new member states play for the European Chemical industry?

Revenues of the EU-25 chemical industry (without pharmaceuticals) reached €455 billion in 2005, which represented 30% of global revenues (€1,496 billion). Therefore, the EU-25 countries are the biggest world manufacturer – with a 30% share of the global market.

The most important sectors of the chemical industry are: petrochemicals, basic inorganic chemicals, polymers, chemical specialties and consumer chemicals. Petrochemicals and basic inorganic chemicals are produced in large volumes and the industry supplies them to other processing industries. Together with polymers they generate approximately 57% of overall revenues. Chemical specialties are produced in smaller volumes and very often for a special use. In total they represent 29% of overall revenues. The last product group – consumer chemicals, include soaps, detergents, cosmetics and perfumeries and their share of revenues – contributes the remaining 14%. In recent years the highest dynamics of revenues and profits has been noted in the sector of basic chemicals, despite a high increase of basic raw material prices. The main reason was an enormous demand in Asia, especially in China.

Four EU member states generate almost two thirds of revenues. The biggest manufacturer is Germany (share of 26.7%), followed by France (13.1%), Great Britain (12.2%) and Italy (11.2%). These big four contribute approximately 62% of overall revenues and together with Spain, Netherlands, Belgium, and Ireland results in 88%. Poland has the biggest share from new member states (1.9%), ahead of the Czech Republic (1.2%) and Hungary (0.9%). This apparently shows that the production of chemicals is concentrated mainly in North-Western Europe. More than 10 thousand people are employed in chemical and pharmaceutical industries in 50 of 116 regions of EU-25. Chemical industry in the 12 new member states is structurally different from EU-15 and the ratio of basic chemicals is remarkably higher. At the same time these countries have altogether a considerable foreign trade deficit. Therefore it is possible to assume that the potential of these countries has been considerably unused until now, in spite of a dynamic growth of production in the industry over recent years. Restructuring and modernization of the industry in the new member states has not yet been completed in a number of cases.

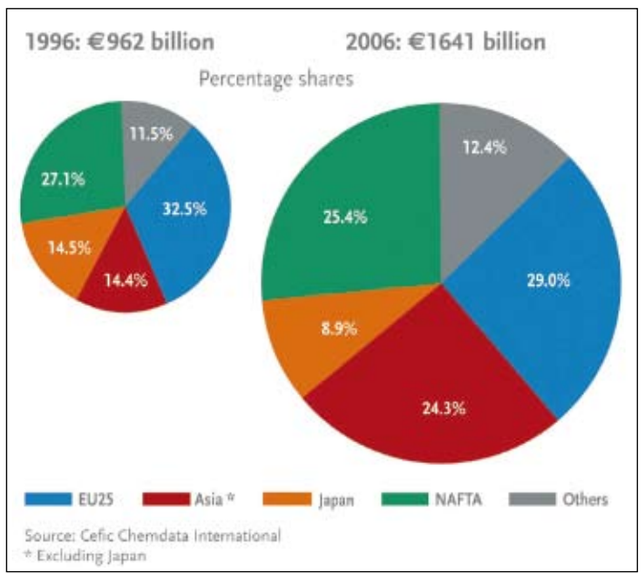

Fig. 1: World chemicals sales in 1996 and 2006 (* Excluding Japan).

In this respect it is also necessary to emphasize a great potential of so-called new countries in the field of consumption. These days the consumption of chemicals in the EU 12 reaches only approximately 20–25% of the EU 15 consumption. This is a great challenge and a chance.

Just 30.3% of chemical and pharmaceutical industry production is sold to final users, the rest is supplied to other downstream industries, services and agriculture. The chemical industry then, more than other manufacturing industries, creates economic activities in other sectors. In opposition to the public perception, SMEs represent the decisive part in the European chemical industry: full 96% of chemical businesses in the EU have less than 250 employees and they take 30% of overall revenues and 37% of employment, whereas in some sub-sectors it makes more than 50%. The importance of SMEs further consists in the fact that decisive inventions and developments are usually born in smaller companies and such companies also play a leading role in transferring innovations along the supply chain towards industrial users and consumers.

Energies and Raw Materials as Decisive Factors of Competitiveness

The chemical industry uses energy-producing raw materials not only as a source of energy but also as basic materials for its final products. The policy of climate change control focused on the reduction of green house gas emissions is consequently logically directly connected with the energy policy. Both have a strong and indirect impact on energy prices and utilization of energies.

Crude oil is the most important raw material and an important source of energy for the European chemical industry. Europe does not have any structural disadvantage in comparison with other world regions due to an oil-based production as the global oil market limits price differences. However, since new investments are directed mainly to regions with expected rapid market growth, Europe often has less modern plants of a size, which is nowadays normal in other regions.

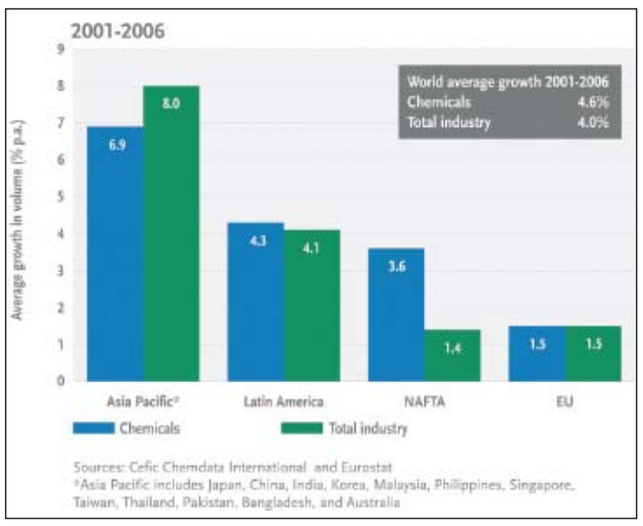

Fig. 2: International comparison of production growth of the chemical industry during 2001 – 2006.

Production of ethylene, as the most important unit of the petrochemical industry is considerably more expensive when based on oil than the production based on ethane, implemented currently in the Middle East. This is also the main reason for an investment boom in building ethylene units in that area. Availability of ethane is however limited and consequently also the impacts of production based on this gas on global market prices are, and will remain, limited.

In contrast to the oil situation, Europe has a disadvantage in case of natural gas. The transportation of gas depends on gas pipelines or on sea transport of liquefied natural gas. Both possibilities are costly and hence the infrastructure is limited. This fact, together with trade restrictions in case of number of suppliers and distributors, explains substantially large differences in natural gas prices in various world regions. Improved functioning of effectively liberalized gas market, at least within the Union, as well as ensuring reliable import of gas for competitive and undistorted prices from neighboring regions (Russia, Algeria and Libya) has an extremely high importance for fundamental parts of the industry (e.g. ammonia production).

In the case of some productions, for example electrolytic chlorine and alkali production, costs of electrical energy can account for up to 60% of the overall production costs. Strong growth of electricity prices in recent years has already influenced investments into chlorine and alkali production in Europe, which on top of this passes through a costly transition from a mercury-cell electrolysis to membrane technology. Expected further growth of electricity prices in coming decades could seriously endanger a competitiveness compared with other regions, where new large capacities are built. The situation is made difficult by the fact that chlorine, as the main output of this industry branch, is difficult to transport over long-distance due to its hazardous character. This substance, however, stands at the initial point of a long and wide value chain within the chemical industry. Primary possibilities are long-term contracts with electricity producers and an increase of own production. Further development on the electricity market, also as a result of the climate change policy, will have a decisive influence on the future of this important part of the European chemical industry.

▶ Contact:
Ladislav Novák
Association of Chemical Industry
of the Czech Republic (SCHP ČR)
Praha, Czech Republic
Fax: +420 266 793 580
mail@schp.cz
www.schp.cz

World's First CO_2 Capture Plant

Germany's Secretary of the Chancellery, Thomas de Maizière, and Prime Minister of Brandenburg, Matthias Platzeck, together with Swedish Minister for Higher Education and Research Lars Leijonborg officially launched the commencement of operations at Vattenfall's pilot unit for a coal-fired power plant with CO_2 capture, the world's first of its kind.

The pilot unit, which has a thermal capacity of 30 MW, was constructed over the last 15 months at the "Schwarze Pumpe" plant premises in the Lausitz region in the State of Brandenburg, Germany. Vattenfall has invested approximately €70 million in the construction of the unit. The carbon dioxide produced in this pilot plant will not be released into the atmosphere, instead it will be separated, liquefied and further treated for long-term secure underground storage.

Vattenfall's CEO and President Lars G. Josefsson announced on the occasion of the official commencement of operations that "The pilot unit is a milestone on the way to converting coal into electricity that is almost free of emissions. It represents the first ever transition from lab to reality. Our intention is to make a decisive contribution to global climate protection." ■

Akzo Nobel Sells Decorative Paint Brands

Dutch Akzo Nobel, the world's biggest paints producer, said it had reached final agreement to sell its Crown Paints brand in the UK and Ireland as well as two Belgian brands. Crown Paints will be sold to private equity company Endless, while French coatings producer Rieu Investissements will buy its DeKeyn and Linitop brands, Akzo Nobel said in a statement. The sale of the brands was a condition for European approval of the £8 billion acquisition of Britain's Imperial Chemical Industries (ICI) earlier this year. The deals, of which no financial details were disclosed, are expected to be finalized in the third quarter, Akzo said. ■

BASF to Sell More Of Styrenics Business Than Planned

BASF said it plans to sell more of its styrenics business than initially planned, also putting the production of styrene copolymer on the auction bloc. BASF also said in a statement it will reorganize its global styrenics operations into independent subsidiaries to be set up in January 2009 while it continues its year-long search for a buyer. The styrenic commodities and copolymers units have a total staff of about 1,600 and generated sales of about €4 billion in 2007, according to the statement. Copolymers accounted for about €500 million in sales, a spokesman said. In February, the company said it was in negotiations with one potential buyer. In June, it said, however, that it would be unable to keep its initial deadline to clinch a deal in the first half. BASF has described the divestment as inevitable because its standard styrenics will not have enough of an edge over rival products in the long run. Styrenics are plastics with applications including packaging, car parts, appliance parts and mobile phone casings. Total plastics made up €13.5 billion, or 23%, of the group's sales last year. ■

Symrise Poised To Buy Two Companies This Year

Symrise has a shortlist of 10 possible acquisition targets, two of which are "hot" candidates he aims to buy this year, Gerold Linzbach, chief executive of the German maker of scents and flavors, told Euro magazine. Symrise "always has about 10 companies on the radar screen" to add new technologies and to expand geographically, he said in an interview to be published in Euro's September edition. Linzbach also confirmed the company's goal for full-year sales to increase 6% to 7% and Ebita to grow 6%, both adjusted for currency swings.

Gerold Linzbach
CEO, Symrise

Evonik Makes Acquisions

Evonik Industries has signed a contract for the sale of its U.S. and Canadian cyanide activities with Oaktree Capital Management. The cyanide business constitutes a part of the CyPlus Group owned by Evonik. Financial terms were not disclosed. The transaction is subject to approval by the regulatory authorities. The transaction comprises of CyPlus Group's business in the U.S. and Canada dedicated to the gold-mining industry. It includes a 50% share in Cyanco, a joint venture with Utah-based Nevada Chemicals, a publicly traded company and two subsidiaries of CyPlus–CyPlus Canada and CyPlus Corporation. All of CyPlus's activities at the sites in Hanau and Wesseling, Germany, and in Antwerp, Belgium, will remain part of Evonik's hydrogen cyanide network and will continue to successfully operate in their current capacity, with a sharpened focus on emerging markets.

At the same time, Evonik has stepped up its activities in the field of lithium ion batteries. Evonik has doubled its stake in Li-Tec Battery to 40%. In the last year, the headcount at the Kamenz site has tripled to over 100. If market growth forecasts prove correct, the number of jobs will increase more than tenfold. ■

Brenntag Buys Dutch Chemical Distributor C.N. Schmidt

Brenntag said it has acquired chemical distributor C.N. Schmidt, headquartered in Amsterdam, Netherlands. Founded in 1921, C.N. Schmidt is focused on the distribution of specialty chemicals in the Netherlands and in Belgium. The company acts as a distributor, agent and logistics service provider with a focus on the food, pharma, rubber and water treatment sectors. Brenntag Nederland, located in Dordrecht is a leading distributor of chemicals in the Netherlands with more than 240 employees. Brenntag recorded 2007 external sales of €6.7 billion. ■

BP Settles Russia Dispute

BP has signed an agreement aimed at solving the dispute over control of its Russian venture TNK-BP. Robert Dudley, chief executive of TNK-BP, will step down as part of the agreement with the Russian billionaires that control 50% of the business. Three independent directors will also be appointed to TNK-BP's board. Dudley's departure had been pivotal in the power struggle between BP and the Russian investors in the venture, which accounts for 25% of BP's profits. The memorandum of understanding also includes the option to list up to 20% of the venture on international markets.

BP has offered a Russian-speaking candidate for the post, with extensive Russian business experience. The Russian shareholders had accused BP of running TNK-BP like a subsidiary and Dudley of favoring the British shareholder. BP chairman Peter Sutherland said that the deal, to be finalized over coming months, would relieve recent tensions. ■

German Chemical Industry Up

The German chemicals industry posted a 5.5% year-on-year increase in first-half revenues as companies managed to pass some of the spiralling raw-material prices along to customers. The advance resulted from a 3.0% increase in output volume and a 3.5% rise in producer prices, the German chemical industry association (VCI) said in a statement. Demand from abroad grew faster than domestic demand and the strong euro and the weakness of the U.S. economy have so far not weighed on exports, the association said. Looking ahead, the group said it now expects the industry's full-year sales to rise 5.5% in 2008, compared with an earlier forecast of 4.5%. ■

Akzo Nobel Poised for Takeovers

Akzo Nobel said it will focus on integrating Imperial Chemical Industries (ICI) this year but will be prepared to buy larger companies again in 2009, Chief Executive Hans Wijers told German daily Boersen-Zeitung in an interview. "Larger acquisitions are rather unlikely this year but there will be no limits thereafter, particularly not in the industrial-coatings and specialty chemicals markets," the CEO said. The Dutch company is seeing keen interest of potential buyers, mainly among strategic investors, in ICI's specialty starches business, which Akzo is trying to hive off, but Akzo is under no time pressure to push for a sale, Wijers said. While many buyout firms are no longer in the market, the size of the potential transaction would still be "doable by an experienced private-equity manager,"he said in the interview. ■

Hans Wijers
CEO, Akzo Nobel

BASF CEO Sees End to Price Bubble

BASF Chief Executive Officer Jürgen Hambrecht said the current surge in the oil price represents a bubble stoked by financial investors and that fuel prices could soon plunge. "We currently have rolling bubbles from the financial industry," Hambrecht told analysts at a presentation in London. "Rolling bubbles sometimes burst. This is a bubble on the oil price," he said, adding that fossil fuel has increasingly become a financial product. BASF, the world's largest chemical company which currently derives more than 40% of operating income from its Wintershall oil and gas subsidiary, lifted its estimate for the average oil price in 2008 to $120 per barrel, up from a previous estimate of $90. The German company also published five-year forecasts of $100 per barrel. ■

Jürgen Hambrecht
CEO, BASF

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Challenges in the Chemical Supply Chain

Rising Transport Costs Call for Supply Chain Optimization

Road Transportation – On a worldwide basis, the forwarding and logistics business speeds along on the fast lane. There is hardly any other economic field featuring such vivid movement as is found in this segment, and all indicators seem to show that it will remain this way in the future. Production and the economic changes linked to it are more and more globalized, whereas technology and product cycles are getting shorter and process chains are getting more and more complex.

Michael Kubenz
Managing Director
Kube & Kubenz

Logistics is developing with a high innovation speed whose driving force for all national economies in the world can no longer be ignored. The progressive division of labour, outsourcing and globalisation generates an enormous growth with the demand for the transportation of goods. According to present estimations regarding the European Union, an increase of 50% goods traffic and 35% passenger traffic is to be expected by 2020. This means that 70 million passenger cars and 1.5 million heavy goods vehicles (HGV) will crowd Europe's roads. In addition, the seaports which are already cramped today are expected to face a doubling of their container handling.

The facilitation of goods and persons mobility in a sustainable way is one of the most important issues facing today's society. Only if we manage to meet this challenge, will we be capable of permanently securing growth, innovation, value creation and employment. In any case, Europe cannot afford to fail here.

Development Of Transport Costs

In recent months, there have been considerable changes with the individual types of cost and one can identify three essential cost drivers.

Firstly, there are personnel costs, in particular driver cost. In Europe, there are new regulations on working and rest periods for drivers and a new law on driving personnel. The implementation of the EU directives on working periods, for example, reduces the weekly working time of drivers from an average 56.5 hours to 48 hours – a 15% reduction.

Consequences of the new legal provisions include organisational, infrastructural, social and particularly financial impacts on day-to-day practices. A study by the Fraunhofer Institute, by order of the German Association for Freight Forwarding and Logistics, shows that the new law causes additional costs of €4.7 billion for Germany alone. This is a 9.4% increase of total transport costs, with the cost increase being generated by additional assignments of drivers, additional drivers and an increased number of vehicles.

In order to compensate this loss of capacity, we are in need of approximately 7% more drivers – Germany alone will suffer from a lack of 50,000 drivers in the coming years. However, this lack of driving personnel is no longer a national but a European problem.

Another essential factor pushing up the cost with road transportation is the Diesel price. In the course of last year, the Diesel price grew by approximately 25%. Having a share of 26% of the total costs, the fuel costs alone contributed to an increase of 6.5% in total costs.

The third important cost-driver are the contribution systems in Europe. As more and more countries start introducing road charge systems, and those countries already implementing such systems continuously increase the charges, partly at a very drastic rate, transport costs rise. In Germany, for example, the average road charge amounts to 13.6 cents per km to constitute a cost burden of €13,600 with an annual mileage of 100,000 km on our motorways. The European Commission threatens to allow for another dramatic increase in road transport prices as a result of the planned charging of external costs.

Taking all this into account, it is safe to say that we will have to be prepared for strongly growing transport costs as all three cost drivers – driver cost, energy cost and road charges – clearly show an upward trend.

"We will have to be prepared for strongly growing transport costs."

Supply Chain Performance

In view of the cost development in Europe, the optimisation of the supply chain is an essential task to be dealt with. It requires the application of the optimum combination of all carriers in the logistics chain.

With goods traffic in Europe predicted to grow by approximately 50% by 2020, all carriers will enjoy considerable growth rates with quantity. Road transport is expected to remain being the dominating carrier by holding an estimated share of 45% in 2020, followed by maritime traffic with 41% and railway traffic with 8%. If only the domestic carriers, i.e. road, railway and inland waterway transportation are taken into account, the share of road transportation in the whole domestic transport performance is estimated to amount to approximately 80%.

In view of these forecasts, there are five essential fields requiring action in order to sustainably assure the mobility of goods transportation in Europe in the future:

- Infrastructure
- Intermodal transportation
- Modern telematics systems
- Innovative vehicle concepts
- Reduction of loading and unloading times

Infrastructure

Today's transport networks constitute the physical infrastructure for the European domestic market. Unfortunately, the infrastructures in Europe are completely overloaded, which causes negative consequences for the national economies and the environment. The overload situation is not only found with road infrastructure but also with the infrastructure of railways, seaports and airports. By 2020, it is expected that 60 big-size European airports located will be heavily overloaded.

What we need are massive investments in transportation infrastructure. These infrastructure investments have been reduced in all EU member states and at present amount to less than 1% of the GNP. This trend must be reversed and more money must be made available for the upgrading and expansion of the infrastructure, also by making use of alternative non-governmental, i.e. private financing sources.

"What we need are massive investments in transportation infrastructure."

Intermodal Transportation

In order to reduce the overload, in particular of the road infrastructure, it is necessary to increase intermodal transportation in the fields of railway and short sea shipping. However, this increase will not be achieved by means of a state-controlled and merely fiscal-oriented policy regarding contributions and transportation. We need more intermodal quality offers meeting the market demands, in particular with regard to punctuality in order to allow for the relocation of transports.

Modern Telematics Systems

It is impossible to improve the supply chain without an intensified use of new information technologies and modern telematics systems. These technologies allow for an essential improvement of the fundamental economic and ecologic conditions of goods transportation in Europe.

Innovative Vehicle Concepts

Shipping space is scarce, and so is traffic space. One solution to the problem is the implementation of innovative utility vehicle concepts, i.e. the EuroCombis. Having a length of 25.25 m and a greater shipping volume, the EuroCombis offer the chance to transport more goods with reduced traffic and thus less fuel consumption and reduced emissions. Simultaneously, they feature the latest technology and the best safety equipment available.

A study in Germany has proven that the higher number of axles with this type of vehicle helps to reduce the road surface load caused by heavy goods vehicles by approximately 30% per ton and to decrease emissions by up to 24% per ton. Thus, we should welcome the European Commission's efforts to deal with this topic by ordering a study on a possible revision of the Directive 96/53 EC on dimensions and weights.

Reduction of Loading and Unloading Times

We must consider it our principle goal to minimize the unproductive standstill times. In this context, we will have to co-operate with the chemical industry to optimise the processes, including the time slot indications for heavy goods vehicles, the extension of these slots and the use of unloading teams. Precious driving time wasted on loading and unloading can be substituted by more cost-effective personnel made available on site. The drastic cost effects of the new law on driving personnel can only be cushioned with the help of new agreements on processes.

"The optimisation of the supply chain is an essential task."

Future Challenges

In principle, I am of the opinion that we will continue investing in the process quality of the chemical supply chain. In the future, we will undertake considerable endeavors to continuously grant further job training to our employees. In addition to the obligatory advanced training for drivers to be started in Europe from September 2009 and providing 35 hours of advanced training measures within a five-year period, we as service providers will invest in driving safety training and eco drive training.

After the 9/11 attacks, it was not only the U.S. who saw the need to develop measures to guard against potential terrorist acts, particular with goods transportation. Although in a very abstract way, Brussels admits that each member of a supply chain holds a potential risk. It is true that the Brussels draft on the safety improvement of European, national and regional supply chains has been put on hold due to the pressure exerted by trade and industry, but the supply chains connecting us to third party countries still remain affected.

Trade and industry have to contribute to the prevention of such dangers, too. The forwarding and logistics branch is well aware of this fact and acts accordingly. Safety is to support economic action and not to block it. Nevertheless, we will jointly have to prepare ourselves for increased expenses with regard to security measures in the chemical supply chain in the future – not least due to the continuous pressure exerted by the U.S.

We will make substantial investments in modern, safe and environmentally-friendly equipment in the future. This includes modern telematics systems and the procurement of state-of-the-art utility vehicles of Euro V standard. Additionally, we will continuously improve transport safety by employing the latest advanced driver assistance systems (ADAS) like cruise distance control and fully automatic brake and lane assist systems.

Being service providers in the field of logistics, we are more and more integrated in the production and supply processes of the chemical industry. This integration is also most favourable for us as we will only be capable of successfully meeting the future challenges regarding the optimisation of the chemical supply chain if we work together. Whether co-modality in transportation processing, answers in view of the new law on driving personnel or measures aimed at increased safety and security are concerned – we will only be able to successfully cope with the future challenges on the basis of a partnership marked by mutual trust and reliability.

Contact:
Michael Kubenz
Kube & Kubenz
Hamburg, Germany
Tel.: +49 40 23 72 07 20
Fax: +49 40 23 72 07 98
michael.kubenz@kubekubenz.com
www.kubekubenz.com

Shedding More Light

ADR 2009 Clears up Numerous Shortcomings in the Tunnel Regulations

Tunnel Regulations – They formally came into force with the introduction of ADR 2007. Nevertheless, in practice they have still not been fully put into effect.

It almost seems as if the responsible authorities are still waiting for the teething troubles to be overcome in the new legislation. The responsible UN Working Party WP15 took a major step towards achieving this goal at its meeting in November 2007. The representatives from government and industry present at this meeting agreed numerous points to ensure a more systematic and practical procedure that is to come into force in ADR 2009. The most important new development is the decision to include the tunnel restriction code in the information in the transportation documentation, thereby closing the existing information shortfall. The tunnel restriction codes for various goods have also been changed and the explanations of the tunnel categories revised. The agreed changes mean it has now become possible to adapt dangerous goods management solutions to the requirements of the tunnel regulations.

Status Quo

The new legislation was precipitated by a spate of serious tunnel accidents in the Alps. Although these by no means all involved dangerous goods, politicians called for new regulations. It was therefore decided that tunnels should be classified in five categories depending on their safety status. However, up till now this has only been on paper. While tunnels in the safest category A are not required to have any signs or identification of any kind, other tunnels in categories B to E carrying restrictions for transporting dangerous goods must display signs by Jan. 1, 2010.

Nevertheless, specific tunnel restriction codes were assigned to dangerous goods in ADR 2007. The tunnel restriction codes are allocated on the basis of the potential hazard. The classification code, compatibility group, packing group and UN number-specific properties also appear here.

The tunnel restriction codes may also be dependent on the net explosive mass and the mode of transport. This means the code may vary for one and the same substance depending on whether it is transported in a tank or as packed goods. For mixed loadings, the most restrictive code for the most dangerous good determines the tunnel restriction code of the whole shipment.

For route planning of dangerous goods shipments, the following rule applies: The lower the safety classification of the tunnel, the lower the potential hazard posed by the transported goods may be. Highly dangerous goods such as UN 1310 ammonium picrate, wetted, are therefore allocated tunnel restriction code B and from now on must only be transported through the tunnels in the safest category A. If the code begins with a B, the goods must not be transported through tunnels in categories B, C, D and E.

Paper Relevance Introduced

When ADR 2009 comes into force, consignors will be obliged to include the tunnel restriction codes in the transportation document. This is not required by ADR 2007.

ADR 2007 says nothing on the subject of how the process required for this must be carried out, i.e. how a driver obtains the required information. Nonetheless, the vehicle driver is responsible for ensuring that the tunnel restrictions are complied with. For a trucker to meet this requirement on his own initiative, he needs both the necessary knowledge and an ADR, hopefully in a language he can understand. In view of the industry's usual time constraints, this seems a somewhat illusory expectation. A correction to the regulations was urgently needed.

More Flexible Documentation for Multimodal Consignments

In its original version, a form of documentation was proposed that was too biased towards road haulage and included the tunnel restriction code in brackets directly after the packing group. Multimodal shipping papers would have led to ongoing conflict between ADR requirements and those of the other modes of transport. In the case of air freight, for example, IATA-DGR requires different information to be provided after the packing group than that required by the ADR. Instead of a tunnel restriction code, IATA-DGR first requires the type and quantity of the packages and the packing instruction number.

As ICAO/IATA and the bodies responsible for the IMDG code see no reason to change their existing, established documentation requirements, there was no other choice but to make the sequence for specifying dangerous goods information more flexible in ADR 2009. To enable multimodal documentation the tunnel restriction codes can in future also be shown in places other than those where pure ADR documentation would require them to appear.

Changed Tunnel Restriction Codes

As described, the tunnel restriction codes are assigned in part on the basis of the ADR classification codes. From a technical point of view, this procedure resulted in a whole raft of contradictions in ADR 2007. A particularly bizarre example relates to tank transportation. Although certain goods must under no circumstances be transported in tanks, they were nonetheless allocated a tunnel restriction code defined as being for packages and tanks. This affected some UN 1950 aerosols, for example. Although it is unlikely that hauliers would have used this option in practice, the ambiguity still needed to be cleared up to prevent misinterpretations. Errors of this kind have now been eliminated in ADR 2009.

WP15 also turned its attention to the explanatory texts for each tunnel restriction code. In ADR 2007, the texts were often not clear or not precise enough. The changed explanations affect all restriction codes that distinguish between tank and other modes of transportation.

A further modification relates to the code structure in ADR 2007 that used the number 1 to distinguish between tank and other modes of transportation. The symbol could easily have led to misinterpretation, leading to the conclusion that the number was a semantic signifier and not, as actually intended, merely a separator. The backslash now chosen to replace the 1 is more appropriate.

More Restrictive Tunnel Restriction Codes

Some tunnel restriction codes are more restrictively formulated in ADR 2009 than in ADR 2007. The UN Working Party based the agreed changes on technical factors. A case in point is the upgrading of oxidizing compressed gases. Because these gases present no direct risk of a large fire, the original classification only prohibited their transportation through E tunnels. However, dangerous goods experts pointed out that oxidizing gases can indirectly cause a major fire because of their fire accelerating properties. In view of this, oxidizing compressed gases have now been assigned the tunnel restriction code D/E in ADR 2009 that prohibits them from passage through both D tunnels and E tunnels when transported in tanks.

The Future of Tunnel Signage

According to a statement by the German Federal Ministry of Transport, Building and Urban Affairs on Jan. 25, it is still uncertain when Germany will start to put signs on its tunnels. In practice, this process is implemented by the responsible authorities in the individual federal states. In the author's opinion, the introduction of tunnel signs is also likely to be used as a political tool, as part of general traffic control or environmental measures. So far, no information has been provided regarding which tunnels are to be posted with signs, when and how this is to take place, and whether tunnels will be posted with signs consecutively or all at the same time within a particular area of jurisdiction. To enable hauliers of dangerous goods to plan with a sufficient degree of reliability, it would be desirable to provide an Internet portal covering the whole ADR-relevant area and offering timely clarification of the procedure, irrespective of the data.

The affected industries have been calling for a portal like this for some time, but the only information provided in the ADR under 1.9.5.3.7 is that "the restrictions must be officially announced and made generally accessible." However, if the situation does not improve considerably with regard to information, the category A tunnels that do not require signs are likely to prove particularly problematic for route planners, because, depending on the procedure of the responsible authorities, it will remain unclear whether the tunnel in question is an A tunnel or a tunnel that has not yet been posted with signage.

Mapping the ADR Requirements in SAP

Changes to regulations always pose a particular challenge for software developers. Customers expect the changed requirements to be rapidly mapped in the IT system. To do this, the providers of dangerous goods management software must constantly monitor the development of the individual regulations. The latest rulings have cleared up numerous areas and made a lot of improvements with regard to the tunnel regulations in the ADR, particularly in terms of IT support. Based on the known regulation status and the rulings, TechniData has prepared a solution for SAP EH&S that allows users to store the tunnel restriction code in the database and output it on dangerous goods documentation in paper or electronic form. This solution is already available as an SAP Note.

Contact:
Klaus Reinhardt
Technidata AG
Markdorf, Germany
Tel.: +49 7544 970 0
Fax: +49 7544 970 110
www.technidata.com

Across The Atlantic

Can European Distribution Models Benefit from Existing U.S. Transport Management Systems?

Compatibility – Transport Management Systems (TMS) have been used effectively in the U.S. and they are increasingly becoming the norm in the American freight business; but do they work as well in Europe, and what would be the effects of European freight businesses adopting the American model?

TMS are software systems designed to manage and control the progress of cargo shipments through all stages of the supply chain. They enable all parties involved to coordinate their actions and to cooperate to ensure the cargo is processed as quickly, efficiently and cost-effectively as possible.

The basic principle of TMS is ensuring that information is used effectively to underpin all supply chain operations. But simply passing information through a system is not going to be effective unless the people involved in the supply chain act upon that information. TMS provides fast and effective methods of data transfer designed to enable each link in the supply chain to communicate effectively, collaborate and thus improve efficiency.

Another important aspect of TMS is that they meet the growing demand from customers for visibility. Businesses are demanding greater visibility to maintain competitiveness and global trade has increased the need for technology to support international transportation. Distribution systems have to keep pace with fast-changing market conditions and the burgeoning information revolution; not only do these systems have to show the current position of cargo, they must also be able to give planned arrival times, condition, value and so on.

The IT World

Trends in information technology, driven by market demand, will inevitably shape the supply chain models of the future, whether operators like it or not. Factors such as customers' needs to reduce risk in procurement, and to limit or reduce growth in overheads growth, will all increase the pressure for change. It is becoming increasingly necessary to integrate all sources of information, in order to encourage the development of collaboration from each supplier in the process, which in turn will affect the behaviour of those further downstream including the end customer.

So it would seem that change to a more IT-based system of transport management is becoming inevitable, but there are differences between the American and European models which may mean European operators will resist adopting American-style TMS.

Europe for a start is a much larger and more complex market than the U.S. Traditionally, European freight companies have competed with each other much more closely – on the doorstep, almost literally – and there are a far greater number of small to medium sized operators than in the U.S. U.S. companies are larger and have tended to invest heavily in technology and more successfully than their counterparts in Europe.

TMS in the U.S. have up to now been fairly straightforward, focusing on capacity planning and the flow of equipment, but now that it is competing in the global marketplace, TMS are becoming more complex and sophisticated, and therefore possibly more appropriate for the European market. Indeed, globalisation is in any case bringing the regions far closer together in practical terms, and it seems likely and desirable that they should both adopt a common – or at least compatible – system of transport management. There can be little doubt that this would ultimately benefit manufacturers and customers in terms of increased visibility and effectiveness in managing their shipments.

Contact:
Andrew Austin
Schneider Logistics Europe
www.schneiderlogistics.com

One Size Does Not Fit All

In the Shipping of Temperature-controlled Pharma, Adaptability is Key

Right Place, On Time – More and more pharmaceuticals are now temperature sensitive, which makes shipping much more complicated than simply putting an order into a box, slapping stamps on it and sticking it in the mail.

Michael Vorwerk
Chief Operating Officer, Lifeconex

Lifeconex has high goals: to be the leading provider of temperature-controlled transportation solutions to the life sciences industry; to set new standards in the industry; and to deliver new levels of supply chain excellence. As a joint venture from industry heavyweights DHL Global Forwarding and Lufthansa Cargo, Lifeconex has been able to make a name for itself over the last several years. Brandi Schuster spoke to the company's chief operating officer, Michael Vorwerk about the challenges in the industry and what the future holds.

CHEManager Europe: Mr. Vorwerk, are there different problems to be overcome when shipping temperature-controlled pharmaceuticals domestically and globally?

M. Vorwerk: Whether domestically or globally, the challenges in shipping are the same. You can't take your eye off the high value goods or leave anything to chance and I think we have developed a model to address these requirements. With transportation for example, more than one participant in the supply chain is normally involved. There is sometimes a lack of integrated end-to-end management of many key partners. Some partners have optimized their own transportation or warehousing or trucking chain, but there are difficulties to be faced in putting the entire supply chain together.

The lack of universal standards and infrastructure for handling temperature-controlled shipments is also a hindrance. For instance, most would consider different climate zones to only be a factor in global transport. However, if we do domestic U.S. transportation, we can also encounter several different climate zones, meaning we sometimes need different package validations than we would globally. This is where an integrated, door-to-door offering is important, particularly when it comes to the handover of the product. This step is the highest-risk factor in the supply chain, and it's our specialty to manage them.

Another challenge we face is temperature monitoring and intervention management. It's of crucial importance to be able to bring the shipments into the chain in the right condition and keep them in the right condition throughout the entire process: transit, warehousing, holding, etc.

In a nutshell, it's important that the process be standardized and that the proper infrastructure is in place to manage shipments throughout the supply chain, keeping them intact, time-wise as well as temperature-wise, for our customers.

Are there any other factors that make standardization particularly important in temperature-controlled shipping?

M. Vorwerk: Because of the developing trend of more companies offering temperature-controlled transport, it is absolutely necessary to have stricter guidance. There is a lot of lip service in the transportation industry as far as service and performance are concerned. There are a lot of providers who see the opportunity of the growing market and want to get a foot in the door, but are not in the position to put their money where their mouth is. The industry needs solutions, not talk. Standardization is key, and Lifeconex is committed to for pushing it.

Standardization is not only driven by government authorities, but also by pharmaceutical associations, such as the Parenteral Drug Association or the Pharmaceutical Cold Chain Interest Group. I expect the situation to become more structured in the future, making it easier to set up the special infrastructures and needs for the transportation of temperature-controlled substances.

With the increased amount of temperature-sensitive products entering the market, how much of this has been reflected in your business?

M. Vorwerk: This is still a very strong-growing market, and that is also impacting us. The market itself has seen growth between 10–15% over the last couple of years, depending on if you're looking at either chemical- or biological-based pharmaceuticals. Many people don't realize that 20% of the world's best-selling pharmaceuticals are temperature-sensitive, which translates into a strong market with continued growth.

What are the drivers behind this strong growth?

M. Vorwerk: Every fifth drug is temperature-sensitive, and the trend is developing more and more in that direction. Regulatory authorities are also becoming more attentive when it comes to transportation, and stricter regulations are driving the need for high-quality and high-value transport. And that is exactly the niche Lifeconex is in, and we have come to benefit from the market growth over the last couple of years.

> *"Whether domestically or globally, the challenges in shipping are the same."*

And how has the increase of biologicals affected your business?

M. Vorwerk: Dramatically. Out of 20 new customers, 12 of them are from the biotech industry – which means there is an increasing need for temperature-controlled shipping here. The volume that this industry ships is not comparable yet to what the rest of the pharmaceutical industry does, but this is a growing market in terms of the need for temperature-controlled transportation.

Do you think biologicals are going to squeeze out chemical-based pharmaceuticals in the years to come, or is there a place for both?

M. Vorwerk: I think there's room and need for both. More and more pharmaceuticals are biological-based, which explains the growth on this side. However, chemical-based pharmaceuticals are still in a growth pattern as well, particularly because of the yet-to-be-conquered emerging markets, such as China and India.

What role do you see temperature-controlled pharma logistics playing in the next coming years?

M. Vorwerk: It will continue to grow strongly. We might have seen a little slowdown from some of the markets, but there is still a double-digit growth. A lot of market participants – especially in transportation logistics – have seen the need for offering solutions to the pharmaceutical world, and there are more and more companies coming to the market and offering those services. So, the market growth will certainly be shared with some more participants.

As the only life sciences industry-specific provider of integrated end-to-end temperature controlled transportation solutions, how closely does Lifeconex work with local service providers?

M. Vorwerk: We work very closely with all of our suppliers in the chain. We manage some 300 suppliers in our current portfolio. They come from a wide range of different areas, such as trucking companies, packaging firms, warehousing providers, airlines, but also ground handlers at the airport, another trucking company at the destination point, dry-ice providers, technology provider for temperature devices etc. There is much more involved than just the regular transportation process of loading goods onto an airplane.

What do you look for when choosing service providers?

M. Vorwerk: We have criteria that are applied to select our suppliers. For example, we work with about 30 airlines on a monthly basis due to network needs. But our preferred-carrier group consists of only 12 carriers that have been selected according to our very strict standards. We also use scorecards on a monthly basis to track and drive continuous process and quality improvements.

How does Lifeconex handle orders that have to be delivered into crisis areas?

M. Vorwerk: If you look at remote markets, it is always more difficult to supply service. We use regulary about 70 airports globally, and those airports make up 80% of the cold-chain business. We have already assessed 35 of them, meaning we have been there and examined their capabilities in terms of infrastructure, emergency procedures, re-icing capabilities and all the other details that we need. Our aim is to have assessed at least 55–60 of these airports by the end of the year. If anything else comes our way and we can offer a solution to the customer, then we will do it, even if it's a crisis area or a remote market with no access to one of the 70 most-frequented airports. It might take a little longer to implement that and to set it up, but we do it.

> *"There is a lot of lip service in the industry."*

In the case of war zones, we work closely with the defense and aid organizations of different countries, which have their own logistical setups. Lifeconex will not act personally in such countries, but we do assist organizations to set up the process or solutions for those areas.

How flexible is Lifeconex in terms of being able to respond to the individual needs of different companies?

M. Vorwerk: On the one hand, flexibility is a dangerous word in cold-chain management, I would rather call it adaptability, but on the other hand, that is our business. Everything we do for our customers is tailor-made. The process always starts with a detailed customer consultation, which then moves into solution development and solution implementation. We only begin the process management step once we are certain that we are able to implement a decent and manageable solution. Once that is in place, only then do we start the process management together with the customer for the shipment. There is no such thing as a one-size-fits-all solution.

Can you recall a particular situation that called for an extra amount of creativity on the part of Lifeconex?

M. Vorwerk: In Tashkent, Uzbekistan, vaccines were needed for small children. We were active from the very beginning with our logistics partners, setting up a cold-chain supply solution for an aid organization; that was something we had never done before. There was absolutely nothing in Tashkent in terms of infrastructure. We had to literally start from scratch, from convincing an airline to bring high-valuable cold containers into the market, getting them out again, and also keeping the products at the integrity that is needed for the vaccines to be delivered to the final user – who were, in this case, children in Uzbekistan.

> *"There is no such thing as a one-size-fits-all solution."*

If we have a solution that we are able to set up, we will do it – from beginning to end.

How does the cold-chain monitoring system differ from a normal monitoring system?

M. Vorwerk: It's much more than just the cold-chain monitoring and the temperature monitoring; for us, it is always about the process and the process management. When we develop a solution for a customer, each and every step is documented and signed off by all parties along the chain, including the customer and all service providers. This means we can have between 40 and 50 milestones and up to 15 different suppliers that have to be monitored in order to insure that the integrity of the goods is secured and that they are in the right condition at the right place at the right time.

And if something unexpected happens?

M. Vorwerk: The integrity of the goods must be kept – particularly the temperature – and we must have the ability to intervene should something go wrong. The fact of the matter is that each unit of product transported potentially represents a patient's life. If a problem arises concerning temperature or timing, we always have contingency plans and emergency procedures in place. In this business, you can't wait until something goes wrong to react.

All in all, it is a very complex and a very intense monitoring process compared to some logistics monitoring done in the industry.

▶ www.lifeconex.com

Hoyer Awarded Contract at Dow Rhine Center

COMPANY PROFILE The international transport and logistics company Hoyer, with its head office based in Hamburg, won a large-scale logistics contract tendered by the chemical company Dow Deutschland. In the Rheinmünster plant, Hoyer will provide a variety of logistics services with 35 employees. The location at Rheinmünster is part of the Dow Rhine Center, a joint cooperation with the plant at Drusenheim on the French banks of the Rhine River six km away.

This success is the second onsite logistics project of Hoyer for Dow in Germany. The established close partnership between the two companies in the Valuepark of Dow Olefinverbund in Schkopau will be further strengthened.

In July, Hoyer took over not only the filling of liquid and solid epoxy resins immediately after production in the plant of Rheinmünster, but also storage, order picking and dispatch. The company is also responsible for the bulk loading, IBC and drum filling of latex. Labelling, sampling and lab analyses as well as storage and loading of packed product are included in the service portfolio. Supporting the styrofoam production, the company checks all pallets received out of production and is also in charge of warehouse management, order picking, repacking and the loading of large-size pallets up to 20 m^3.

All three production units rely on Hoyer for on-time deliveries of rail tank cars containing raw materials. Dow provides a diesel locomotive, which is operated by radio remote control. Hoyer coordinates the shunting of rail cars onsite. Additional packed raw materials and supplies are delivered by truck. The company is in charge of proper unloading, sampling and storage in specified warehouses, including a warehouse for flammable liquids.

The handling for packaging material includes its administration, the call off and the disposal as well as the handling of returns. Different access authorisations to Dow's SAP system have been created in order to book incoming or outgoing stock as well as raw materials. A new warehouse management system has been installed to monitor all movement of goods until they are dispatched.

Within the scope of the logistics services Hoyer will introduce a continuous improvement process programme, monitored by an Improvement Committee of Hoyer and Dow employees. This will ensure a permanent streamlining of logistics processes and workflow in the plant of Rheinmuenster with the objective to generate annual savings possibilities.

During the tender process, Hoyer made use of its Logistics Costing Audit Tool (LAT). The LAT enables Hoyer to analyse, visualise and calculate existing as well as completely new and unknown process flows on a very detailed and accurate basis.

The conversion of process frequencies into number of FTE is based on time benchmarks for each process. These benchmarks are the result of a comprehensive research and define the length of each standardised logistics process. Taking the frequency into account, the LAT is able to calculate the overall required number of FTE for the entered process frequencies. Specific customer processes, which deviate from the standard processes, are adjusted accordingly. Hoyer has evaluated the number of equipment units required for the execution of all logistical activities within a service package.

▶ Contact:
Hoyer GmbH
Hamburg, Germany
Tel.: +49 40 21044 416
sylvelin.reif@hoyer-group.com
www.hoyer-group.com

chemanager-europe@gitverlag.com

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New Biotech Tools for Green Chemistry

Harnessing Microbes for a Cleaner Environment

A Promise for the World – Moving towards greener solutions in the chemical industry requires emphasis on innovation, standardization of production and the reconciliation of new biological feedstocks with the products that industry and consumers demand. This will require the evolution of a large set of technical and infrastructural measures. It is not clear that policy makers recognize the need to integrate green chemistry all the way from the agricultural feedstock to the finished product.

Brent Erickson
Biotechnology Industry Organization

Janet E. Nelson
Biotechnology Industry Organization

Industrial biotechnology (IB) holds immense promise for transforming a wide variety of industrial processes by preventing pollution, reducing costs, conserving natural resources and delivering innovative products to improve our quality of life. It also creates new markets for agricultural crops and crop residues as renewable feedstocks, chemical intermediates and energy sources. Sustainable development cannot be achieved without continuous innovation, improvement and use of clean technologies and green chemistry. Several of the 12 principles of green chemistry can be met through the use of IB including waste prevention, increased energy efficiency and incorporation of renewable resources as inputs.

What Is IB?

Rudimentary IB actually dates back to 6000 BC when Neolithic cultures fermented grapes to make wine and Babylonians used microbial yeasts to make beer. Over time, mankind's knowledge of fermentation increased, enabling the production of cheese, yogurt, vinegar and other food products. In the 1800s, Louis Pasteur proved that fermentation was the result of microbial activity. Then in 1928, Sir Alexander Fleming extracted penicillin from mold; later large-scale fermentation techniques were developed to make industrial quantities of this wonder drug.

Today IB uses the techniques of modern molecular biology to develop new processes that reduce environmental impacts while improving efficiency in numerous industrial sectors. No matter what stage of industrial production – inputs, manufacturing process or final product – IB is providing innovative new tools, techniques and know-how to enable companies to move beyond regulatory compliance to the proactive pollution prevention and resource conservation strategies that are the hallmarks of industrial sustainability. IB's greatest promise it that it results in new industrial processes that both reduce costs and result in pollution prevention.

The Current Situation

A 2001 Organization for Economic Cooperation and Development (OECD) report examined cases where traditional industrial processes were replaced with or modified by a biotechnology process. The results show that biotech invariably leads to a reduction in either operating costs, capital costs or both, and to a more sustainable process – a lowered ecological footprint in the widest sense – by reducing some or all energy usage, water usage, wastewater production and greenhouse gas production. Interestingly, OECD found that cost reduction and improvements in product quality were usually the primary forces driving the decision to incorporate a biotechnology process. In 2004, Biotechnology Industry Organization (BIO) released a report which provides a first look at the potential impact this technology can have to significantly green the industrial landscape while helping companies cut costs and bring new consumer goods to market. As a result of recent technological advances, IB could revolutionize current environmental protection strategies and the whole industrial landscape.

The expansion of the biobased chemical industry reflects the continued utilization of IB and its increasing commitment to green chemistry. The sector is increasing its production of bio-based drugs, commodity chemicals, food ingredients, and biodegradable plastics. A recent report issued by the U.S. International Trade Commission (USITC) examines the competitive conditions affecting certain industries that are developing and adopting new IB processes and products. It finds the application of IB can improve the efficiency of the industries and lead to the development of new products. The 2008 U.S. Department of Agriculture (USDA) report on biobased products concludes that the biobased industry is poised for substantial growth between 2007 and 2025.The science for producing biobased products has advanced substantially, but a number of factors including policy, scientific hurdles and economic feasibility affect the rate of growth of the biobased industry.

A 2007 study by the European Commission's Joint Research Centre focused on case studies to quantify the economic, social and environmental impact of bioethanol production. It concludes that modern biotech offers unique opportunities to address many needs and could consequently serve as a major contributor in achieving EU policy goals on economic growth and job creation, public health, environmental protection and sustainable development.

Reports such as these can deliver information on these powerful new biotech tools to the public, policymakers and non-governmental organizations. All of these groups have a stake in a greener future and need to be informed about the latest technological developments that can improve our world.

IB Holds Great Potential

Substantial analysis indicates that many biotech applications would actually prevent pollution by substituting a biotech process for a traditional industrial process. In a chemical synthesis, enzymes might replace toxic chemicals; the amount of energy consumed could be reduced by replacing high temperature chemical reactions with enzymatic reactions run at much lower temperatures; IB might lead to the development of an innovative end product that replaces an existing product that is less environmentally friendly.

IB is beginning to be deployed in several important industrial sectors, including forestry, pulp and paper, chemicals and plastics, mining, textile production, and energy. In North America alone these sectors account for roughly 40% of energy usage, 50% of industrial pollution and 60% of greenhouse gas emissions. In many cases, use of IB processes can also reduce the risk of toxic chemical spills and chemical exposure. Biotechnology process changes in the nutraceutical and pharmaceutical sector in the production of riboflavin (vitamin B2) and the antibiotic cephalexin have shown that associated air emissions can be reduced by 50% and 80%, respectively. However, more analysis is needed to draw out additional empirical information about possible environmental benefits in this rapidly expanding field.

Educating The Stakeholders

IB is one of the most promising new approaches to pollution prevention, resource conservation and cost reduction. The application of biotech to industrial processes is not only transforming how we manufacture products but is also providing new products that could not even be imagined a few years ago. These new tools, however, cannot help move us toward a more sustainable future unless government policymakers and corporate leaders comprehend their value and take proactive steps to incorporate them in a wide array of manufacturing processes. Public officials and even chemical engineers often seem only vaguely aware of the existence of these new biotech tools and their ability to green the industrial landscape. In many cases the tools are so new that even engineers in the private sector are not yet aware that they are available for deployment. This technology gap, the lag between availability and widespread use of a new technology, must be overcome to accelerate progress in developing more economic and sustainable manufacturing processes through the integration of biotech.

Is Our Future Green?

As use of IB spreads, it could enable us to significantly cut our energy use, industrial pollution and emissions of greenhouse gases. Because IB reduces – and even eliminates – industrial waste, businesses will spend less on cleanup, disposal and control of pollution. IB could be on the leading edge of the development of a renewable carbohydrate economy that could replace a petroleum-based economy. If developed to its full potential, IB offers business a way to reduce costs and create new markets while protecting the environment.

Contact:
Brent Erickson, Janet E. Nelson
Biotechnology Industry Organization
Washington D.C., U.S.
Tel.: +1 202 962 9200
Fax: +1 202 488 6301
berickson@bio.org
jnelson@bio.org
www.bio.org

Next-Gen Sequencers

Drawbacks and Opportunities of Available Tools

Sequencers – In the early days it was more about testing, validating and approving, rather than using the systems in daily lab routines. Nowadays, the experience from a vast variety of projects indicates the drawbacks and opportunities of each technology. In many cases, a combination of the technologies provides the best solution. Generating a useful bioinformatics analysis is the pivotal point for an in-depth comprehension of its biological relevance.

Dr. Kerstin A. Stangier
GATC Biotech

During the last three years, the sequencing market completely changed due to the availability of the Next Generation sequencers (table 1). The technical capability of the systems, particularly embodied by the Roche/454 GS FLX and the Illumina/Solexa Genome Analyzer, generate huge amounts of sequence information. The most important difference to traditional Sanger sequencing is the tremendous increase of data output. On the other hand, the read length of all machines which are available on the market right now is shorter than the read length generated using the Sanger method. These two points – high data output and shorter read length – are the parameters which influence the usefulness for projects and special applications.

Applications

In choosing the right technology or combination of technologies, it is important to understand the aim of the project, as well as to have access to all available information about the organism.

Having performed many projects, each with a different set of questions and goals, various points have emerged: For complete de novo sequencing, e.g. of prokaryotes and eukaryotes for which no very closely related genome is available to be used as a reference sequence, a hybrid strategy of GS FLX, Genome Analyzer, and Sanger sequencing is highly recommended. The long Sanger reads are needed for finishing and gap closure, in particular for longer repeat structures, while the Roche/454 technology provides a good data backbone. Homopolymers can be solved using short reads, e.g. generated by the Illumina Genome Analyzer II technology.

If there is a reference genome available to be used for mapping (e.g. re-sequencing projects), the Illumina Genome Analyzer II is the method of choice. It is the best technology for all applications for which short reads are sufficient, e.g. for an identification such as CHiP, small RNA, 3'UTR or SAGE. In addition, the huge number of reads from the Genome Analyzer II are perfect for quantification projects, e.g. expression level studies.

Data Analysis And Assembly

At the moment, there is no reliable algorithm for de novo assembly of short reads below 50 base pairs (bp) available. In the past 12 months several software packages have become available that address these challenges. However, few have been subjected to thorough testing and none have a track record that ensures success. Each application and analysis method has to be tested for each project goal and the analysis must be optimized and repeated. All this developmental effort is being pushed to the limits by the ever-increasing data output of the machines. The new Genome Analyzer II gives a tremendous increase of reads per run compared to the former version. The Titanium run for the GS FLX (to be releases this autumn) will enhance read length and number of reads per run.

As the bioinformatic analysis is the key challenge, different tools should be used for different applications, also depending on the size of the organism. It is very likely that sequences from small organelles/BACs which contain many repeats need a different bioinformatic tool than data sets for hybrid assemblies. GATC offers a wide range of bioinformatic solutions for genome assembly, transcriptome analysis or small RNA analysis. Proprietary tools are used for the analysis and handling of Next-Gen sequencing data, while third party tools are available for optimized de novo assembly of sequence data from the Genome Analyzer (GA) or improved hybrid assemblies. For example, SeqMan NGen (DNASTAR) assembles Illumina, Roche and Sanger data.

Visualization

The analysis of the huge amount of data needs high computer capacity and the experience for handling projects of this size. The visualization of the results has to be easy and user-friendly. Genome browser desktop applications for data visualization allow a convenient overview experiments. The visualization of the coverage helps to identify smaller InDels and rearrangements within the genome. In addition, SNPs, coding regions and other annotations can be displayed.

Barcoding Systems

There is a number of barcoding systems available on the market that allow an additional level of parallel processing. While the Roche MID kit allows tagging of up to 12 samples, some proprietary tagging systems are suitable for use with different Next-Gen systems and with virtually an unlimited number of samples processed. These barcoding methods are particularly well suited to cDNA libraries, de novo sequencing of BACs, fosmids, or viruses whose sequencing would otherwise be impractical and expensive. Some techniques are highly efficient, resulting in 99.9% of sequences successfully tagged.

Table 1: Overview of Next Generation sequencing technologies (in alphabetical order)

Manufacturer	System	Method	Read length	Samples
Applied Biosystems	SOLiD System 2.0	sequential ligation of oligonucleotides	35 bases; 2 * 25 bases	16 samples per slide/ 2 slides per run
Dover Systems	Polonator G.007	polymerase colony (polony) sequencing by ligation	(2*) 26 bases	18 wells per flow cell 2 flow cells per run
Helicos Bioscience	HeliScope Single Molecule Sequencer	True Single Molecule Sequencing (tSMS)	25 to 35 bases	25 discrete channels per flow cell / 2 flow cells per run
Illumina/Solexa	Genome Analyzer II	reversible terminator-based sequencing	(2 *) 36 bases; up to 75 bp coming beginning 2009	8 discrete channels per flow cell / 1 flow cell per run
Pacific Bioscience	not yet defined	SMRT technology (Single molecule real time; using phospholinked nucleotides)	long reads (not defined yet)	not yet defined
Roche / 454	GS FLX	Pyrosequencing	Ø 100 bases or Ø 250 bases: up to 400 bases (Titanium run) coming soon	16 samples per pico titer plate
VisiGen	The VisiGen sequencing system	interaction between fluorescently-tagged polymerase and fluorescently modified nucleotide	not yet defined	not yet defined

More Technologies

Besides the already established technologies of Roche and Illumina, additional sequencers have entered the market (table 1). Applied Biosystems and Helicos BioSciences machines are already available. Applied Biosystems has released the version 2.0 of its SOLiD System. Helicos announced that they had problems with unstable reagents but the problem has now benn resolved for their Helicos Genetic Analysis System. In addition, Pacific Biosciences and VisiGen have announced plans to bring brand new methodologies to the market in the next few years. The new era in sequencing started with the Roche GS 20 system a few years ago and it was just the starting point for completely new developments.

Conclusion:

There are two main parameters which need to be observed to ensure the in-depth understanding and interpretation of the sequence data:

- The use of various Next-Gen systems to take advantage of each technology and
- The combination of different bioinformatic tools and their stepwise application.

Contact:
Dr. Kerstin A. Stangier
GATC Biotech AG
Constance, Germany
Tel.: +49 7531 81600
Fax: +49 7531 816081
k.stangier@gatc-biotech.com

Plantdustrial

Linking Plant and Industrial Biotechnology

Evolution – Life on Earth evolved from a mèlange of chemical compounds via microbial organisms and algae towards plants. During this process, evolutionary pressure has driven plants to develop an extremely efficient catabolic system, producing a huge variety of high value substances in their complex secondary metabolism. The very same natural laws are underlying chemical processes.

Dr. Peter Welters
CEO Phytowelt + Green Technologies

The usage of fermentation is only the first step to a sustainable chemistry and should be followed by an implementation of knowledge from plant science in a synergistic process to reduce the ecological impact of chemical industry and improve economical rewards. Today, the chemical industry is still a raw material and energy intensive industry. Due to the scarcity of fossil resources, steadily increasing oil price and a need to reduce greenhouse gases, renewable resources from plants will be an increasingly important issue for the chemical industry over the coming years.

Germany, fourth in the world for the production of chemicals, will take a leading role in these efforts because of the high investments of the chemical industry in R&D. Already around 10% of basic material for the chemical industry and 70% of the renewable energy in Germany stems from renewable resources, mainly plant material (fig. 1).

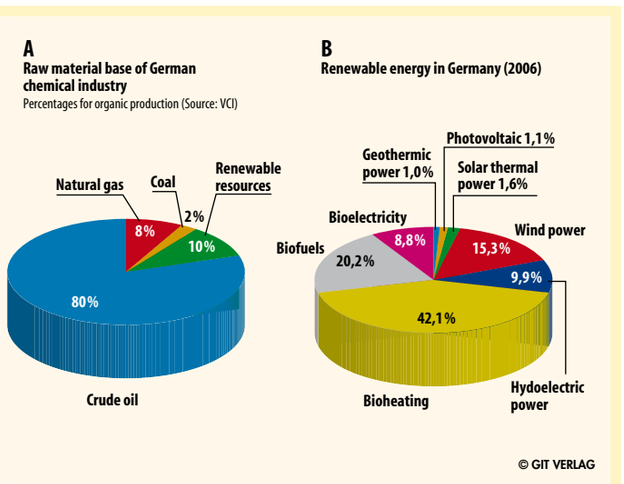

Fig. 1: A) Raw material basis of the German chemical industry; currently more than two million tons of renewable raw materials are used in German chemical industry. One third originates from home market.
B) In 2006, about 200 TWh of German final energy consumption came from renewable, with 70% coming from bio sources.

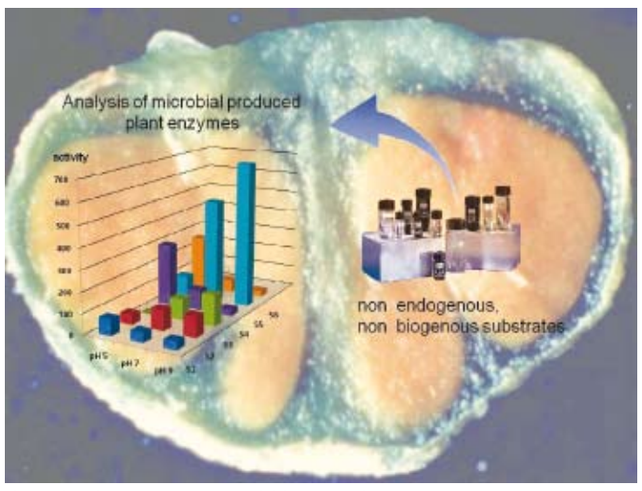

Fig. 2: Diversity of plant enzyme activities concerning substrate, co-factor and pH specificity. Shoot nodules of the leguminous plant *Sesbania rostrata* with the symbiotic bacterium *Azorhizobium caulinodans*.

A World Of Enzymes

The sustainability of chemical processes, especially those where chiral products are synthesized, can be increased by the use of fermentation processes or direct biocatalytic steps. Unlike most chemical reactions, biocatalytically driven reactions are highly stereo-selective for the substrate and the resulting product due to the intrinsic properties of the involved enzyme activities resulting in particularly high substrate and reaction specificities (fig 2).

In addition, natural enzyme-based processes operate at lower temperatures and produce less toxic waste and fewer emissions than complex conventional chemical processes, e.g. the conversion of elemental nitrogen to ammonium is done by plants in symbiosis with bacteria at room temperature and normal pressure, whereas the chemical process demands high pressure and temperature, and metal catalysts (Haber-Bosch process).

The symbiotic process of nitrogen fixation is an example where nature leads the way to a strong collaboration between plant and microbial processes solving hardy problems in an elegant way. This has been the model for our motto "plantdustrial – linking plant and industrial biotechnology" and is intended to result in a strong interdisciplinary collaboration with a high synergistic potential, e.g. to produce aromatic substances in a sustainable fermentation process.

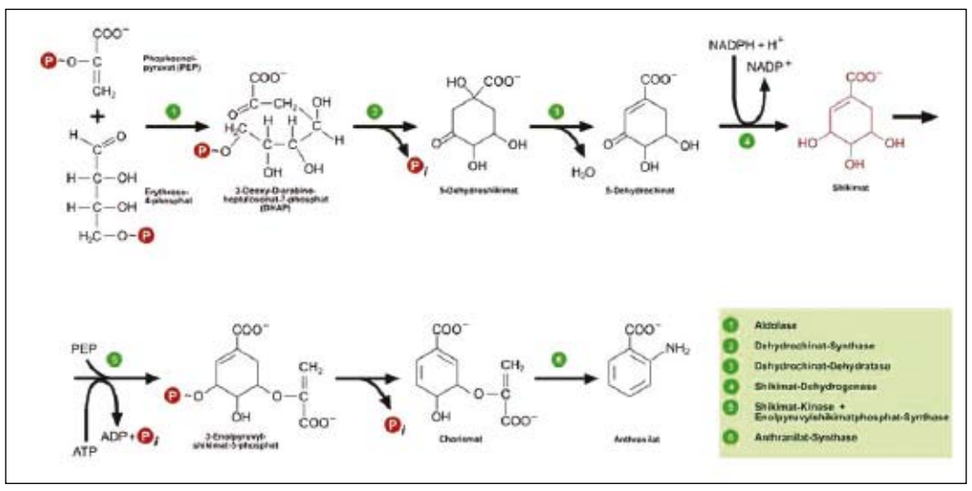

Fig. 3: Shikimi pathway in plants for the production of aromatic substances from sugars.

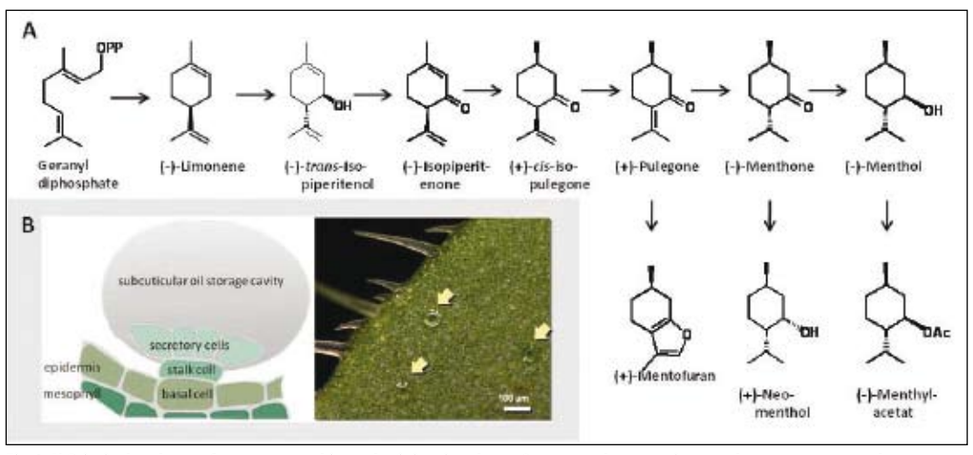

Fig.4: A) Principal pathway of monoterpene biosynthesis in mint plants. Over several enzymatic steps the precursor geranylpyrophoshoate is converted to menthol
B) Trichomes of peppermint (mentha)

The Future

The formation of diversified clusters with partners from academia, large international corporations and SMEs are very important for further exploitation of the hidden treasures of plants. Good examples for such activities are the Cluster Industrielle Biotechnologie 2021 (CLIB2021) and the European Technology Platform for sustainable Chemistry (SusChem) with its German affiliation SusChemD, a combined initiative of Dechema and VCI.

These clusters with a broad array of technologies and the implementation of substantial information available from plants will enable partners to generate value over the whole supply chain, improving sustainability and the impact of renewable resources, reducing cost and time to market by a synergistic approach of microbial and plant science as demonstrated by nature in symbiotic nitrogen fixation.

Contact:
Dr. Peter Welters
Phytowelt Greentechnologies GmbH
Nettetal, Germany
Tel.: +49 2162 77859
Fax: +49 2162 89215
contact@phytowelt.com

Until now, microorganisms, such as fungi and bacteria were used as the main sources for enzymes. The growing complexity of reactions required for the production of fine chemicals, especially for the pharmaceutical industry, draws the attention of industrial biotechnology more and more to plants. The high complexity of plants' secondary metabolism – thus demonstrating the huge number and synthetic abilities of the plant enzymes – as well as the fact that most of today's small molecule drugs (SMDs) can be traced back to a plant metabolites as the basic structure, are certainly major reasons for this development. Moreover, nature has optimized plant enzymes to work best at relatively low temperatures. Their use therefore opens new chances for energy reduction in novel industrial applications. Besides their unmatched range of biosynthetic pathways and reaction mechanisms, plants have found during their long lasting evolution on earth unique possibilities to produce, store and enrich even highly toxic substances by utilizing compartmentalisation, as well as specialized cell organelles or special tissues like trichomes in mint species (fig. 4 B).

In fact, compartmentalisation of biosynthetic reactions within plant cells is another key factor for solutions delivered by plants, e.g. for the synthesis of hydrophobic products and intermediates. Plants can be used as models to develop reaction compartments to produce a desired product at room temperature and normal pressure and have the blueprint for the required enzyme. Plants are especially potent in synthesizing a class of substances called terpenes e.g. carotinoids are well known representatives of this class. Another important class are monoterpenes produced by mint plants which have been utilised for industrial purposes for a long time (fig. 4).

The understanding of the underlying genetic and biosynthetic regulation, of the interaction of compartments and organelles, and of the sequential synthesis steps involving a multitude of different reaction conditions (oxidative, reductive, high or low pH) in mitochondria, plastids, peroxisomes, the cytosol or the ER will open new routes and possibilities to produce a vast amount of complex chemical products that until now have not been possible with classical chemical or enzymatic methods.

It is most important to note that usage of plant enzymes and their biosynthetic abilities is not restricted to the use of whole plant systems (e.g. as bioreactors). Through the targeted use of biotechnology and biodiversity, Phytowelt GreenTechnologies isolated plant genes and optimised their coding regions to produce enzymes in microorganisms with specificities and stabilities tuned to particular industrial purposes.

Times Have Changed

Energy Management as Important Factor in Global Competition

Need For Action – The first oil crisis was in 1973, the second in 1979; rationing, production and marketing controls were established to try to resolve these crises. Yet, oil did not exceed the price of $34/barrell. The oil price in August 2008 was $120/barrel, and some people think that the price will hit $187/barrel within the next 36 months. Trends in the market suggest that the demand for energy will dramatically rise over the next 25 years: The global demand for all energy sources is forecast to grow by 57 %. Because of this, energy management is an important aspect – today, but especially tomorrow.

If energy prices continue to rise dramatically the business impact could include: reduced profits as a result of high operating costs; decline of sales of energy-using products or energy intensive products and disruptions in supply chains as suppliers are unable to meet cost obligations or to stay in business. To remain competitive, it is necessary to reduce the demand side of the energy equation. This requires investments in technologies or programs to reduce the cost and consumption of energy. A number of areas exist that should be addressed when looking at energy efficiency/reduction, including: energy used for manufacturing, energy in product/process design and energy used in the supply chain. An additional reason for energy reduction is its contribution to greenhouse gases (GHG).The Hadley Center for Climate Change says that CO_2 makes up 63 % of GHG. Energy generation is the largest contributor to CO_2. A reduction in energy consumption reduces the need for energy generation, which in turn reduces the CO_2 being generated. Thus, you can reduce CO_2 produced by reducing energy consumption.

Energy In Manufacturing

One area that people think about when energy efficiency is talked about is manufacturing. The U.S. government expects energy consumption in most manufacturing sectors to decrease in the future. Each company must do their part in decreasing energy usage in manufacturing. So each energy consuming system should be examined. Comparisons between equipment and systems can give an indication that inefficiencies exist. Continual monitoring of equipment and systems energy can lead to identifying problems. Benchmarking against the equipment manufacturer, industry, and own internal standards can identify problem areas. One example: steam traps. In a steam system which has not been maintained for 3–5 years, between 15–30 % of the installed steam traps may have failed, thus allowing live steam to escape. In properly maintained systems leaking traps should account for less than 5 % of the traps. Just repairing steam leaks can save 1–2 % in energy. Rohm & Haas projected an annual savings of $50,000 by improving the steam system maintenance in its Knoxville plant.

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Energy in Product and Process Design

When designing a product, improved energy efficiency processes should be considered. These processes might not be possible with existing equipment, but, with the amount of new facilities being built; it is a significant missed opportunity not to use the latest technology. Manufacturers should not just replicate the existing facilities and processes; but use the opportunity to design energy efficiencies into the complete process. Carnegie Mellon University chemical engineers have devised a new process that can improve the efficiency of ethanol production. These researchers have used advanced process design methods combined with mathematical optimization techniques to reduce the operating costs of corn-based bio-ethanol plants by more than 60%.

Energy In Maintenance

Properly maintained equipment and systems are a fundamental part of energy efficiency and can reduce energy consumption by 6–11 %. While preventative maintenance will keep the equipment running without break down and will result in moderate energy reduction, having the maintenance being triggered based condition of the equipment and system is a proven way of reducing maintenance costs and energy consumption. Including a condition of energy intensity can indicate that the equipment or system needs maintenance, even though there is no other indication of a problem. An improperly tuned engine, for example, hurts gas mileage by an average of 4.1%. The decline in gas mileage, in this case an indicator for energy intensity, indicates the engine needs a tune-up.

Energy in the Supply Chain

With an increasing number of goods are being shipped internationally, the energy used and the environmental impact can be reduced through better, more efficient coordination and tracking. Global transportation solutions can increase efficiency by improving the co-ordination, strategy and logistics surrounding the movement of goods through multiple countries. Each jurisdictions regulation has to be taken into consideration. Modes of transit, trade restrictions, container size, and route restrictions are all part of the planning process. By including the amount of energy for each option an effective and efficient transport plan can be created. One aspect of these cross jurisdictional shipments that is often overlooked is documentation. Every jurisdiction has its own documentation requirements. Being held up due to incomplete documentation is a problem. Extra storage time, goods movements, resources for storage (heating, lighting, cooling, etc.) all contribute to additional energy usage. Planning solutions which provided an optimized schedule and routing can be undone by something as simple as the incorrect form. These solutions must be integrated into the execution systems so that the complete documentation for the shipment can be provided. Even domestic shipments can benefit from better planning.

United Parcel Service (UPS) for example, wanted to cut down on the fuel its fleet of 94,000 ground vehicles uses. UPS began experimenting with a software program it developed itself. This program helps optimize driving time on routes by programming, for example, right turns only on certain New York City runs. Using this software UPS trucks drove 30 million fewer miles last year, or a reduction of almost 2 % in the company's annual global mileage. UPS is saving an average three million gallons of fuel a year, while reducing carbon emissions by 31,000 metric tons, the company says.

Energy Reporting And Visibility

One of the initial problems with energy efficiency is that most companies do not have any energy data other than that at a summarized level. Little information on the energy consumption by individual equipment or lines is available. This means that one of the first things energy efficiency projects encounter is the requirement to install metering equipment. Once the metering is in place and the data can be collected either manually or via data collection system such as data historians, then analysis can proceed.

Energy usage of individual equipment can be displayed and compared to the manufacture's specifications, industry standards, and own benchmarking data. By integrating this information with Enterprise Asset Management systems and Production Planning systems it is possible to associate energy usage, production, and maintenance information. Other analysis are now possible, comparison of like types of equipment can identify better performing equipment which can be used as part of justification for upgrades. In multi-plant environments comparing identical or similar equipment between plants can identify different maintenance and operational strategies. Further investigation enables companies to standardize on the most appropriate procedures.

Energy Planning

Industry should consider establish its own long and short term energy plans. Energy should be planned and viewed like any other production resource. It is possible to include energy consumed into a products definition the enterprise resource planning (ERP) system, just like any other resource. Treating energy this way is the start of the process in transforming energy from an overhead to a direct material. Once this is done, the ERP systems can give the company visibility into the energy demand from production, since energy demand is now calculated based upon the production schedule.

Planning energy usage in production is just the start. As investigation into the consumption of energy in all aspects of the business and supply chain continues other opportunities become visible. A carbon adjusted supply chain is now possible, transportation routes can now be optimized to reduce energy consumed, along with the other traditional supply chain optimization parameters. Decisions about the location of a plant or warehouses can now take into account the energy costs and the associated carbon impact and balance this information with the labor and material costs.

Making Efficiency Pay

A growing segment of customers favor companies that can credibly demonstrate reduction of the carbon footprint. Not every company can get customers to pay a premium for "green" products. But, by having this information displayed differentiates you from the competition. Tesco, for example will become the first supermarket chain in the world to assign a "carbon label" to every product on its shelves, in an effort to attract ever more environmentally conscious consumers. The UK's biggest chain said the labels would record the amount of carbon dioxide emitted during the production, transport and consumption of the 70,000 products it sells.

There is another side of reducing energy usage and the subsequent reduction in CO_2 emissions. This is making use of carbon credits or offsets. Signatories of the Kyoto Protocol have agreed to have caps or quotas on the maximum amount of GHG emitted by developed and developing countries. Each business is assigned an allowance of credits, which the gives the business the right to emit one metric ton of Carbon dioxide" carbon dioxide or other equivalent Greenhouse gas" greenhouse gas per credit. Those companies whose emissions are underneath their allowance can sell their unused allowances as carbon credits, and companies that are about to exceed their quotas can buy these unused allowances as credits. It is even possible that, being seen as environmentally conscious, with programs to reduce green house gasses and energy usage, could make your company more attractive to investors. The Scotia Bank has established an investment fund of companies that are developing strategies to adapt to or mitigate the effects of climate change.

Energy Efficiency 'Now Important'

Energy management and the resulting efficiencies is everyone's business, not just the engineers'. As a major factor in the generation of green house gasses, it is in everyone's best interest to conserve energy as part of caring for the environment. It is also a double benefit that conserving energy adds to the bottom line in reduced costs, potentially added revenue and increased return on assets.

Contact:
John Harrison
SAP Canada, Industry Business Unit Chemicals
john.harrison@sap.com
www.sap.com

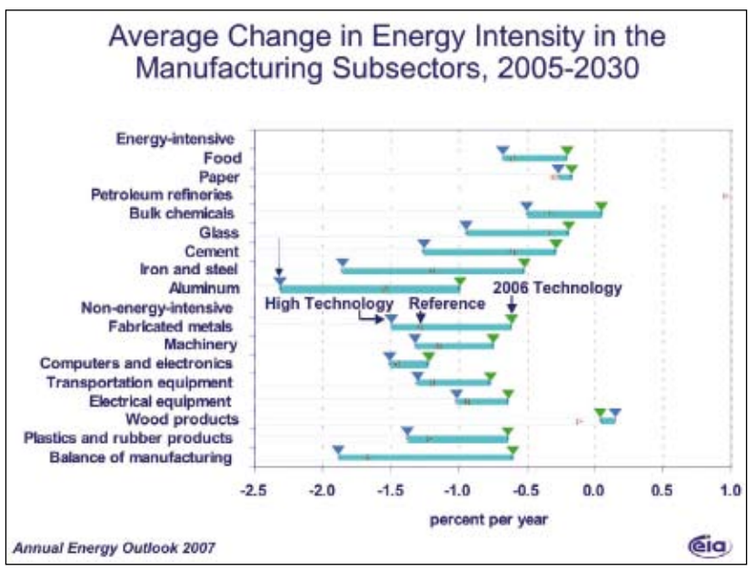

Fig. 1

Fig. 2

Praxair to Supply Hydrogen to BP Praxair said it has finalized an agreement with BP whereby Praxair will supply hydrogen and steam to BP's Whiting, Indiana, refinery complex. Praxair will build two new hydrogen plants with a total capacity of 200 million ft^3/day. The plants, designed and constructed by Praxair, are scheduled to start up in the second half of 2010. The use of hydrogen will allow BP to produce very low-sulfur gasoline and diesel fuels in the refining process and to upgrade heavy Canadian crude oil to lighter, cleaner-burning fuels.

Praxair has been operating in northern Indiana for almost 100 years. Today, BP and other customers in the region are supplied from four locations where Praxair operates 10 air separation plants, a rare gas facility and four smaller hydrogen plants. A state-of-the-art operations center in East Chicago, Indiana, controls 130 miles of pipeline that deliver oxygen and nitrogen as well as hydrogen. ■

Emerson Main Vendor at Nalco Plant Emerson Process Management has been selected by Nalco Industrial Services, as the main instrument vendor for a new water treatment chemicals plant in the Nanjing Chemical & Industrial Park in China. The plant, scheduled for completion early in 2009, is being constructed by the U.S. Nalco Company. Nalco is investing about $25 million in the new plant in Nanjing City. It will have a total annual capacity of 37,000 t.

"The factory in Nanjing will become our largest and most important production base in China," commented Louis L. Loosbrock, Group Vice President of Nalco. "Products made there will be capable of implementing the most advanced water treatment strategies." ■

Praxair Expands Agreement Praxair Investment has signed a long-term supply agreement with Guangdong Shaoguan Iron & Steel Group (Shaoguan Steel). Under this contract, Praxair China will build a large air separation plant to go on stream in mid-2010. The new plant will supply oxygen, nitrogen and argon for Shaoguan Steel's increased production capacity. The plant will be the fourth Praxair air separation unit constructed at Shaoguan Steel and will increase Praxair's total production capacity to 3,550 mt of oxygen per day. ■

ExxonMobil Chemical Steps Up ExxonMobil Chemical will improve the supply of its specialty compounds in Asia Pacific following the establishment of a compounding agreement with Resin & Pigment Technologies (R&P), a subsidiary of EnGro Corporation Limited, according to the company. Under the agreement, R&P will manufacture a broad range of ExxonMobil Chemical's specialty compounds for use in automotive interior and exterior applications, appliances and consumer products.

The R&P facility is located on Jurong Island, Singapore, just two kilometers from ExxonMobil Chemical's petrochemical complex. ExxonMobil Chemical will leverage its global portfolio of specialty plastics and elastomers using the Singapore complex as the primary source of polyolefins for the production of its specialty compounds. The R&P facility is ISO 9001 certified and recently achieved ISO/TS 16949 automotive certification. ■

Linde to Invest $180 Million Linde will invest $180 million to expand city-owned gas production facilities in South Korea, Seoul's energy ministry announced. Industrial gas is used in sectors such as crude refining, chemicals, steel and shipbuilding, and generates about 60 trillion won ($58.98 billion) per year worldwide. South Korea's industrial gas market grew to 1 trillion won last year and has been expanding at a double-digit growth rate. Seoul's vice-energy minister Lee Jae-hoon will sign a memorandum of understanding (MOU) with Aldo Belloni, a member of Linde's executive board, on the development of the facilities in Yongin, south of Seoul. ■

Air Liquide Invests €100 Million in Two Gas Projects in Poland Air Liquide is to invest €100 million in two industrial gas production projects in Poland. The first project involves the construction and operation of two air separation units for Polish company ZA Pulawy. The first unit will enter service at the start of 2010. The two units together will produce more than 1,200 t of oxygen for the region's industry. The second project involves the construction of an air separation unit in Gdansk, which will operate from 2010. ■

Shell Chemicals Seeks Partners for New $500 Million Singapore Facility Shell Chemicals said it is seeking potential partners for a $500 million styrene monomer/propylene oxide (SMPO) manufacturing facility it plans to build in Singapore, the Business Times reported, quoting a senior company executive. Strong demand for SMPO, which are chemicals used in the production of polystyrene containers and rubber soles, is underpinning the project, said Fang Yea-Yee, Shell Chemical's general manager for SMPO and derivatives.

"A lot of work is going on and we are in discussions with possible joint venture partners," Fang said. Shell Chemicals has an existing SMPO joint venture with Germany's BASF in Singapore. The joint venture company, called Ellba Eastern, produces 250,000 t of propylene oxide and 550,000 t of styrene monomer annually. "Shell believes the strong growth in the Asia-Pacific demand for both styrene and propylene oxide will continue to create attractive opportunities for new SMPO investments," Fang said. ■

Getting Innovation Right

Overcoming Obstacles to Innovation in the Chemical Industry

Innovation – Leading chemical companies have long been aware that innovation is a key success factor in the chemical industry. Global champions such as BASF, Bayer or Evonik all emphasize the importance of new, innovative products as a source of competitive edge, increased profit margins, enhanced customer relationships and high reputation within the industry.

In the future, innovation may become even more important for Western companies wanting to compete with chemical companies from emerging markets such as China and India. With competitors from these countries, Western players are often not able to compete on price, and their initial edge on quality is gradually eroding as the emerging competitors improve. In the long run, only innovation will remain as a source of competitive advantage and differentiation.

Research vs. Development

In order not to be misunderstood, it is necessary to make a clear distinction between development and research. While research relates to activities aiming to create truly new chemicals, development describes the modification of existing chemicals, for example the modification of chemicals so that they match the needs of a specific customer. Development activities tend to be more short-term, less risky and at the same time also potentially less profitable than research activities (fig. 1).

Chemical Companies: Difficulties With Basic Research

Many chemical companies focus on development and not on research, that is, on providing good technical service and products customized to specific customer requirements, not on major product innovations. However, in the long run, the weakness of these companies in being truly innovative seems problematic. Any product that does not substantially change over time will undergo commoditization. Customers will get more and more familiar with the product and its properties, and will be less willing to pay a premium for product-related services. Correspondingly, they will be more likely to switch to cheaper suppliers, exposing the producers of these chemicals to stronger competition from emerging markets.

Furthermore, any position obtained as a preferred chemical supplier via development (as opposed to innovation and research) is very difficult to leverage globally. Development services typically are localized and depend strongly on the staff-delivering them, and thus are difficult to transfer to a business relationship in another country. In contrast, once a chemical company is known as innovative, such an image is a truly global advantage. Thus research – as opposed to development – gives a competitive advantage that is much more in line with business realities in a globalized world.

Given these facts, it is surprising that many Western chemical companies are relatively weak with regard to innovation, and it seems worthwhile to look for the causes. The most likely reason is that the companies are run by operations people with a limited understanding of the way innovation works, and the requirements innovation needs (fig. 2).

Development	Research
• Primarily adaptation of existing knowledge and existing products to slightly changed circumstances	• Creation of substantially new knowledge, new technology and new products
• Oriented at specific problems of present customers	• Not necessarily oriented at specific problems of present customers
• Defined target market	• Unknown target market
• Relatively short timeframe	• Long timeframe
• High likeliness of success	• Low to medium likeliness of success
• Limited investment of resources	• Potentially high investment of resources
• No big advances in knowledge required	• May require big knowledge advances
• No substantial new IP created	• Potential to create substantial new IP

Fig. 1: Basic differences between development and research in chemicals

Operations	Innovation
• Short-term results	• Ambitious long-term results
• Cost controlling	• Investments with unclear result
• Strict utilization of controlling systems	• Acceptance of ambiguity
• Emphasis on stability and planning	• Emphasis on flexibility and changes
• Monitoring of results	• Acceptance and tolerance of failure
• Adherence to guidelines and rules	• Creativity, breaking free of rules
• Performance and efficiency	• Growth and innovation

Fig. 2: Key focus in operations- and innovation-driven environments

As a consequence, whole companies – including those functions responsible for innovation – are run based on the principles of operations-driven businesses. Thus the mindset is short-term, risks are avoided and failure is not allowed. While pure development work (such as the customization of a product to the needs of the requirements of a specific customer) may still be possible, truly groundbreaking innovation cannot happen. This would require investing a larger amount in a longer project with an uncertain result.

The Innovation Process

If a chemical company wants to change this situation and thus embrace the opportunities that truly innovative chemical products bring, it is well advised to look at the individual steps of the innovation process in detail (fig. 3).

In the first step, a company needs to identify the areas in which it is to look for innovation. These should be those areas which are in line with company strategy, and in which innovation is considered to be the most likely to be successful and the most profitable.

In the next step, ideas need to be developed that can be pursued. Here, it is advisable to look for input not only from internal but also from outside sources to avoid limiting oneself to a small pool of innovative ideas. It is best to start with a large number of ideas – even though some of them may sound very unlikely – and to reduce them later in a systematic evaluation step.

Step in Innovation Process	Benefit of Optimizing Step
Identification of businesses in which innovation is the most profitable for a chemical company	• Research resources are focused on genuinely worthwhile areas • Innovation in target areas, not accidental
Development of ideas for successful innovative products that give chemical companies an edge	• Idea development is broad-based and conclusive • Thus only high-quality ideas are pursued
Management of research projects to give quick results with limited resource input	• Clear provision and management of research resources • Timely progress of research projects
Optimization of market success of innovative products by entering the market in the right way	• Optimized market entry • High profit impact of new, innovative products

Fig. 3: Different steps in the innovation process

Innovation management is the key to the third step. Once projects have been selected, it is necessary to provide the required resources, set realistic timeframes and readjust project goals.

Finally, once a project gets close to a product ready for market entry, the transition to the market has to be well prepared in order to maximize the potential of the new product. This often involves removing barriers between marketing and research staff.

A Tool to Promote Innovation

In order to help chemical companies optimize the innovation process within their companies, the consulting company Stratley has created a tool, the Stratley Innovator, that gives detailed advice on how to handle each step of the process (fig. 4).

Depending on the specific situation of a company, and the detailed input derived from this situation, the Stratley Innovator tells chemical companies all information relevant to innovation, from focus areas of research over lists and prioritization of ideas and resource requirements to market entry plans and measures.

There are strong indications that many Western chemical companies will need to become better at basic research to stay competitive. Otherwise, these companies run the risk of their markets getting more and more attacked by companies from emerging countries with cost advantages, big domestic markets, and rapidly improving product quality and technological knowledge.

▶ Contact:
Dr. Kai Pflug
Stratley AG, Shanghai, China
Tel.: +86 21 2890 9677
Fax: +86 21 2890 9999
k.pflug@stratley.com
www.stratley.com

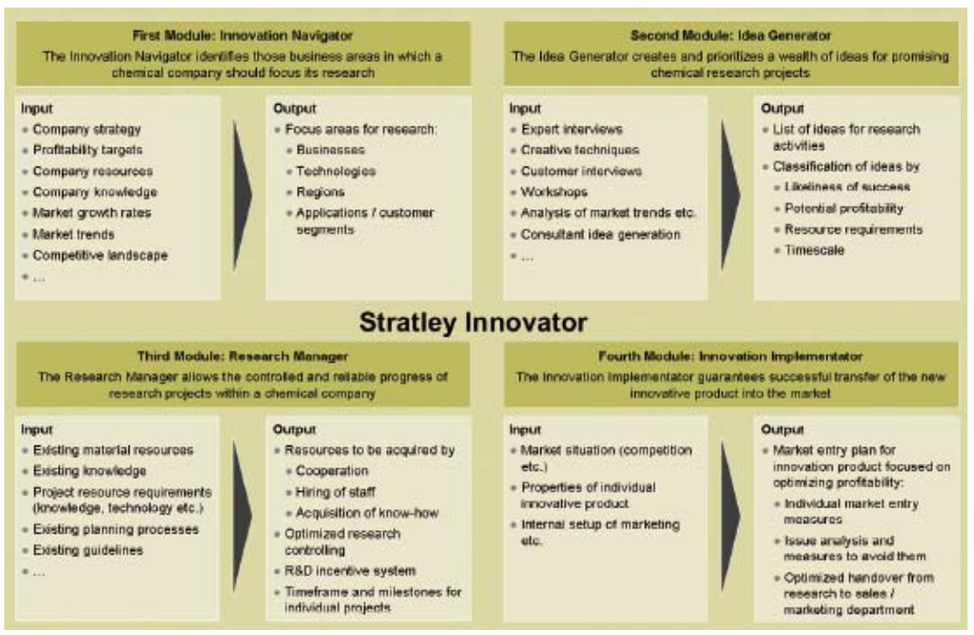

Fig. 4: The Stratley Innovator optimizes innovation of chemical companies

EFCG Pharma Business Conference

Massive Inflow of Rogue Pharmaceutical Ingredients into Europe

Looking For Solutions – The European Fine Chemicals Group (EFCG), a sector group of the European Chemical Industry Council (Cefic), held their Third Pharma Business Conference in Lisbon in May. The event was co-organised by EFCG and Concept Heidelberg to discuss current problems and possible solutions to ensure the compliant sourcing of APIs and excipients.

Many major stakeholders, such as representatives from U.S. Food and Drug Administration (FDA), the European Medicines Agency (EMEA) as well as representatives from major active pharmaceutical ingredients (API) and pharmaceutical manufacturers and traders, presented their views on strategies for compliant pharma sourcing.

The problem of non-compliant, unsafe pharmaceutical ingredients was illustrated to all parties involved, for example, through the recent heparin case. This involved the contamination of a life-saving pharma ingredient, heparin, resulting in many casualties in the U.S. Guy Villax, CEO of Hovione, an API manufacturer with sites in Portugal, U.S. and Macao, summarised the information available and presented in addition the results of his own studies.

Today, more than 80% of all active ingredients in medicinal products consumed in Europe are produced outside Europe, with the larger majority coming from China and India.

Call for Excipients Certification Scheme

Dr. Arnulf Heubner, Merck KGaA, Germany, outlined the situation in the global excipients market. He pointed out that this market is expected to grow at a compound annual growth rate of 3.8% through 2011. Although the introduction of new materials for use as excipients takes a very long time, thus delaying innovation processes, new excipients applications are topics of many research and development activities. Examples are excipient blends for increased functionality, new grades of existing excipients to enhance performance, excipients for controlled release and new drug delivery compounds for various applications.

Dr. Tim Boelke, BASF Germany (for EFCG) and Dr. Ian Moore, Croda Chemicals (for International Pharmaceutical Excipients Council Europe) presented their respective views on the need for a certification scheme for excipients. EFCG and IPEC Europe then publically announced the signing of a memorandum of understanding that will lead to close collaboration of the two associations on matters relating to pharmaceutical excipients. Initially the two associations will work on the development of a certification programme for manufacturers and distributors of pharmaceutical excipients, which will cover both good manufacturing practices (GMP) and good distribution practices (GDP).

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Finding and stopping illegal manufacture of APIs is not a simple task.

APIs Entering Europe from Asia

Charles Hu (BimSifram Group, Paris), a trader with many years of experience in importing pharmaceutical ingredients from China into Europe, explained the key problems related to the purchase of APIs from China. He stated that quite often the contents of the involved CEPs and DMFs do not reflect reality and do not correspond to GMP-compliant operations. It is even not always certain whether the site as defined in the dossier exists at all. He went on to say that the producers sometimes submit false documents and refuse any audits or inspections. The announcement of an audit or an inspection in such a situation leads to the immediate close-down of the site.

Hu emphasized that current competition that mainly focuses on price is increasingly causing major problems, especially for the European pharmaceutical industry. Unlike the FDA regulations, the European laws are not or are hardly being enforced by the supervisory authorities. Therefore the EU regulations are often not respected in China. Because of the combination of a lack of respect for strict regulations and low prices, Europe is becoming "the last served market after the U.S., Japan and the rest of the world," Hu stated.

Another speaker from a trading company, Erol Thomas Isim of Pharma Action, Germany, stated that around 90% of API material entering the EU via traders does not comply with the mandatory standard ICH Q7 GMP. During his presentation, he explained what he felt was a root cause that had contributed to the heparin disaster:

- The supply chain preceding the final manufacturing steps of heparin is complex and not transparent
- A large number of brokers and traders as well as hundreds of often small workshops are involved early in the supply chain
- None of these involved parties are subject to supervision by any Chinese or foreign authorities.

Non-transparent Supply Chains Make Raw-materials Tracing Impossible

Another detailed analysis of what led to the heparin disaster was presented by Villax. According to the FDA, possibly as many as 100–150 deaths in the U.S. were connected to the counterfeited, contaminated ingredient. Villax emphasised that better data collection systems would probably have established an even bigger number of additional victims in other parts of the world. He explained the "crime scenario" known so far. Following the slaughtering of pigs, fraudulent blending of raw heparin with the contaminant took place at certain points in the supply chain, in order to enhance the yields. Complex and non-transparent supply chains make the origins of the raw material almost untraceable. Heparin is the most recent case, but not the only one related to counterfeited pharmaceutical ingredients of Chinese origin. On several occasions during the past decades other counterfeited ingredients such as glycerin (contaminated with or replaced by diethylene glycol) and gentamicin reached the world market and caused many deaths.

There are strict EU regulations and numerous supplementary guidelines in place that manufacturing authorisation holders' and pharmaceutical ingredients manufacturers have to follow to ensure that their medicinal products will contain high-quality APIs. However, the growing threat to human health of counterfeit pharmaceutical ingredients entering the European market is breaching all regulations and guidelines. Therefore, this problem requires top priority attention from the supervisory authorities.

Consultation Paper

Francois-Xavier Lery from EMEA, London, gave an update on EMEA's activities relating to inspections and compliance of APIs. In the consultation paper on a possible legal proposal to combat counterfeit medicines for human use, which was issued for public consultation on March 11, the European Commission envisaged a combination of tightened requirements for APIs, such as a mandatory notification procedure for manufacturers/importers of APIs, tightened GMP standards and enhanced audits and enforceability of GMP. In addition, the EurdaGMP database linked to other community databases, would offer relevant information regarding GMP histories of API manufacturing sites as well as huge search capabilities, thus facilitating exchange of information between the competent European member state authorities and potentially with certain other countries' authorities. According to the consultation paper, the competent authorities shall carry out repeated inspections of API manufacturers in third countries if the third country applies lower GMP standards or if the supervision and oversight are not at least equivalent to those in the EU. Lery emphasized that despite these recent initiatives, inspections performed by authorities should not be regarded as a substitute for a better supply chain control by the pharmaceutical companies themselves.

Having been confronted with the danger of substandard or counterfeit pharmaceutical ingredients, the FDA formed a pharmaceutical ingredient safety task force in mid 2007, mainly in response to the diethylene glycol (DEG)/glycerin incidents. This task force convened in CDER's Office of Compliance in May 2007 to prevent DEG-like contamination of pharmaceutical ingredients, to address the issue of raw material supply chain integrity and the risks posed by sourcing poor quality materials and to propose specific ways to enhance FDA's oversight of pharmaceutical ingredient safety.

Dr. Nicholas Buhay from the FDA Center for Drug Evaluation and Research explained the activities and the recommended action items developed by the task force. Key issues are a broader control of sources of precursor material for raw material manufacture, a reporting requirement for industry regarding material contaminants and dedicated investigation resources focusing on contamination as well as new approaches to testing. Buhay pointed out that joint operations with "sibling regulators," information acquisition and exchange, common investigations and response plans will be necessary to meet the challenge of fraudulently adulterated materials.

▶ Contact:
Tony Scott
European Fine Chemical Group (EFCG)
Brussels, Belgium
tscott@tsassoc.eu
http://efcg.cefic.org/

Premium Products for the Process Industry

Synthetic Organic Heat Transfer Media Offer Many Advantages

Heat Transfer – Specialty chemicals group Lanxess recently showcased its Diphyl heat transfer media at the 15th international Oil, Gas, Petrochemistry 2009 exhibition in Kazan/Russia. "We want to continue actively driving business in Russia," said Ralf Krueger, Marketing Manager, Chlorotoluenes & Derivates, in the Basic Chemicals business unit.

Many processes in the chemical and petrochemical industry and the rubber and plastic processing sectors would be inconceivable without the use of some form of heat transfer medium.

Heat transfer plays a major role in the petrochemical industry, and many processes would be inconceivable without the use of some form of heat transfer medium. Because the most suitable heat transfer fluid for a given plant concept is selected according to technical and economic aspects, synthetically produced organic heat transfer media are being increasingly used instead of mineral oils in demanding applications such as synthesis processes, reactor cooling and heat recovery.

The classic product Diphyl is a eutectic mixture consisting of diphenyl and diphenyl oxide. It can be used not only in liquid form but also in the vapour phase at temperatures of +13 °C to +400 °C. This makes it possible to operate complex facilities at low pressure with ideal temperature distribution and relatively simple system design.

Diphyl DT is a mixture of isomeric ditolyl ethers. One reason for the increasing popularity of this heat transfer medium is its outstanding heat transfer performance compared with mineral oil-based heat transfer media. The spiralling oil prices have also made it even more attractive for applications in the chemical industry. Because of its high thermal stability, it can be used at higher service temperatures (up to 330 °C) than mineral oil-based heat transfer media. Diphyl DT also has better heat transfer properties and can be pumped at lower temperatures (down to –30 °C).

Diphyl THT, because of its polyphenylene structure, has extremely high thermal stability with an application range of between 0 °C and 345 °C. It can be used in pressureless systems even at very high temperatures, which means that the product offers an opportunity not only to save costs but also to increase the functional reliability of the heat transfer units. With Diphyl THT, Lanxess is following the mounting trend towards pressureless heat transfer systems – especially in the chemical industry for polymer production.

Diphyl KT is a low-viscosity, organic heat transfer medium with favourable heat exchange properties, and is suitable above all for combined heating and cooling processes in the liquid phase. Typical fields of application, in a temperature range of –45 ° to +350 °C, are the chemical and petrochemical industry and the rubber and plastic processing sectors.

▶ www.diphyl.com

A Fervent Advocate of Biocatalysis

BASF Chemist Klaus Ditrich Receives 2008 Siegfried Medal

Teamwork – On Sept. 4, Professor Dr. Klaus Ditrich, who works in BASF's biocatalysis research, received the 2008 Siegfried Medal for Trendsetting Work in Process Chemistry. This renowned prize is awarded every other year by Swiss fine chemicals company Siegfried in cooperation with the Organic Chemistry Institute of the University of Zurich.

Chiral intermediates, marketed by BASF under the Chipros brand, are used by the company's customers as key building blocks in synthesizing active ingredients for crop protection products and pharmaceuticals. Klaus Ditrich was particularly involved in the development of an industrial manufacturing process for optically active amines. The key step in this process utilizes an enzyme-catalyzed reaction that allows the two enantiomers present in the starting material to be separated in a highly efficient manner. Dr. Michael Reubold interviewed the laureate about his research.

Prof. Dr. Klaus Ditrich
BASF

CHEManager Europe: Prof. Ditrich, the award recognizes your research team's work in the development of technically practicable production processes for optically active amines, alcohols and carboxylic acids. When did you start working in this field, and how did you approach this task?

K. Ditrich: I started working in this field in the middle of the 1990s. By education, I am a classic organic chemist, and I was working on asymmetric hydrogenation reactions at the time. I was very skeptical about whether biocatalysis is in fact a suitable process for producing optically active intermediates on an industrial scale and, to be honest, I went to great lengths trying to prove that it is not. In the end, however, I had to acknowledge that biocatalysts are in many cases superior to chemocatalysis with respect to selectivity and efficiency, so I gave up the struggle in a way: Today, I am a fervent advocate of biocatalysis.

What are the advantages of biocatalysis as compared to conventional processes?

K. Ditrich: There are many aspects I can give you here. Availability is important. Once you have got hold of the microorganism that produces the desired enzyme, you can very easily produce the required catalyst by means of fermentation. Optimizability is another thing. You can fairly easily adapt an enzyme to a given substrate, if necessary, by means of modern methods of genetic engineering. Optimizing a phosphine ligand for a metal-containing catalyst is certainly a more complex task. In most cases, enzyme-catalyzed reactions are highly selective and proceed in moderate reaction conditions so that the resulting straightforward processes and reduced need for cleaning cut the consumption of energy, solvents, etc. A point that I think is essential for technical feasibility is the fact that biocatalysts are often highly tolerant to impurities, which would kill catalysts that contain metals. Oxygen, sulfurous components or water are generally tolerated without complaints, and of course this goes along with the significantly less laborious purification of industrially available starting materials and solvents.

As I said at the outset, I went to great lengths to avoid becoming an advocate of biocatalysis, but I must say it does have its advantages.

What were the major obstacles that originally prevented the upscaling of the syntheses created in the lab and blocked the path to industrial practicality?

K. Ditrich: The biocatalytic step is generally the least of the problems, because we use catalysts that have been optimized by nature in the course of about 1.5 billion years – or that our biologists have optimized by biotechnological methods. The desired products are as a rule obtained highly selectively and with very good yields. In many instances, however, isolating the products does pose problems. Most of our customers are pharmaceutical companies who, quite understandably, demand extremely high purity of the intermediates they use to synthesize active ingredients. Customers often will not tolerate more than 0.1% of a by-product, and of course you must prevent any undesirable side-reaction that may occur in preparation.

How did you solve these problems?

K. Ditrich: Most of these side reactions are the result of impurities that act as catalysts, of long residence times and thermal exposure, and can be avoided only if you apply intelligent process and preparation concepts and ensure optimum plant design. This has been accomplished in BASF's plants producing optically active amines. It is only owing to the special design of the preparation part of the production facility that we can achieve high chemical and optical purities in the manufacture of optically active amines. Our smart engineers have done a wonderful job there.

So, it really was a team effort.

K. Ditrich: Indeed! I do not consider the award of the Siegfried Medal to be a personal success of mine, but rather as a reward for the work done by the whole Chipros team, which includes many colleagues from research, process development, production facilities and, last but not least, marketing. In my experience, a successful project is always the result of a committed team working together, with everybody working in the same direction. In the case of optically active amines, working in this way, we needed no more than six years from the first steps of working out the process until we put into operation a purpose-built plant that is designed to fit this particular process.

At which sites do you operate the processes you helped to develop, and what are their output volumes?

K. Ditrich: We currently operate two facilities that produce Chipros in Ludwigshafen, Germany, and one in Geismar, La. (U.S.). While the Ludwigshafen plants are designed to function as multi-product facilities, we use the U.S. production facility exclusively to make an optically active amine that is needed as an intermediate in synthesizing a corn herbicide which BASF markets. The total production capacity of all facilities is around 5,000 mt/y.

The biotech pilot plant is equipped with a large number of pilot-scale reactors complete with process control system for the active further development and optimization of existing processes and the development of new large-scale fermentation processes.

Could you tell us what projects you are dealing with at the moment?

K. Ditrich: My work focuses on the synthesis and production of optically active amines. I am convinced that we have every right to claim that BASF has built an excellent reputation in the pharmaceutical industry as a source for this category of substances. True to our motto – "We help our customers to be more successful" – we are prepared to support even very early stages in the development of new active ingredients by synthesizing small kilogram batches of optically active intermediates that may be required. At present, we have some very promising amines in our pipeline, which we hope will represent a highly interesting sales potential in the future. Bearing in mind our agreements with customers, I cannot name any specific molecules, but I can assure you that we are not getting bored.

BASF has nearly three decades of experience in biotechnology. The company employs biotechnological processes to manufacture different products, including enzymes, and chiral intermediates, using live cells or enzymatic processes.

Chiral intermediates are examples of white biotechnology, also known as industrial biotechnology, being used successfully. Since when has BASF been looking at biotechnological processes?

K. Ditrich: BASF has been working in white biotechnology since the early 1980s. Our first successes were intermediates obtained by biocatalysis for the synthesis of optically active herbicides, and the fermentation processes for making vitamins (vitamin B2) and amino acids.

What potential for this key technology of the 21st century do you see in other areas?

K. Ditrich: Whether white biotechnology will ever play a significant role in the production of simple bulk chemicals that are currently produced on a petrochemical basis seems doubtful to me. I am, however, firmly convinced that in the future it will play a major role in producing fuels like bioethanol, biobutanol or biogas from renewable resources. At a time when fossil resources are becoming scarcer, it is increasingly important that we use nature's synthesis potential – which in most cases is carbon-neutral to boot – more efficiently, and precisely in this area biocatalysts will be essential.

▶ Contact:
Prof. Dr. Klaus Ditrich
BASF SE
Tel.: +49 621 60 41734
klaus.ditrich@basf.com
pharma-intermediates-europe@basf.com
www.basf.com

Staying One Step Ahead

Industry Leaders Discuss This Year's Hottest Topics

Divided Opinions – One evergreen issue at the CPhI is the regulation of APIs and excipients. Is there enough regulation or not? The opinions here are as varied as the industry leaders CHEManager Europe interviewed for its annual CPhI Roundup. Find out what else they are saying about the future of the industry, technological development, competition and much more.

What issues do you see shaping the industry in the coming year?

Lukas von Hippel
Vice president, marketing and sales, AllessaChemie

L. von Hippel: The housing crisis in the U.S. is not only an issue for the bankers, but for all of us – if consumers for whatever reason do not consume, we will not be able to sell our products – and we have seen the effect on the stock markets this year as well as in the automotive industry. Inflation is back and will become an issue for all of us as well. Reach will have effects on the cost position of the producers of specialties. We might have to face the fact that some specialties will not longer be produced.

David Hipkiss
CEO Prosonix

D. Hipkiss: Our customers are increasingly understanding the importance and impact of how right, first-time advanced particle engineering can have major impact on formulation performance and clinical benefit. We believe that this will not only have a major effect on the efficiency of primary API manufacturing, but will also fundamentally change the way drug product is manufactured, with unnecessary secondary manufacturing operations becoming increasingly outdated.

G. Haering: It would be nice to know. A positive factor for Western fine chemicals companies has been the rapidly closing gap of value for API manufacturing between low-cost countries such as China and India and the western countries. is closing much faster than expected. We have noted recently that quotations for some non cGMP starting materials from China and Europe were almost equivalent and at the end not so far for a cGMP production in Switzerland or Ireland.

Bob Hartmayer
Business group director, president and CEO of DSM Pharmaceutical Products

B. Hartmayer: The issue of products coming off patent combined with less-than-robust pipelines is creating a major issue for the pharma market in general. This, of course, affects all areas of the supply chain. For the CMO, this has created opportunities as large pharma looks to outsource more as a means of reducing costs.

F. Wicks: Pharmaceutical growth remains robust, but the rate of introduction of new drugs is still relatively low. As a result, the pharma industry remains in cost-reduction mode, which means there are a lot of opportunities for providers of contract manufacturing and other key services. Another industry trend is the continued shift away from traditional small-molecule API-based drugs to biologic drugs, and those based on high-potency APIs. Risk mitigation and quality assurance is also a growing issue for pharma firms, particularly in the wake of problems with the blood-thinning drug, heparin, which was blamed on problems at a Chinese supplier.

W. Schmitz: In the west, consolidation of the fine chemicals sector is at an early stage and is long overdue after the excessive increases in capacity during the 1990s. At Saltigo, our focus is on developing our custom manufacturing business – with attractive models for technology, plants, sourcing, service and partnership – into flexible, cost-efficient customer service units. Additionally we are following the consolidation developments in the fine chemicals market closely and are open to any suggestions that will help us make our range of services even more attractive to our customers.

R. Chantillon: The pharmaceutical industry is undergoing dramatic change. A major trend is the outsourcing of many services by the major pharma companies including manufacturing. The pressure from generics and competition within the generics industry, with increasing Asian presence, is putting pressure on prices when the market is moving in the opposite direction because of oil and energy price rises. This is compounded by increases in regulation and higher supply chain costs.

What issues do you see shaping the industry in the coming year?

T. Hoshiba: There are a number of important issues for the industry in the upcoming 12 months. Not least of these is in which direction energy prices will move. In the last few weeks, the trend has been downward, but it is hard to see exactly where things are going in the mid to long term. Another very important point for our line of business is the roll-out of Reach. This will have a big impact even for companies not directly affected, as many larger client companies are making assisting them with their Reachcompliance an important criterion when choosing suppliers.

M. Aslam: Increased competition from Asian countries coupled with increased pricing pressure from customers is prompting fine chemical manufacturers to come up with new technological solutions to reduce cost and still be able to maintain margins. A good example is continuous processing. Need promotes innovation, and in the pharmaceutical fine chemical industry, the need to lower operating cost will trigger development of efficient technologies such as continuous processing. Green chemistry initiatives will play a major role in the next few years. Increased pressure from regulatory agencies coupled with increased public awareness and high waste disposal cost will drive pharmaceutical fine chemical manufacturers to develop atom efficient processes that minimize waste and reduces carbon footprint.

Dr. Dieter Gothier
Managing Director at hameln pharmaceuticals

D. Gothier: The rising energy costs will draw a higher attention to the transport costs for finished goods especially for low margin products. The need for a tougher regulation of the whole pharmaceutical supply chain in a globalized business will be a mayor discussion in the next years. The recent problems with heparin quality and the world wide bulge of drug counterfeit will be a booster for the call for additional regulation.

What new technologies have you recently implemented into your portfolio?

A. Meudt: We have developed several new technologies in the areas of organometallic chemistry, enzymatic reactions, air oxidation of glycols and nitrations. To give just a few examples, we have introduced a nickel-catalysed synthesis of boronic acid esters that are not accessible by standard methods, improved enzymatic methods for making chiral mandelic acids and oxiranes, processes for making high-purity oxa acids by air oxidation of glycols, and semi-continuous processes for nitric acid ester formation of diols.

C. Le Ret: Within Umicore's business line Precious Metals Chemistry, and within the life science industries, we strive to develop at industrial scale of catalysts with improved efficiency. That was the case about 18 months ago when we launched Neolyst M4 series: metathesis catalysts based on Ghent University Professor Verpoort's technology having as main feature to be latent. They are very stable catalysts and they need specific thermal or chemical conditions to become activate, which make them of great interest in reactions such as polymerization or ring closing metathesis, the latter being of great interest to synthesize molecules containing large rings.

Do you think APIs and excipients are adequately regulated? If no, what must be improved?

P. Murin: No. Look at some of the very real – and tragic – problems that have occurred over the past few years. I believe the regulations should be harmonized globally to something like we have here in the U.S.

Wolfgang Schmitz
CEO of Saltigo

W. Schmitz: The production of APIs is adequately regulated to ensure patient safety. However, these regulations are not equally enforced throughout all countries and companies. Therefore, not every company is producing according to these standards. In the interest of patient safety globally consistent standards have to be enforced by the authorities in order to avoid fatalities like in the recent heparin case.

G. Haering: APIs are definitely well regulated. It is important to highlight that the quality requirements of the pharma partners are often much higher than the authorities themselves. Having regular audits from partners once or twice a month, from the Swiss authorities once every two years and from the U.S. Food and Drug Administration once every three years with no major remarks is a confirmation for us that we are doing well.

It will be interesting to monitor the future trends of more stringent requirements from the quality point of view in conflict with the request of reducing the cost of the pharmaceutical products. As we all know: Perfection is desirable, but is unaffordable from an economical point of view.

M. Aslam: AFC's primary focus is cGMP production of intermediates and APIs. In our view, regulatory agencies, such as the FDA, are doing a great job in ensuring that fine chemical manufacturers are building quality into their processes – a key attribute for producing high quality products. We truly believe that APIs are well regulated in U.S. We also believe that regulatory agencies are working with industry to truly understand the needs and challenges of producing fine chemicals in a regulated environment. For example, the recent revision of cGMP requirements for Phase I products will allow more flexibility and thus allow faster development of new drugs.

D. Hipkiss: Yes. We were also pleased to see a relaxation in the rules from the U.S. Food and Drug Administration requiring Phase 1 material to be made to full cGMP standards.

L. von Hippel: According to our understanding, we have regulations which are strong and well defined. We believe it is not necessary to improve the regulations themselves. However, what might be improved is the performance of those claiming to follow the rules. That's why we have worked for some time at European level within the AIME group of Cefic's EFCG to come to voluntary guidelines – to improve quality, safety and standards. Not with the intention to set a new standards, but to make those we have to be applied – on a voluntary basis for the benefit of all consumers.

B. Hartmayer: The need for FDA audits around the world is constant and has a direct impact on current viable partners for API delivery. As the industry becomes more globalized, the issue of resources needed to keep up will only continue to intensify.

R. Chantillon: The framework for regulations of APIs and excipients is well established with the latest EU directives like GMP Part II and industry sponsored guidelines like those from the International Pharmaceutical Excipients Council (IPEC), of which Univar is member. However, I believe that in order to enhance efficiency, standard formats need to be implemented so that suppliers can demonstrate to manufacturers the quality of their products. Currently, each pharmaceutical manufacturer still has their own system for checking raw material quality especially with the regard to excipients. The result is that the suppliers and distributors, in particular, are inundated with quality questionnaires which add significantly to our costs. For this reason, Univar fully supports initiatives such as the Excipient Information Pack (EIP) currently being drawn up by IPEC which will provide consistent information for a given product for many customers.

D. Gothier: Yes, I think there is an adequate level of regulation but of course the enforcement of these regulations has become more difficult in a globalized economy.

Martin Widmann
Head of global business unit Pharma Ingredients and Services at BASF

M. Widmann: Current good manufacturing practice (cGMP) regulations are the key to reliable pharmaceutical product quality and ultimately patient safety. Apart from the production of active pharmaceutical ingredients, the manufacturing of pharmaceutical excipients has not been subject to certified cGMP standards until now. BASF certainly considers pharmaceutical excipients cGMP certification and its legal enforcement as absolutely necessary and is therefore actively supporting the activities of EFCG and IPEC Europe in this respect.

> *"Perfection is desirable, but is unaffordable from an economical point of view."*
>
> Gabriel Haering, Director Head Business Development Chemical Operations, Helsinn Chemicals

A. Meudt: With regards to U.S. Food and Drug Administration inspection of API production plants, there is need for improvement for Asian plants. Especially the frequency of inspections need to be higher, given the significant risk for consumers if quality standards are inadequate.

Where do you see opportunities for technological progress in the field of API development and synthesis?

Andreas Meudt
MD New Business Development/Global R&D Director, Archimica Group

A. Meudt: We see significant potential in the application of enzymatic technologies in organic synthesis. The outstanding potential of these technologies is far from being fully utilized. For instance, an enzymatic Archimica technology allows synthesis of enantiopure oxiranes in almost quantitative yields – such reactive intermediates are extremely versatile building blocks for a variety of APIs, including products which have been made by different and less economic routes before.

C. Le Ret: Any new product or technical service that would simplify the chemist's life is a progress. That is why Umicore concentrates on developing more active, more selective as well as more versatile catalysts, together with more efficient and reliable metal recovery technologies and services. Shortening synthesis pathways by using a metathesis reaction and reducing wastes by having an increased metal recovery is where we see ultimate progress.

What role do countries such as China and India play in terms of competitiveness for your business?

Tom Hoshiba
General manager, TCI Europe

T. Hoshiba: Ask anybody in our business, and they will tell you that the challenge coming out of India and China is intense. The primary impact is of course on price competitiveness although rapidly-improving quality and logistics on the part of suppliers in both of these regions is also a major factor. There is absolutely no room for complacency. To stay ahead of the game we must strive for ever greater efficiency and competitiveness. We also need to innovate. Then again, when thinking about the challenges presented by the rise of India and China, I am reminded of the Japanese word kiki which means "difficulty" or "crisis." It is composed of two Chinese characters which when written separately mean "danger" and "opportunity." This always serves to remind us that where there is a challenge, there is also an opportunity.

F. Wicks: China and India have, to date, offered the benefit of lower production costs, although costs are starting to be in closer alignment with those in the west, particularly with their need to improve quality, HSE standards and fuel costs. That said, they do offer efficiencies in manufacturing that we are embracing. Efficiencies are not the only driver. It is also important to have a presence in China and India because of the size and growth of their respective markets and the presence of many major global pharma firms there.

L. von Hippel: China and India have been the countries challenging the industry. This helped to push custom synthesis to improve processes, efficiency and to speed up processes. In addition, our customers understood to use the resulting overcapacity to bring prices down, sometimes too low, leading to the consolidation we have seen. However, besides that, sometimes it was a squeeze-out process leading to capacity shut down. Once the capacity was gone, prices came up to former levels or even higher. As a consequence, the geo-political risk for some companies became more and more relevant, especially when the last western source disappeared. We have noticed movements back to Europe especially for the nonGMP intermediates we offer over the last year. This

shows us that doing our homework has paid off. We will most likely never be able to have the cost structure of a Chinese or Indian company, but we claim to have high standards at reasonable costs: When we ship a batch of 20 t in 100 drums, it will be just one batch, but not 100, which influences at least costs of analytics.

B. Hartmayer: Cost reduction is becoming more and more of an issue. We do see opportunities to improve our competitiveness by sourcing raw materials in these regions. Additionally, China can be seen as a developing market of pharmaceutical consumers.

W. Schmitz: Indian and Chinese companies have made noticable progress on improving their service offerings. According to our customers, they are widely accepted in the areas of generic APIs, raw materials and early intermediates. However, there still seem to be some concerns around IP. More importantly, the recent Heparin case proved that CGMP standards are not fully implemented everywhere. These quality issues have raised serious concerns regarding patient safety as widely discussed in the media. Regarding cost competitiveness, we have seen remarkable cost increases from materials we source from India and China. With growing standard of living, salaries, energy cost etc. we have witnessed that much of the previous low cost advantage disappeared and we expect this trend to continue.

Roger Chantillon
Industry Business Director of Univar Europe

R. Chantillon: Univar has been sourcing from China and India for over 20 years. The local offices continue to grow and are an increasing source of new materials for us. We remain vigilant to ensure we are targeting the right partners who can offer products with the appropriate quality standards and we offer the advantage of a Reach program which overseas suppliers can leverage. Clearly some of the manufacture is moving to Asia, and yet pharma manufacturing in Europe remains strong.

Peter Murin
CEO of Halocarbon

P. Murin: Their recent rise pushed down pricing for a lot companies, including ours. Fortunately, we were able to compete, although it was painful and have growing sales into Asia. Pricing is improving recently, and I expect that trend to continue as the true costs of responsibly manufacturing chemicals are reflected in their prices.

Dr. Henning Witte-Abel
Global business unit manager Customer Manufacturing at DyStar

H. Witte-Abel: China and India will develop further in future and play an important role in the market. We expect further grow for our division to come from focusing on our strengths: service, solution-provider and an enormous range of chemical syntheses at production facilities around the world.

M. Aslam: India and China provide the raw materials that allow us to focus on our core technologies and thus enhance our competitive position in the pharma industry. However, in order to ensure quality and assurance of supply, we work very closely with our suppliers.

A. Meudt: For the highly differentiated "high-tech building block" business, Asian competition still does not play a major role. Western companies who can offer differentiation won't suffer massively from Asian competition. In addition, many pharma firms who have "tested" Asian suppliers in the past years have had to learn unpleasant lessons, so there is a significant return to reliable Western suppliers. However, in the area of generic APIs, particularly Indian competition is taking over more and more market share from Western companies.

D. Hipkiss: Being a technology-led business, we have been largely immune to cost pressures exerted by Indian and Chinese companies on more typical API producer companies. We do, however, expect to forming one or two key CMO partnerships with leading Indian based firms in the year ahead in order to meet the increasing demands of our pharmaceutical customers who are requiring us to provide highly engineered API particles for their own use.

"Where there is a challenge, there is also an opportunity."

Tom Hoshiba, General manager, TCI Europe

Competition for pharmaceutical projects is getting tougher. How have development partnerships been changing over the years?

R. Chantillon: Univar is typically involved in projects focused around improving the efficiency of raw material supply chains. This has the two-fold benefit of reducing complexity and cost for both suppliers and customers alike. There is increasing interest in these approaches as outsourcing, in general, becomes a major trend in the industry.

Frank Wicks
President of SAFC

F. Wicks: It is our opinion that pharmaceutical companies are placing greater importance on their external partnerships as the outsourcing trend continues to grow in the drug development business. Companies such as ours are benefiting from this trend as we have developed a one-stop shop for our partners, providing them with support all the way along the development pipeline, from sourcing to commercialization.

W. Schmitz: Drug development partnerships have been the established relationship format for the interaction between custom manufacturing and development organizations and emerging and virtual mid-size pharma companies for some time now. With the recent reduction of manufacturing and scale-up capacity at major pharma companies, we have experienced a change of the interaction towards the same format. The main difference is the formation of teams across companies and more intense interaction on all levels and within all disciplines involved in the process.

M. Aslam: Competition for pharmaceutical projects is getting tougher. However, with a long term view on relationship and our ability to provide value through our core technologies, we have expanded our customer base. In our view, it is critical to maintain open communication with our customers, provide excellent technical support, and focus on cost reduction initiatives to retain our competitive advantage. This has helped AFC expand the customer base and the product portfolio.

T. Hoshiba: Not only has competition been getting tougher, but setting up projects has become very much more complicated over the last few years. Back in the day, such partnerships were generally much more localized affairs conducted between a local client and a local business partner. Of late however, the whole process has become globalized. This has opened the market up to a greater number of players, and contracts are increasingly likely to be concluded between partners in different continents and time zones. As a result, firms bidding for projects have to be much more aware of differences in business culture and communication. On top of this, developments in information technology mean that differences in price and lead time between suppliers are much more accessible than previously and much more rapidly communicated to the client. With more potential partners providing more information more quickly, things are very much more complex and competitive than they used to be, even five years ago. Responding to these new business realities whilst maintaining high levels of confidentiality, customer service and professionalism is a real challenge to everybody in the industry.

D. Hipkiss: We are focused on our core area of expertise of providing commercially viable ultrasonic particle engineering solutions and the ideal means to practice them at industrial scale. Given our increasing track record across all scales, in actuality the number and quality of partnerships with pharmaceutical companies has increased significantly. We expect this trend to continue over the year ahead.

Gabriel Haering
Director Head Business Development Chemical Operations, Helsinn Chemicals

G. Haering: I would say that nothing has changed over the past years. Human relationship and communication are the keys to a healthy partnership. Talking with our partners and understanding what we do well or where we could improve means also working on good partnership management. Face-to-face meetings and regular teleconferences keeps alive a good partnership alive and creates trust over time.

B. Hartmayer: With a growing need for outsourcing partners, those with the capabilities, costing and quality to meet their needs in a sustainable, long-term relationship will be essential. We see these as critical parameters that pharma companies are looking for in their strategic partners.

A. Meudt: The large pharmaceutical firms have been focusing more and more on preferred supplier relationships to reduce complexity in their supply chains. This results in few contract manufacturing organizations ,which will be performing quite well because of being selected into this premier league and many others who will lose business. Archimica feels well situated in this rivalry, having been selected already by four of the top 10 pharma firms as a preferred supplier.

What are the major requirements of pharmaceutical customers when choosing a development or manufacturing partner?

W. Schmitz: Our customers expect first and foremost high-quality standards and full compliance with industry standards such as cGMP, flexibility, long-term committment. An established track record in applying a broad variety of chemistries and technologies is a prerequisite. Proactive efforts on continuous improvement of all aspects of the project are required to maintain the business. Innovation like establishing new technologies such as micro reactors is important as a differentiation factor.

L. von Hippel: That's a difficult question, because requirements vary not only from company to company, but also from project to project. As a general conclusion, professionals want to deal with professionals. And professionals have clear criteria what they are looking for and what they can expect. The expectations are not only driven by technical facts, but also by the ability of companies to interact and the company culture: Every project has its own challenges and its own key decision criteria. We will never be the right partner for every project, and we are even not trying to be it. We work hard to be efficient, honest and reliable, right from the beginning. This is part of the service we offer and this is why professionals like to cooperate with us.

B. Hartmayer: I think we must assume that quality and reliability are not negotiable. In addition, cost competitiveness is rapidly increasing in importance. Finally, a long-term track record of performance is essential to instill a high level of trust and confidence.

F. Wicks: Pharma firms want a trusted, financially strong partner with strong chemistry knowledge and project management expertise, backed up by a wide breadth of products and services that can provide support at all points of the drug development pipeline. It is also key to be able to offer an array of complex technologies to support the latest generation of drugs, including high-potency APIs, biologics and conjugates. Having a global footprint is also important when dealing with the large, multi-national pharmaceutical firms, and possessing the ability to deal with regulatory compliance requirements around the world is equally sought after.

R. Chantillon: The major requirements are quality of procedures and processes, security of supply and demonstrable added value. Pharmaceutical customers want to reduce complexity of the apparently simple process of the supply of raw materials. It is in fact highly complex as a consequence of the narrow specifications and the requirement to consistently demonstrate the quality of each delivery.

D. Gothier: The requirements of pharmaceutical customers are as multifaceted as the requirements of their international markets and the different cultures and businesses. In the end it all comes down to providing a high level of customer perceived quality at a competitive price.

P. Murin: For raw material suppliers, they're cost and reliability. Reliability, quality and confidentiality – Halocarbon's strengths – are a higher priority for customers worried or who know because of past disappointment that they may get more problems than savings when going with the lowest price.

Malik Aslam
President of AFC

M. Aslam: Trust. Pharmaceutical customers need to have a level of confidence before they entrust you with the manufacturing of their product. In our experience, pharma customers are looking for a few basic criteria such as assurance of supply, quality, technical competence, safety, environmental and flexibility. Naturally, price is also an important factor. Ability to provide globally competitive pricing coupled with ability to reduce price by continuous improvement initiatives is key to winning projects from pharmaceutical customers.

T. Hoshiba: Obviously, precise requirements will vary from project to project and between business partners. However, in general, pharmaceutical companies require high product quality, technical competency at both the manufacturing and quality assurance stages, as well as appropriate manufacturing specifications and security of supply. They also need the assurance of absolute confidentiality and professionalism in the management of every stage of the project. In addition, I don't think I have yet met a customer who thinks price and lead time on a project are unimportant!

G. Haering: From recent surveys we have done with our partners, the top four requirements include soft factors such as timeliness, flexibility, relationship and value. The only hard factor in the top five was having U.S. FDA-inspected facilities. Other things, such as price, one-stop shopping service and geographic proximity were less important. Of course, this all can vary from company to company, but it also confirms that the human factors in the relationship are key in the success or the failure of the partnership.

A. Meudt: One-hundred percent reliability, service attitude, a broad technology portfolio including both classic technologies and modern chemistry capabilities, e. g. in organometallic/cryogenic chemistry and enzymatic applications, are amongst the key requirements.

Have you upgraded production plants or have you made investments in capacity expansion recently?

A. Meudt: Archimica is currently investing into expansions of its cryogenic capacity at its sites in Frankfurt, Germany and Bon Encontre, France. This goes along with the companies' strengths in organometallic chemistry which very often requires performing reactions down to –85 °C. With the success of Archimica's boronic acid product line and other cryogenic products, this expansion has become necessary to cope with growing customer demand.

Dr. Wilhelm Stahl
Head of Saltigo's Business Line Pharma

W. Stahl: In February 2008, we officially inaugurated a state-of-the-art multi-purpose unit for the production of active pharmaceutical ingredients and intermediates. This cGMP facility was built in 2006–07 based on an existing plant complex and cost around €10 million.

The unit has four production modules, three of which are approved for the production of APIs. With a total vessel volume of 142 m³, the plant has 44 m³ of stirred reactor volume with vessels ranging from 2.5 to 8 m³, plus a storage tank volume of 100 m³. It can produce both orally and intravenously administered APIs, including corrosive substances such as hydrochlorides. The plant is equipped with apparatus for performing reactions, work-up, crystallizing and recrystallizing under cGMP conditions. The well-trained production team has many years of manufacturing experience, also in dealing with customer and official audits. Furthermore, the plant is also very well integrated in the site's infrastructure, providing access, for example, to the piloting potential in the neighboring Central Organics Pilot Plant (ZeTO).

At the beginning of this year, Lanxess announced the establishment of a new site in Redmond, Washington, for Saltigo. We intend to use the facilities of the kilo lab and pilot plant, both of which meet cGMP standards, to produce APIs for early clinical testing up to and including Phase IIa in particular as a local service to emerging pharma companies. Timothy Fitzpatrick has been appointed manager of the new U.S. site, where up to 25 people are to be employed.

Christophe Le Ret
Director of business development, at Umicore

C. Le Ret: In May 2008 Umicore finalized the construction of a new Platinum API plant in Argentina. This plant strongly increases Umicore's production capacity and allows us to better accommodate our Platinum API customers worldwide. Oncology Platinum APIs are produced there according to the highest quality- and social standards. The cGMP approved plant, is compliant with ISO 9001 and 14001 and produces according to USP, EP and JP.

What do your investment plans look like for the foreseeable future?

A. Meudt: We will continue to invest into technology expansions as our technology and service offering in this area is amongst our most important differentiators for customers. The clear focus of these investments will be in our core technologies which are organometallic chemistry, enzymatic chemistry, hazardous reactions like nitrations and aseptic/sterile filtration.

W. Stahl: We will continue our process of investment to further enhance Saltigo's performance and competitiveness, and continuously adapt our facilities to the market requirements. In total, we plan to spend about €50 million before the end of 2010.

C. Le Ret: We plan to maintain our high R&D costs over the coming years, in order not only to keep more than 50% of products being less than 5 years old in our portfolio, but also to stay innovative towards our own processes and to keep optimizing them and improving our customers' satisfaction.

Principles Of Heterogeneous Catalysis

Part III: Catalyst Design

Catalysis – Parts I and II of this four-part series were published in CHEManager Europe 7-8/2008, and CHEManager Europe 9/2008, respectively (www.chemanager-europe.com). This sequel focuses on catalyst design.

Given that the performance of a catalyst is controlled by a limited number of kinetic parameters, it is unclear why it is so difficult to design a catalyst from molecular-level concepts. As noted above, during the early stages of research into a catalytic process, first we do not know which steps in the reaction mechanism are kinetically significant, and which species are most abundant on the catalyst surface under reaction conditions. Second, we do not often know the structure of the active site and its dependence on the nature of the reaction conditions. Third, we do not usually know how the activity and selectivity for the catalytic reaction depend on the structure of the active sites. Fourth, we do not typically know during these early stages the rates of various modes of catalyst deactivation (e.g., sintering, phase changes, deposition of carbonaceous deposits on the surface, etc.), and we do not know whether the catalyst can be regenerated following deactivation. Finally, we must ensure that the texture of the catalyst and the geometry of the reactor are designed in such a way that mass transport of reactants and products to and from the active sites is sufficiently rapid that high rates of reaction per unit volume of reactor can be achieved.

Catalyst Material

Because of these difficulties, the field of heterogeneous catalysis is highly interdisciplinary in nature, and involves close collaboration between experts in such areas as catalyst synthesis, catalyst characterization, surface spectroscopy, chemical kinetics, chemical reaction engineering and, most recently, in theoretical calculations of catalyst structure and performance using density function theory. These broad studies can be grouped into three levels.

All studies of heterogeneous catalysis begin at the materials level. High-surface area catalytic materials must be synthesized with specific structures and textures, the latter referring to such features as the sizes of the various phase domains and the details of the pore structure. Clearly, the synthesis of catalytic materials must be guided by detailed characterization studies to determine the structures, compositions, and textures of the materials that have been prepared. These characterization studies should be conducted after the catalyst has been subjected to various treatment steps (such as those treatments employed during activation of the catalytic material), and it is most desirable to carry out characterization studies of the catalyst under the actual reaction conditions of the catalytic process. Indeed, the properties of a heterogeneous catalyst are inherently dynamic in nature, and these properties often change dramatically with changes in the reaction conditions (e.g., phase changes, surface reconstructions, changes in surface versus bulk composition, etc.).

Catalyst Performance

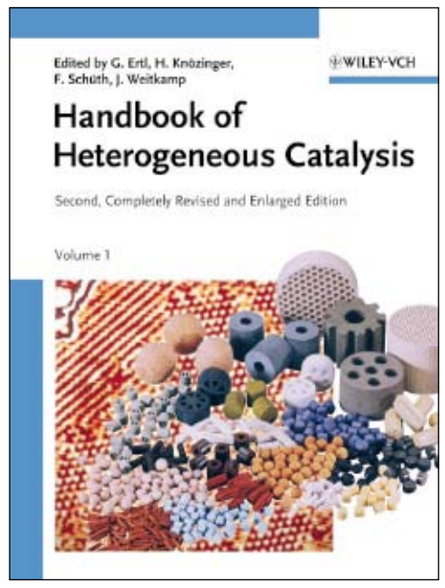
The central level of research and development of heterogeneous catalysts involves the quantification of catalyst performance (this is known as the catalyst performance level). These studies can be carried out in a preliminary fashion over a wide range of catalytic materials (e.g., high-throughput studies) to identify promising catalysts and reaction conditions for further studies. The performance of the catalyst is then documented in greater detail by determining catalytic activity, selectivity, and stability with respect to time-on-stream for various reaction conditions. These measurements must be made at various conversions when multiple reaction pathways exist, because catalytic selectivities in these cases are different, depending on whether the desired products are formed in primary vs. secondary reactions, or in series versus parallel pathways. We note here that various definitions of catalytic activity are used, depending on the nature of the study. For practical studies, catalytic activities can be reported as rates per gram of catalyst or per unit surface area. However, for more detailed studies or for research purposes, it is often desirable to report catalytic activities as rates per surface site (i.e., TOFs), with the number of surface sites measured most often by selective adsorption measurements (e.g., adsorption of H_2 or CO to titrate metal sites, adsorption of ammonia or pyridine to titrate acid sites). In some cases it is possible to report catalytic activity as rate per active site (also called TOF), when it is possible to distinguish active sites from the larger number of surface sites using special probe molecules (e.g., dissociative adsorption of N_2 to titrate sites for ammonia synthesis; selective poisoning by adsorbates that compete with the reactants of the catalytic reaction); or by transient isotopic tracing.

Fig.: Levels of study in heterogeneous catalysis research

Elucidation

For the purposes of catalyst development, it is probably sufficient to work at the materials level and the catalyst performance level. However, research into heterogeneous catalysis is dominated by studies conducted at a third level – the elucidation level – where the aim is to identify the fundamental building blocks of knowledge which can be assembled to build a molecular-level understanding of catalyst performance in order to guide further investigations to improve catalyst performance. At the Elucidation Level the studies are designed to determine the surface composition and nature of the surface sites on the catalyst. Clearly, these investigations must be conducted with the catalyst under controlled conditions (e.g., under ultra-high vacuum, after treatment with H_2, after calcination, etc.) and, where possible, such measurements should be made with the catalyst under reaction conditions. Moreover, the studies may be carried out on real catalytic materials and on more well-defined surfaces (e.g., single crystals, or model samples formed by depositing known amounts of materials onto well-defined supports). Most measurements at the elucidation level involve studies of the interactions of specific probe molecules with the catalyst surface. These probe molecules may be the reactants, intermediates, or products of the catalytic reaction, or they may be more simple species chosen to monitor a specific functionality of the surface. Alternatively, a molecule may be used as a probe because it has an advantageous feature for spectroscopic identification (e.g., CO for infrared studies, a 13C-containing molecule for NMR studies). These studies of the interaction of probe molecules with surfaces are designed to determine the surface concentrations of different types of surface site, to determine the nature of the adsorbed species formed on the surface sites, and to determine the reactivities of the surface sites by monitoring the adsorbed species on the surface versus time, versus temperature or, most commonly, during a temperature ramp (e.g., temperature-programmed desorption).

The third pillar of studies at the elucidation level involves the use of DFT calculations to assess the structures, stabilities, and reactivity of species adsorbed onto the surface sites (with the sites being composed of clusters of atoms or as periodic slabs of atoms). These studies are used to help interpret the results obtained from spectroscopic studies of catalyst surfaces (e.g., to predict the vibrational spectra of species adsorbed in different orientations on different sites), to calculate heats of adsorption for various intermediates in a reaction mechanism (e.g., to predict which species are expected to be abundant on the catalyst under reaction conditions), to estimate the energy changes for possible steps in a reaction mechanism (thereby eliminating from further consideration steps with very positive energy changes), and to determine activation energy barriers for steps that are suspected as being kinetically significant in the reaction scheme. Indeed, a key feature of these theoretical studies is the ability to predict how the surface properties are expected to change as the nature of the surface is altered (e.g., by changing the surface structure, or by adding possible promoters). This in turn will provide feedback to the materials level with regards to new materials that should be synthesized and which are likely to lead to an improved catalyst performance. In addition, these theoretically based studies provide information about highly reactive intermediates which might be difficult to obtain by direct experimental measurements. Most importantly, studies conducted at the elucidation level provide a scientific basis about the working catalysis that may, in future, be used to design different reaction pathways.



► James A. Dumesic (corresponding author)
University of Wisconsin, Madison, WI/USA
Tel: +1 608 262 1095
dumesic@engr.wisc.edu
George W. Huber, University of Massachusetts, Amherst, MA/USA
Michel Boudart, Stanford University, Stanford, CA/USA

* References available on: www.interscience.wiley.com/reference/hetcat

Part IV (Catalyst Development, Bridging Gaps in Heterogeneous Catalysis) will be published in CHEManager Europe 11/2009 (Oct. 30).

Water is Nowhere Near Enough

The Sepawa/EDC-Congress has Reached an International Level

Soaps and Detergents – From Oct. 15 – 17, 2008 Wuerzburg, Germany, will again be the centre of the Sepawa/EDC-Congress. The increasingly international orientation of the event shapes its themes and the expectations of visitors.

In personal care and laundry products, chemistry is the key not only to cleanliness, but nice looks and alluring scents. Photo: Henkel

The move from the familiar and well-acquainted surroundings of Bad Duerkheim has contributed to the progress of Sepawa (Association of Soap, Perfume and Detergent Experts e.V.). The move itself to the geographically more central but nevertheless beautiful city of Wuerzburg already sent out a very positive signal that was further amplified by the EDC event (European Detergents Congress), which from then on took place in collaboration with the Society of German Chemists (GDCh). The synergies of two strong partners, Sepawa and GDCh, could thus develop beneficially. Prof. Dr. Andre Laschewski, Potsdam, also considers this to be a very important aspect: "The combined event of Sepawa Congress and European Detergent Conference in Wuerzburg is a successful and at the same time highly informative event. It presents the state of the art in the developments of surfactants, detergents and formulations in Europe on an exceptionally broad level reaching from science to development and application to the regulatory sector." With the third pillar of the event, the incorporated exhibition of various kinds of businesses – small and medium-sized (SMB), research institutions and large-scale businesses of the chemical industry – the organizers of the event have completely realized their objective of creating a forum for science, application and business.

Sepawa is on the Right Track

In the run-up to the fourth mutual Sepawa/GDCh – event and after having worked together for meanwhile three years, an additional trend has become obvious: The congress that originally had a bonding effect on a national scale is increasingly adopting an international profile. This was confirmed by Robert Fischer, member of the Sepawa-executive board, when he said, "Increasing numbers of visitors and the continuously high demand for exhibition opportunities prove that Sepawa is on the right track. Hence, in 2007 we had about 200 participants from non-German speaking countries and in 2008 there will even be 31 exhibitors from abroad who have registered their participation." Latest developments and trends within Europe are also essential information for smaller businesses that are not in a position to switch to English as their business language at any given time. Following the example of Sepawa very active groups have been formed in several European countries in order to ensure the rapid, uncomplicated exchange of expertise locally. Lothar Rasthofer, president of Sepawa, is sure that "the specific experiences of these sections from countries such as Scandinavia, Benelux, Austria, Switzerland and the Ukraine are going to enrich the discussion," and goes on by confirming "the goal of reaching ever more internationality will continue to be pursued for all four market segments: detergents and cleaners, cosmetics, perfumery and the chemical industry. This is also an important impulse for our specialized groups who in turn encourage and pursue professional discussions with their own events."

Discussing Future Subjects Today

With the growth of the event into a European meeting point, businesses have a chance to address and discuss topics concerning the European Economic Area already at an early stage. "The increasing marketing of many products throughout Europe raises the issue of necessary regional differences in various product groups. Thus, in the case of foodstuffs it is a known fact and common practice to adjust the taste of products to regional preferences. "This means, tomato ketchup in Italy may well taste different from the product of the same brand name sold in Germany or Scandinavia," said Prof. Dr. Klaus-Peter Wittern, Beiersdorf.

These are issues that result from the regional variety in Europe and do not only apply in the food industry. The current world market situation is going to be an additional central topic among the participants. Horst Waltenberger, member of the Impag and Sepawa-Executive Board, said: "The Sepawa-Congress will become ever more significant to the European extractive industry and formulators. Especially in times when the supply of raw materials has become unstable there is a great need for networks to intensify their cooperation – in other words they have to close ranks." The fact that this closing of ranks can take place here in such an uncomplicated manner every year is an important argument for the "Future of Germany Inc." In his formal address, Wolfgang Grupp, Trigema, will focus exactly on this topic, especially in the face of growing markets in the East. "Sepawa and particularly the European Detergent Conference offers an excellent market for innovations and trends," said Dr. Thomas Mueller-Kirschbaum, Henkel, and continues, "I do not know of any other annual conference that offers nearly the same abundance of chemical-technical information and the opportunity to interact with our innovation partners of the supplying industry. Therefore, I am in great expectation again of gaining many impulses from discussions with smaller and larger suppliers as well as from the many talks."

During his tour of last year's Sepawa Congress, Prof. Dr. Klaus Töpfer shows himself impressed by the great diversity displayed in the exhibition.

A Forum Of Generations

Practice-related and economic problems are not examined to the same degree in every study course; therefore, the association wants to lend a helping hand. "I see it as a special responsibility of Sepawa to introduce young professionals to its topics. Thus we invite academic students to attend our conference free of charge and award Sepawa-grants to PhD students and students of technical colleges," said Prof. Dr. Ulrich Buller, 2nd President of Sepawa and head of the Research Committee of the Fraunhofer-Gesellschaft.

The Magic Of Scent

The event of the DGP (German Society of Perfumers) has the very promising title "In Every Sense." Whoever though feels he can still somewhat resist this magic can find out more about the scientific reasons behind the magic of our senses and it's clever application, by listening to Prof. Dr. Th. Hummel, Dresden, and Simon Harrop, Brand Sense Agency, Oxford.

► Contact:
Tel.: +49 821 3258 321
Fax: +49 821 3258 322
www.sepawa.com

Rare In Nature

Fluorinated Compounds Becoming Increasingly Important for Pharma, Agro

Many Possibilities – Organofluorine chemistry has achieved great importance in numerous significant industrial and technological developments over the last few decades and today represents, more than ever, a vast and rapidly expanding field.

Wolfgang Ebenbeck
Head of Saltigo's
Fluorine Team

The development of chlorofluorocarbons (CFCs) and fluorocarbons (FCs) in the 1930s as inert refrigerants earmarked the beginning of widespread industrial applications of organofluorine compounds and gave the impetus for the development of other fields of applications for fluorocarbons such as fire-extinguishants (Halons) and foam blowing agents (e.g. CFC-11). Fluorocarbons have also been used in the health care as inhalation anaesthetics (Desfluran) or artificial blood substitute (perfluorodecalin). The discovery of polytetrafluoroethylen (PTFE) in 1938 established the presently largest industrial application of fluorine chemistry and has opend the field for new applications derived from fluoropolymer-industry (e.g. fuel cells). Other important fields for future industrial applications are the use of fluorocompounds for liquid crystals and electronic chemicals. Fluoroaromatic compounds have first been employed as reactive intermediates for dyestuff, and more recently in the life science sector as intermediates for pharmaceutical and crop protection products.

Fluorine Chemistry in Life Science

Organofluorine chemistry has recently entered the life science sector – particularly the area of drug discovery – and fluorinated compounds have become increasingly important as key building blocks for highly effective drugs in pharmaceutical and crop protection products.

However, given the fact that fluorinated products are quite rare in nature (only 13 naturally occurring organofluorine metabolites) and the fact that one key approach in traditional medicinal chemistry is to revert to the naturally occuring pool of biologically active compounds for indentifying new lead structures reflects the consequence that until the 1970s fluorinated compounds have been rarely encountered as starting points for new drugs in medicinal chemistry.

Since then organofluorine chemistry became an essential tool in the design and synthesis of new biologically active substances. Today, more than 150 fluorinated drugs have come to market and 20% of all pharmaceuticals and 30–40% of all agrochemicals are estimated to contain at least one fluorine atom; in development stage at least half of the drug candidates contain fluorine. This growing demand for fluorinated compounds in the life science area is due to the unique and significant effects by incorporating fluorine or a fluoro containing group into a biologically active compound changing its biological and physical properties including its stability, lipophilicity and bioavailability.

Recent Developments

Despite the abundant array of new fluorinating agents and the growing inventory of synthetic fluorinated compounds, there is still an increasing demand for developing scalable and cost efficient fluorination methods and new synthesis strategies for fluorinated compounds. Saltigo's Fluorine Team and its process development units have recently made major achievements in various fields of organofluorine chemistry, in particular in the development of new scalable fluorination methods and technologies applied in custom synthesis and custom manufacturing:

- **New phase-transfer catalysts for Halex**
  The Halex reaction (halogen-exchange reaction) represents one of the most commonly used transformations in organofluorine chemistry and plays an important role in the large scale manufacturing of fluoroaromatics, the most widely used class of biologically active compounds in the pharmaceutical and agrochemical sector.

  In general, chloroaromatics activated towards nucleophilic substitution by electron-withdrawing groups, are reacted with a fluoride source at high reaction temperatures (160–240 °C) to yield the corresponding fluoroarenes. Typically, the reaction is supported by the presence of a phase-transfer catalyst to increase of the effective fluoride concentration and to improve the rate of reaction. Saltigo's Fluorine Team has developed a new generation of highly effective and thermally stable CNC- and PNC-phase-transfer catalysts, and has opened the way for new synthetic routes in HALEX chemistry by enabling the halogen-exchange of even unactivated substrates, such as 3,5-dichloropyridine or 1,3,5-trichlorobenzene.

- **PBSF: A mild and selective fluorinating agent of chiral hydroxy groups**
  The conversion of chiral hydroxy groups into enantiomerically pure fluoro compounds on technical scale presents a significant challenge to process chemistry. Many reagents have been developed for this type of transformation, such as DAST, Deoxo-Fluor, fluoroalkylamines (FARs) or complexes of amines with HF (NEt3*3HF, Olah's reagent), but due to their limited stability, availability or high price these reagents are often limited to lab scale synthesis. Saltigo has developed a safe and robust industrial fluorination process for the selective conversion of chiral hydroxy compounds into the corresponding fluoro compounds using perfluorobutanesulfonyl fluoride (PBSF), which is produced at Lanxess, is stable to air and moisture and allows a safe and easy handling on technical scale.

- **Saltigo's custom research service in organofluorine chemistry for life science R&D**
  Saltigo's Fluorine Team provides custom research service for life science R&D in the field of organofluorine chemistry. Our team of experts supports the activities of our customers in medical research and preclinical development by providing innovative methods and custom-synthesis of new and non-commercial fluoro compounds. Access to more than 4,000 rare fluorinated building blocks on stock and more than 24,000 reports for the synthesis of fluorinated synthons enables us to offer the best possible service for our customers in the life science sector.

Technical Requirements

Handling fluorine chemistry still remains a specialist's field and requires special technical equipment, highly skilled people and extensive experience to gain the best results.

Numerous fluorinating methods for the selective incorporation of fluorine or fluoro-containing groups (e.g. CF_3, OCF_3, SCF_3) often require reagents such as anhydrous HF, elemental fluorine or SF_4. These reagents are often toxic, corrosive, dangerous and difficult to work with and therefore require special equipment (autoclaves, safety measurements, special apparatus for HF-distillation etc), which does not belong to a standard set-up in most research labs. While anhydrous HF is the preferred reagent for industrial fluorinations at technical scale (HF-diazotisation, halogene-exchange) many new and versatile fluorination agents (Deoxofluor, electrophilic fluorination reagents, fluoroalkylamines (FARs)) have been designed and developed in recent years, which allow easy handling and are useful reagents for fluorinations on lab-scale, e.g. in medicinal chemistry. Due to their limited stability, availability and high price these reagents are not preferred for technical scale.

The Saltigo Fluorine Team represents more then 40 years of profound expertise in organofluorine chemistry, which embodies a major key competence within Saltigo's widespread research and technology platform. The Fluorine Team has developed a broad range of fluorination methods and technologies including anhydrous HF-chemistry and high-pressure Halex reactions and our team of experts will assist clients in handling this chemical challenge right from the beginning, in their research and development activities.

Contact:
Ilona Bolz
Lanxess, Leverkusen, Germany
Tel.: +49 214 30 61684
Fax: +49 214 30 44865
ilona.bolz@lanxess.com
www.lanxess.com

Never Out Of Style

How Chemicals Improve the Look, Feel and Durability of Leathers

Innovation – Nothing moves faster than fashion trends, and leather is one of the most exciting materials that meets all demands each season.

Tanners often comment that there has been a lack of real innovation in the wet end, at least for the last decade. However, the same old problems they have always been facing are getting much worse as the quality of raw hides and skins continues to decrease. Lanxess is among the few suppliers to the leather industry who has virtually all necessary chemicals in its product range. These are inorganic and synthetic tanning agents, preservatives, fatliquors, dyestuffs, as well as tanning and finishing auxiliaries. Cooperation agreements with Rohm and Haas and Atlas Refinery have enlarged Lanxess' product range even further.

Structural Upgrading

The use of thermoexpandable microspheres in the retanning process for structural upgrading of collagen is a technology that opens up completely new possibilities. These opportunities include improvement in leather quality, and in turn the ability to attain higher yields in terms of area utilization with a more regular surface appearance.

This new technology consists of a new functional product, a special polymer dispersion that contains the micro-spheres, and a new, customized expansion technology.

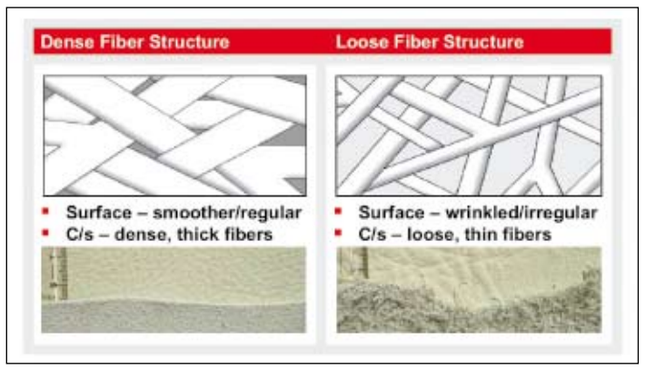


Fig. 1: Structural Defect No. 1: Looseness

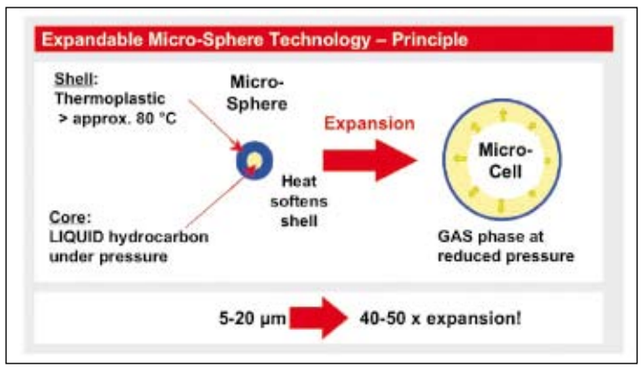


Fig. 2: From Micro-Spheres to Micro-Cells

Fig. 3: How to Expand Micro-Spheres Effectively

The polymer dispersion, known as Levotan X-Cel, contains compact microspheres of an average diameter approximately between 5 and 20µ. The spheres, which are filled with a liquid gas, can expand up to 40 times their original volume size, thereby becoming bigger microcells.

The use of this polymer dispersion system always has to be followed by a thermo-activated expansion step. During this expansion process the liquid gas in the unexpanded microspheres converts into the gas phase. The pressure inside the sphere becomes reduced by enlargement and the density of the particle changes significantly from approximately 1,000g/dm³ in the unexpanded form to about 30g/dm³ in the expanded form. It is important to know that in both forms the shell of the microcells is absolutely impermeable. The gas cannot escape without the destruction of the cell itself.

One of the main reasons for the use of microsphere technology in the leather making process is the upgrading of the internal structure of leather. This new application for the leather industry gives tanners the new potential to upgrade lower quality leather, something tanners have long wished for.

The microcells, through expansion, can fill open and loose areas inside the leather. It can be described as a type of "internal stucco" to upgrade the structure of leather. The polymer containing the microspheres is added in the retanning step at a relatively early stage of this wet end process.

In contrast to conventional retanning chemicals, the distribution of the micro-spheres is by diffusion. Their final distribution in the leather is complementary to that of standard retanning chemicals. Therefore, through expansion they can "fill" areas inside of the leather in a manner that cannot be achieved by syntans, retanning polymers or resins.

Once the microspheres have been added to the process, retanning and drying processes follow as usual. Since the customary drying process, through vacuum or toggling, is not sufficient to activate the unexpanded microspheres, an additional process step is required for activation. This is performed using a special machine where the dry crust leather is passed through a channel where it is treated with hot, saturated steam for several seconds only.

The hot steam penetrates into the leather without making it wet, and the humidity transports the temperature, within seconds, internally to the unexpanded microspheres. These special conditions of humidity and temperature lead to a softening of the microspheres shell, and they expand instantly to form the much larger microcells.

Once the microspheres are expanded, they cannot be removed, and permanent elastic filling has been achieved. The voids, veins and loose parts in the leather are filled with the microcells, without making the leather heavy and hard. Depending on the quantity of microspheres offered during the retanning, open areas are not only filled after expansion, but there is also a significant increase in the overall thickness of the leather. Depending on the amount of added Levotan X-Cel, and the recipe, the leather can even be "pumped up", and an increase in thickness most commonly of between 0.1 to 0.2 mm is achieved, but up to 0.8 mm in thickness is also possible in certain cases.

Protective Finishing

With trends toward light colored leathers being used for a variety of applications including automotive interiors, the need for protective finishes has never been more important. In a joint venture, Lanxess and Daikin Industries developed an innovative system that anchors organic, soil-repellent fluorine products firmly to the leather surface and is resistant to mechanical abrasion. The Aquaderm X-Shield system is a VOC-free, aqueous dispersion that is applied to leather like a top coat. The desired gloss level can be achieved by varying quantities of the two components Aquaderm X-Shield G and Aquaderm X-Shield M. The effectiveness of the antisoiling system has already been proven in numerous trials and shows an outstanding performance, especially in terms of cleanability. The system compares favourably with conventional finishes in regard to other desirable properties, such as surface touch which had been problematic with previous fluorocarbon finishes.

Preserving Agents

Due to extended times in transport and storage, leathers in the wet blue and wet white conditions need protection against bacterial and fungal contamination. Compared to the loss in value associated with damage, the cost of fungicidal treatment is relatively low. Within the chemicals for the wet end, however, fungicides are among the most highly priced on a per kg base. This cost element, combined with the fact that use in leather production often involves uncommon conditions for biocide application, requiring a lot of application research and formulation development, means there are only a very limited number of active substances available in Europe.

▶ Contact:
Dr. Dietrich Tegtmeyer
Lanxess Deutschland GmbH
Leverkusen, Germany
Tel.: +49 214 30 52891
Fax: +49 214 30 27627
dietrich.tegtmeyer@lanxess.com
www.lanxessleather.com

Everywhere There's Science

Sigma-Aldrich's Buchs Site: Center of Excellence in the Swiss Alps

SWISS PRECISION Sigma-Aldrich is a name that is readily recognized by scientists around the world. Its biochemical and chemical products and kits are used in scientific and genomic research, biotechnology, pharmaceutical development, the diagnosis of disease and as key components in pharmaceutical and other high technology manufacturing. Over one million scientists and technologists around the world use products from Sigma-Aldrich and a significant proportion of these products originate from Buchs in Switzerland. Nestling in an alpine valley on the banks of the river Rhein, Sigma-Aldrich has here its largest European facility.


A significant proportion of Sigma-Aldrich products originate from Buchs in Switzerland, the company's largest European facility.

The company's presence in Europe grew significantly when it acquired this manufacturing facility containing its own R&D laboratories in 1989. The acquisition added further breadth to its already large product range and provided a center from which to coordinate many of its European operations. The Swiss company brought with it an impressive range of chemicals and reagents for analysis, quality control and environmental monitoring.

The Buchs site provides a center of excellence in analytical reagents targeted at customers with high demands for high purity, reliable quality and easy-to-use products. Steeped in the Swiss tradition for precision, reliability and innovation, the Buchs location in eastern Switzerland can serve these needs well. With over 100 scientists in its 550 strong workforce it is certainly well qualified and experienced in the science of chemical production, quality control and R&D. It has been operating under ISO 9001 for many years. In 2007 it launched a commercial laboratory with double accreditation for production of certified reference materials under ISO/IEC 17025 and ISO Guide 34.

Within the global R&D structure of Sigma-Aldrich the Buchs R&D team represents the center for product and service innovation in Europe. Besides classical synthesis capabilities more new cutting-edge technologies have been established, for example, microreaction technology for continuous synthesis or simulating moving bed (SMB) chromatography for preparative chiral separation. In close cooperation with universities, external R&D partners and the innovative product management team up to 1,000 new products are developed every year.

Buchs provides a central manufacturing base for Sigma-Aldrich in Europe. Sigma-Aldrich has other manufacturing locations around Europe concentrating on specialty products for Life Science and High Technology. Yet it is the Buchs location that takes care of the core product range that laboratory scientists commonly use every day as well as high quality products used in analytical laboratories.

Sigma-Aldrich took on the facility when it was still known as Fluka and this remains the brand name for these products. Its traditional catalogue continues as the main catalogue for all analytical reagents and standards from Sigma-Aldrich and still carries the Fluka name. Sigma-Aldrich, and previously Fluka, in Switzerland has built up its reputation on this large catalogue containing over 25,000 products. As part of the global organization it now represents the 130,000 products in the complete range.

Since becoming part of the Sigma-Aldrich Corporation, the Buchs location has increasingly been playing a major role in building up another successful part of the company's business. The SAFC unit serves manufacturing customers in the life science and high technology industries. The Buchs location has been contributing to this growth with development and production of large-scale commercial and custom chemicals especially for the SAFC Pharma business unit.

Custom-manufacturing projects are managed from here on a global basis, coordinating manufacturing activities and services around the world for its pharmaceutical customers. Products for these customers coming from the Buchs factory are manufactured there under cGMP conditions. Recent investments ensure that the entire supply chain from sourcing through production, quality control, storage and distribution is controlled to the standards and norms of the pharmaceutical industry.

With dedicated staff managing compliance, health and safety, sales and marketing and central services, the Sigma-Aldrich facility in Buchs, Switzerland is a fully-integrated company bringing global business into Europe and Swiss precision to the world.

▶ Contact:
Trevor Jones
Sigma-Aldrich
Buchs, Switzerland
Tel.: +41 81 755 2745
Fax: +41 81 755 2770
trevor.jones@sial.com
www.sigma-aldrich.com

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Changing Lanes

The Future for OTC Distribution in Europe

Fortunes Made – Europe's population will consume some €47 billion of over the counter (OTC) medicines, dietary supplements and remedies for minor illnesses in 2008. By 2010 the figure is expected to top €50 billion.

While this represents only 16% of Europe's pharmaceutical retail market, it is a jealously guarded monopoly by the region's 141,000 mostly independent pharmacies that provides a valuable profit stream and a hedge against diminishing margins from dispensing state subsidized prescriptions. However, it is becoming increasingly evident that political, social and economic drivers are behind the dynamics fueling the consolidation and restructuring of the supply chain, and the erosion of the power of the independent pharmacist to act as the consumers' advisor and sole reseller of non-prescription medicines.

The OTC Market

Growing concentrations of Europe-wide retail groupings and the emergence of new aggressive channels are among the key factors gradually shifting the balance of influence over consumers' choice, access and demand for self-care away from brand owners to organized distribution channels. However, this change in the influence over consumer behavior has to be seen in the context of slowing demand and maturing markets.

85% of non-prescription medicines for OTC self-medication are purchased from pharmacies. Whereas this is largely due to restrictions on distribution, some 60% of European consumers value the advice given by pharmacists in helping them select the right treatment for minor ailments. Yet, first and foremost, pharmacies are responsible for dispensing prescriptions, OTC medicines are very much a secondary business for the majority.

This said, the impact of health reforms has begun to squeeze pharmacy earnings from their traditional business, particularly in Germany and France. Combined with a general trend towards commercialism among younger pharmacists, this has begun to raise the importance of OTC medicines and personal care in their business mix.

Non-Pharmacy Channels

Unlike the situation in the U.S., retail distribution of OTC medicines, other than through pharmacies, is highly restricted in most European States, including Austria, Belgium, France and Spain. Germany, Switzerland, the Netherlands and more recently Italy license non-pharmacy outlets to sell a limited range of OTC medicines under the supervision of a qualified druggist or in the case of Italy a pharmacist.

A so called general sale list (GSL) of medicines that can be freely sold in any outlet has long applied to Britain, but in recent years has extended to the Czech, Poland, Norway, Denmark, Portugal, Hungary and the Netherlands. Nevertheless, in Europe only 15% of self-medication distribution reaches the consumer through non-pharmacy outlets. This is up from 13% in 2005, a percentage that had remained very much the same since the late 1990s. Even so, the potential for expansion of so called GSL medicines is immense.

James Dudley
Managing Director
James Dudley Management

With the numbers of markets for medicines licensed for sale in non-pharmacy channels, such as supermarkets and convenience outlets, expanding as part of a continent-wide process of deregulation, more and more major chain retailers are being drawn into the OTC self-medication sector. Major international chains including Auchan, Leclerq, Carrefour, Tesco and Wal-Mart as well as druggist chains Schlecker and A.S. Watson are among the international chain retailers aggressively looking for a share of the European pharmacy market – pharmacy acquisition and channel access to non-prescription OTC medicines appear to be high on the retail agenda along with dietary supplements, parapharmacy and medical devices. The very presence of these companies in the supply chain alters the balance between manufacturer and consumer.

Pharmacy Ownership

An important trend in the processes of deregulation concerns pharmacy ownership. In 2000, Norway followed the Netherlands in changing pharmacy ownership regulations, thus enabling retail pharmacy chains to develop. Most recently the Slovakian Medicines Law was amended to permit companies to run pharmacies. Before the regulatory changes in Norway, the Netherlands and Slovakia retail pharmacy chains were only permitted in Belgium, the Czech Republic, Ireland, Poland, Switzerland and the UK.

86% of pharmacies in Europe are single outlet, independent owner managed, down from 91% in 2005. However, 6% of pharmacies are members of small multiple groups of between 2–50 outlets. The number of these groups has increased due to new group ownership rules introduced in Germany in 2004, which permit a pharmacist to own up to four outlets. Around 2% of Europe's pharmacies are under state or public ownership, excluding hospital pharmacies. These are mainly located in Sweden and Italy, but this could all change soon as the Swedish government has given itself until early next year to wind down its state monopoly, Apoteket. In broad terms it is expected that the government will auction off Apoteket in chunks to interested multinational chains in early 2009.

At the same time the pharmaceutical supply chain is concentrating around key players. Together with their associate companies, the leading three wholesalers Celesio, Phoenix and Alliance Boots control over half of the European intermediary pharmacy market (fig.2). With all three companies having holdings in Anzag in Germany this adds approximately 3% to their combined market share, which represents about 52% share of the total European average. However, retailers with a global reach should not be ignored. A.S. Watson is one in point. In Europe, the group now operates nine health and beauty chains and operates over 7,800 retail stores in 36 countries. Furthermore, it has the potential to continue its global expansion by acquisition.

Regulatory Barriers

Despite the strategic intentions of the major international players the expansion of retail pharmacy chains has been prevented by regulators in most European States especially France, Germany, Italy, Spain, Portugal, Bulgaria and Austria. Barriers to the development of pharmacy chains are based on prohibitions on outside and multiple pharmacy ownership and on restrictions on the freedom of establishment for pharmacies. The European Commission has initiated seven infringement proceedings and is acting against currently applicable pharmacy legislation in these States.

In September 2008, the European Court of Justice (ECJ) will settle the future of pharmacies in Europe. In a hearing of joint cases, the German and Italian ban on outside ownership are to be debated. If the national regulations are overturned in Luxembourg, pharmacy laws in all other EU countries will come under scrutiny.

The reference for preliminary rulings from Germany concerns the Dutch mail-order pharmacy DocMorris (Celesio) that opened a pharmacy in Saarbrücken, Germany, in 2006, despite the effective ban on outside ownership. This is not the first time DocMorris has used the European Court to fight its corner. In 2003, the company took on the German establishment to overturn laws restricting distance selling of pharmaceutical products. The ECJ found in favor of DocMorris and in the process ended up legitimizing distance selling of non-prescription medicines across the EU.

Virtual Pharmacy Groupings

Large retail pharmacy chains already exist in virtual forms. In Europe, 34,000 pharmacies are members of voluntary groupings or virtual chains (table 1). This is equivalent to a quarter of all retail pharmacies in the region. With the main international wholesalers Celesio, Alliance Boots, Phoenix, Galenica and OPG as the drivers behind this form of retail grouping it is fully expected to expand across the whole continent in a very few years.

Table 1: Emerging Virtual Pharmacy Groupings in Europe

Country	Group	Sponsor/owner
Baltic States	Apteek	Phoenix
France	Pharmactive	Celesio/OCP
	Alphega	Alliance Boots
Germany	Commitment /DocMorris*	Celesio
	MVDA/Linda & Midas	Phoenix
	Meine Apotheke	Sanacorp
	Vivesco	Anzag
	EMK	von der Linde
	Parmapharm	Independent co-operative
Italy	Alphega	Alliance Boots
	SPEM	Phoenix
Netherlands	Mediq	OPG
	Kring	Alliance Boots
Norway	Selmos Valstine	Phoenix
Spain	Alphega	Alliance Boots
Switzerland	Winconcept/Amavita	Galenica
UK	Numark	Phoenix
	Vantage	Celesio/AAH
	Pharmacy Alliance	Alliance Boots/Unichem

*) Acquired May 2007
Source: James Dudley International Ltd. 2007

Future Company Strategies

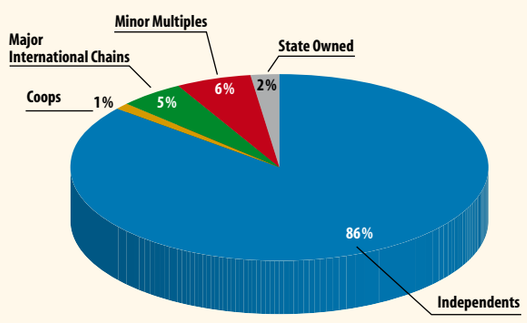
So how do the unfolding changes to OTC distribution channels affect future company strategies? The consumer driven OTC self-medication sector has been drifting from its mainstream research based prescription core for over a decade, and increasingly the abolition of reimbursement for products not requiring a doctor's prescription have forced a rethink among many companies traditionally wedded to the reimbursement system. While German companies have proved the power that can be generated by a marketing model that combines the influencing of prescribers, motivating and educating pharmacists and driving consumer demand through public adverting, the health reforms introduced in the Act on the Modernization of Statutory Health Insurance (GMG), which came into force Jan. 1, 2004, have effectively shut down this approach. Even so, the legacy of brands cultivated and nurtured by this model will endure for many years. This is a pattern repeated across the European region in varying degrees and companies have to become much more consumer focused. They are also becoming aware of the demands being made by organized chains, whether wholly owned or virtual.

Hence, the future opportunities and challenges to the consumer healthcare sector will be based more on developing strategies to generate consumer led market share to ensure listings with the emerging retail groupings looking for a cut of the European non-prescription market, rather than adherence to any particular marketing approach. While the role of the pharmacist and physician will continue to provide a major influence on consumers' trust and loyalties to brands, companies are being forced to make big leaps in their business cultures. Even diehard traditionalists are recognizing the need to adapt from meeting the rules of reimbursement systems to matching market share driven category management criteria demanded by a growing number of efficient retail groupings.

James Dudley, Managing Director
James Dudley Management

Contact:
James Dudley Management
Kidderminster, UK
Tel.: +441562 7474705
information@james-dudley.co.uk
www.jamesdudley.info

Pharmacy Ownership in 18 Country Study Figure 1



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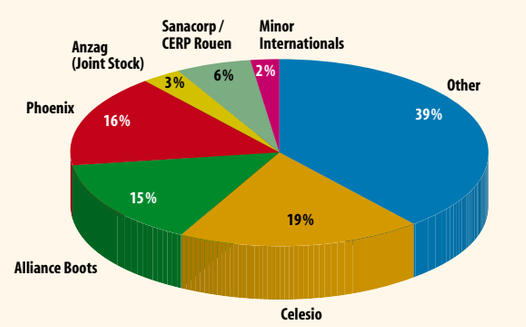
Leading Wholesalers % Share Top 20 European Markets Figure 2



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Biologics: Challenge Or Opportunity?

International Tendencies in Generic Markets

New Trends – In 2005, pharmaceutical expenditure accounted for an average of 19.6 % of the total health expenditure in the EU. Gudrun Neises and Janine Stangl of the Hochschule Fresenius – University of Applied Sciences, explain how biologics offers opportunities for companies that are well-positioned to enter the generic biologics sector.

Between 1995 and 2000, the total health expenditure per capita increased by about 4 %, and the average expenditure for pharmaceuticals by about 4.6 % in the Organization for Economic Cooperation and Development (OECD) countries.

In recent years, health insurers and politicians have placed their hopes on the ability of generics to deliver noteworthy savings to overstretched health care budgets due to their lower costs and potential for more efficient resource allocation. The biologics market promises potentially rewarding opportunities for companies that are well-positioned to enter the generic biologics sector.

What Are Generic Biologics?

Biologics are imitations of living sources, such as humans, animals or microorganisms. They can be composed of sugars, proteins or nucleic acid, or a combination of these substances. They may also include living entities such as tissues and cells. These molecules are produced through biologic processes, such as fermentation or cell culture. Most biologics are complex mixtures that are not easily identified, often manufactured by using biotechnology.

Cost Is A Factor

Nowadays, biologics are on the cutting edge of medical science and research. These products raise the expectations of many people to treat severe medical conditions and even diseases which are incurable, for example the treatment of oncological patients or patients with chronic diseases. Biologics necessitate specific delivery systems – such as injections or infusions have to be administered intravenously – because oral medications will be decomposed by the digestive system. Drug prescription, dosage and administration of follow-on biologics are key responsibilities held by medical doctors.

The issue of generic biologics has evolved since the first blockbuster biologics were patented. Furthermore, the subject of generic biologics generates several additional questions, such as: How will differences in development and manufacturing costs and associated regulations affect the market for generic biologics? Will generic biologics be as competitive as chemical drug generics? What about safety, consumer acceptance and the prospects of significant cost savings?

New evidence indicates that generic biologics will be expensive due to incalculable fixed costs necessary for clinical trials, capital costs and manufacturing. International regulatory guidelines advocate comprehensive pre-clinical and clinical testing of biosimilars prior to market authorization, which differs from traditional chemical drugs and their generics. This is because of the complexity of biological manufacturing processes; minor modifications in the bioprocess can lead to adverse effects in quality and safety. Recent estimates indicate that the fixed costs could range from $2–200 million. There is also the fact that process approval costs are higher for biologics than for chemical entities.

Capital investment will be a lot higher for generic biologics compared to traditional chemical generics. Either new facilities have to be constructed or manufacturers have to enter into partnership agreements based on geographical locations with other manufacturers in countries with low production costs, such as China or India. The present scarcity of capacity enables contract manufacturers to be able to exert considerable pressure in negotiations. This means that they prefer to develop relationships with innovators.

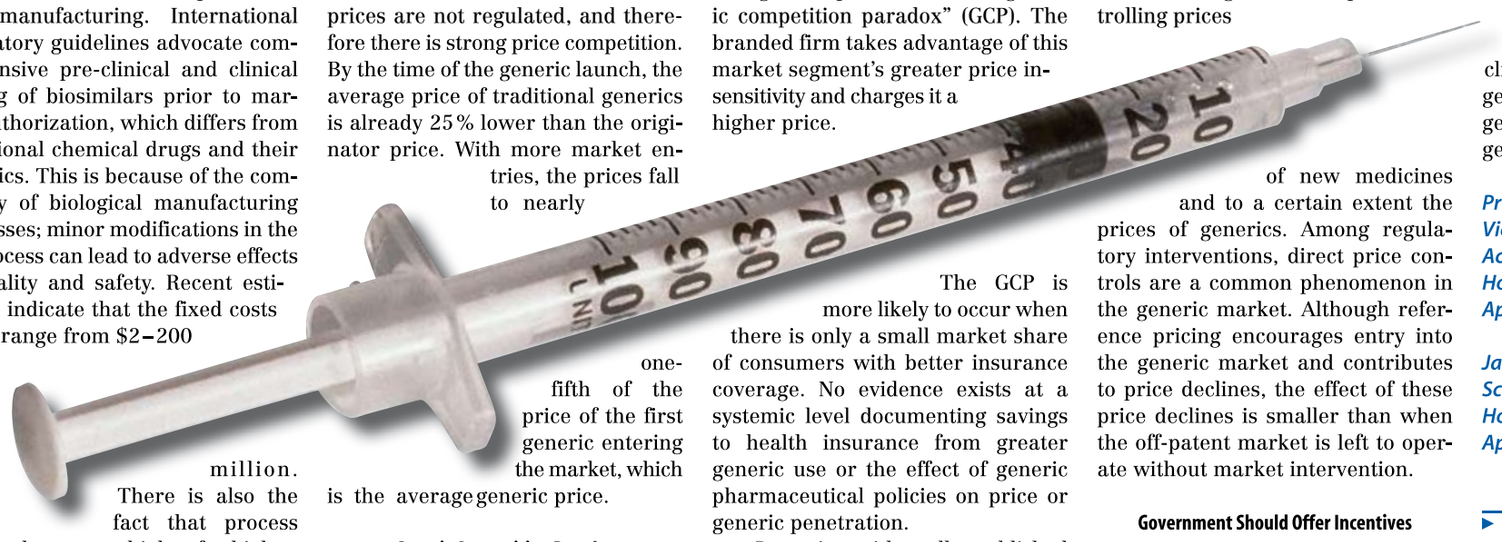
Fewer Competitors

Finally there will be less biogeneric companies entering the market than would be expected for generic pharmaceuticals. With fewer generic competitors, the price for generic biologics will be nearly the same as the price for branded biologics.

Preliminary estimates assume that the generic-to-brand price ratio is 90 %, with one generic substitution entering the market, 63 % with five generic substitutions entering the market and 40 % with 10 generic substitutions entering the market. As years go by, the price for generics will become cheaper, and the prices will also vary according to the therapeutic class.

In comparison, one year after a chemically identical or traditional generic product enters the U.S. market, it captures a large share of prescriptions dispensed (44 %) and market sales (50 %). Of course, in the U.S. prices are not regulated, and therefore there is strong price competition. By the time of the generic launch, the average price of traditional generics is already 25 % lower than the originator price. With more market entries, the prices fall to nearly one-fifth of the price of the first generic entering the market, which is the average generic price.

Nowadays, biologics are on the cutting edge of medical science and research.



Generic Competition Paradox

Moreover, there is evidence that an increase in generic medicine uptake does not necessarily imply a reduction in total pharmaceutical expenditure. To make matters worse, an increase in volume of traditional chemical generics could result in an overall increase in pharmaceutical expenditure. This phenomenon is known as the "generic paradox" or the "generic competition paradox" (GCP). The branded firm takes advantage of this market segment's greater price insensitivity and charges it a higher price.

The GCP is more likely to occur when there is only a small market share of consumers with better insurance coverage. No evidence exists at a systemic level documenting savings to health insurance from greater generic use or the effect of generic pharmaceutical policies on price or generic penetration.

Countries with well-established generic markets may or may not impose regulations on pharmaceutical prices. Generic penetration is more common in unregulated markets. In the U.S. and in Germany, price ceilings on new pharmaceutical products can not be found – Germany even has a reference price system for generics. Other countries such as France, Canada, Denmark and Italy have authoritarian arrangements in place controlling prices of new medicines and to a certain extent the prices of generics. Among regulatory interventions, direct price controls are a common phenomenon in the generic market. Although reference pricing encourages entry into the generic market and contributes to price declines, the effect of these price declines is smaller than when the off-patent market is left to operate without market intervention.

Government Should Offer Incentives

Because of the unique position of generic biologics as the cutting edge of medical science and research, politicians should introduce a totally different system of promoting faster uptake and price competition. Considering the weak evidence for the efficiency of supply-side policies side (price ceilings on reimbursement; reference pricing) demand-side policies should be conducted. The government should create incentives for greater entry by establishing push or pull mechanisms. Follow on biologics or generic biologics are medications which are only applied by physicians, usually for patients with serious or chronic conditions. But pharmacists and their pharmaceutical assistants also face new challenges concerning the quality of advice given to clients. Educational programmes on generics have a positive impact on generic uptake and acceptance of generic substitution.

Prof. Dr. med. Gudrun Neises
Vice President for Research and Academic Development Mentor
Hochschule Fresenius – University of Applied Sciences

Janine Stangl
Scientific assistent
Hochschule Fresenius – University of Applied Sciences

Contact:
Prof. Dr. med. Gudrun Neises
Hochschule Fresenius – University of Applied Sciences
Idstein, Germany
Tel.: +49 6126 9352810
neises@fh-fresenius.de
www.fh-fresenius.de

Pharma Convergence

Challenges in Drug Development and Manufacturing Methods

A Changing Business – The global pharmaceutical world has been changing and its pace has accelerated in the last three years. Not only do they need to develop a new business strategy, they need to improve their manufacturing methods and technologies.

Girish Malhotra
Epcot International

If the current scenario of "drying of the blockbuster pipeline" and generics increasing their market share holds, we could see most of the API manufacture, formulation and clinical testing moving to low cost countries. Since laws of economics prevail, this could be considered inevitable. Ethical and generic companies have to develop and implement strategies that could give them the competitive edge and allow them to move forward on their chosen path. Since ethical and generic producers are adversaries, it would be interesting to see the playing out of the respective strategies. Let the match begin!

Ethical Pharmaceuticals

Major pharmaceuticals have developed and commercialized blockbuster drugs. However, they have not retained these drugs in their portfolio after the patents expire, as they have been busy developing new drugs. Producing patent expired drugs has not been part of their strategy.

Due to high profit margins, generics have taken over the patent expired drugs and have lately made every effort to do so through litigation. With aggressive entry of generic producers from Israel, Iceland and India, the turbulence in the pharma field has dramatically increased.

With the drying of blockbuster pipelines, escalating clinical trial costs and relentless pressure of generics to capture the market, ethical drugs producers are trying to implement strategies to reduce their costs and retain their stronghold on the drug development chain. Some of the strategies being implemented are as follows:

- Outsource drug development
- Outsource active pharma ingredients (API) manufacture and formulation
- Synergize small molecules and/or biotech combinations
- Acquire small/large biotech companies
- Whatever else works i.e. collaborations

Some of these strategies might work as a short term fix to retain profits, however, the long-term impact of these strategies is going to be significant. The biggest consequence is going to be the shift, disappearance and/or reduction of the knowledge base from "Major Pharma" companies to the outsourced companies. Since the outsourced companies are in low cost countries, they have dual benefit of the above relationships. It makes them intellectually and financially stronger to become formidable generic competitors. We are beginning to see this happen.

Generic Pharmaceuticals

Generic pharmaceuticals are enjoying what I will call the best of all worlds. They are basking in an unprecedented growth. I do not believe any of the financial analysts and pundits would have predicted this in the beginning of 2005. Customers would like to have drugs at lower prices, generics are able to fulfill this need in every market and as a result the demand for generic drugs has increased. This surge has increased generic business dramatically in recent years. They have utilized profits to grow organically and acquire sites that are being shed by API producers and formulators at significantly low costs. They have also benefited from the technology and intellectual property that comes with these acquisitions. Strategies being implemented by the generic companies are unconventional and this is causing additional turmoil in the pharma field.

Future And Strategies

Pharmaceutical companies have achieved handsome profit margins by inventing new drugs and by producing generics. Customers have paid for every inefficiency in the development, clinical testing, manufacturing and supply chain. Since pharma companies have been able to make respectable profits there was never a burning need to minimize the costs of each step. Everyone has been comfortable in their respective arenas. However, the drying of the blockbuster pipeline and generic companies trying to encroach on the playing field of ethical companies is changing the market dynamics.

The price consumers pay for drugs in the U.S. and some other countries are not market driven but rather driven by what the market can bear. Many consider these prices high and are getting low cost drugs every way they can e.g. Canada, Mexico, imports and/or internet. This has led to considerable debate and discussions as healthcare costs increase. Wal-Mart and a few other companies are offering drugs at low prices. This puts pressure on the companies in the supply chain to continuously lower their costs. Therefore, companies will have to consider and implement new strategies.

If the major pharma companies are not able to develop new blockbuster or biotech drugs, they could start making generic drugs. This could lead to consolidation and formation of "mega" companies. My definition of a "mega" merger is a combination of an ethical and generic company to be players in both markets. These mega companies will not only develop new drugs, but will also have to make every effort to retain the patent expired drugs as part of their portfolio. If this happens, every step of the supply chain, especially manufacturing technologies, would be critically evaluated and methods implemented to reduce costs. The business model of mega companies could be a combination of market and consumer driven companies trying to maximize their market share. This should reduce global healthcare costs.

The Indian government has announced an innovative drug discovery program combining global IT firms (Sun Microsystems), researchers (Royal Society of UK, Imperial College of London, Medicine Sans Frontiers etc.), companies, and young minds at India's scientific laboratories to invent drugs at a fraction of the cost of a multi national company (MNC). An open platform of drug research like Linux development is an interesting and innovative concept and path. Success here would genericize and commoditize pharmaceuticals and add additional pressures on pharma companies to implement technology improvements to reduce costs. Other business models will emerge. I expect that more than 50 % of the pharmaceutical market will become a commodity market in the next five years and we will see prices drop.

Manufacturing Methods

Improvement of manufacturing technologies has not been part of any business model. In the last few years, there has been a considerable amount of discussion on the need to improve the manufacturing technologies, nevertheless, progress has been very slow.

New business models for ethical and generic pharmaceutical companies will have to include improvement of their manufacturing technologies. Today, active ingredients and formulation are dictated by "quality by analysis" methodology. It is not the way of the future. Pharmaceutical companies have to move to "quality by design (QBD)." QBD is being talked about in the pharma world but it needs to be put into practice. Specialty chemicals, petrochemicals and other industries have produced products following QBD.

Technologies to achieve QBD exist, but need to be adopted. Improving manufacturing practices and QBD is not difficult. It requires discipline and dedication. Implementing QBD methods will change the landscape and it will be interesting to see what develops.

Contact:
Girish Malhotra
Epcot International
Pepper Pike, U.S.
Tel.: +1 216 292 0626
Fax: +1 216 591 0932
epcotint@ix.netcom.com
www.epcotint.com

Advertising Regulations

Repercussions Of The Gintec Case

Clear Text – What were the leading events that resulted in the ruling by the European Court of Justice (ECJ) in the case against Gintec in November 2007, and what effects has this resulted in?

Dr. Christian Tillmanns
Law firm of
meyer/meisterernst

The German Gintec International Import-Export GmbH (Gintec), in May 2000, advertised various ginseng preparations, which are registered in Germany as OTC medicinal products. Gintec's advertising was accompanied by a consumer survey evaluation, in which testimonials of patients were described. In addition, Gintec announced on its internet site a monthly price draw with the chance of winning a pack of "Gintec's Red Imperial Ginseng Extract Powder."

German Legislation

Subject matter of the main proceedings was paragraph 11 of the German law on advertising of medicinal products, Heilmittelwerbegesetz (HWG). Paragraph 11 of HWG states:

"(1) Outside professional circles medicinal products, procedures, treatments, items or other remedies may not be advertised.....(11) using statements made by third parties in particular using statements of gratitude, recognition or recommendation, or by reference to such statements... (13) using competitions, price draws or other procedures, the outcome of which is dependent on chance..."

With regard to the wording of this regulation the German fair-trade association, Verband Sozialer Wettbewerb (VSW), argued that Gintec's advertisings were incompatible with the abovementioned provisions of the HWG and the matter was sent to the German Federal Supreme Court. Firstly, the VSW stated that the advertising, including the consumer survey evaluation, contained prohibited references to statements from third parties within the meaning of paragraph 11 (1) (11) of the HWG. Secondly, the VSW stated that the prize draw announced on Gintec's internet site was in violation of paragraph 11 (1) (13).

Community Legislation

The provisions of directive 2001/83/EC of the European Parliament and of the Council of Nov. 6, 2001, on the Community Code relating to medicinal products for human use concerning advertising medicinal products are contained in titles VIII and VIIIa thereof. They are entitled Advertising (articles 86 to 88) and Information and Advertising (articles 88a to 100) respectively. Article 90 does not prohibit the use, in an advertising message, of statements by third parties in such a general and unconditional way as paragraph 11 (1) (11) of the HWG. Article 87 (3) requires that advertising should encourage the rational use of the medicinal product by presenting it objectively, without exaggerating its properties and that it should not be misleading. Article 90 also contains specific directions regarding the content of advertising for medicinal products to the general public, prohibiting the use of various specific types of material. For example, article 90 (j) forbids using material, which refers, in improper, alarming or misleading terms, to claims of recovery.

Preliminary Ruling

With regard to the fact that paragraph 11 (1) (11) of the HWG contains stricter rules than directive 2001/83/EG concerning the advertising with statements by third parties, the German Federal Supreme Court requested a preliminary ruling by the ECJ. The German Federal Supreme Court called for clarification as to the degree of harmonisation brought about by directive 2001/83 in the area of medicinal product advertising. The main and among the EU-Member States heavily discussed question was, whether the directive 2001/83 provides minimum standards only, allowing the Member States to provide stricter rules on advertising – that was the position of the VSW and the German and Polish Governments – or whether the directive brought about complete harmonisation, which leads to the conclusion that the Member States are not entitled to provide for stricter rules than those laid down in the directive 2001/83.

The Court's Decision

The ECJ stated that titles VIII and VIIIa of directive 2001/83 lent support to the view that the directive brought about a complete harmonisation in the field of advertising medicinal products, since it lists expressly the cases in which Member States are authorised to adopt provisions departing from the rules laid down by that directive. Moreover, the court referred to the goals of the directive and held that it was adopted on the basis of article 95 EC, which permits the adoption of measures for the approximation of the provisions laid down by law, regulation or administrative action in Member States, which have as their object the establishment and functioning of the internal market. Accordingly, recitals four and five in the preamble to directive 2001/83 state that the directive aims do remove the hindrances to trade in medicinal products that are created by disparities between national provisions relating to medicinal products thus directly affecting the functioning of the internal market.

With regard to paragraph 11 (1) (11) HWG the court stated that the directive must therefore be interpreted to the effect that a Member State may not provide, in its national legislation, for an absolute and unconditional prohibition in the advertising of medicinal products to the general public, on use of statements from third parties, whilst their use can be limited, under directive 2001/83, only by reason of their specific content or the type of person making the statement. Such advertising can only be prohibited if it is not in line with the regulations of the directive either, e.g. because the advertised product does not possess the alleged properties and therefore the advertising campaign has to be considered as misleading.

The ECJ nevertheless considered the two advertisings of Gintec as not in line with directive 2001/83. The court states that the testimonials gave the impression that the medicinal product contributes to the reinforcement of general well-being. This is incompatible with article 90 (c), which prohibits any suggestion that the health of the subject can be enhanced by taking the medicine. Moreover the testimonials have to be considered as misleading, if the product does not possess the claimed effects. Furthermore, the court states that articles 87 (3), 88 (6) and 96 (1) of directive 2001/83 prohibit the advertising of Gintec's product by means of a prize draw on the internet, because it encourages the irrational use of that medicinal product and leads to its direct distribution to the general public and to the presentation of free samples.

Effects of the ECJ Ruling

In consequence of the fact that the directive 2001/83/EC sets a definitive minimum and maximum standard – complete harmonisation – in the field of advertising for medicinal products which limits the regulation by the member states, in future all national provisions, particularly with regard to the OTC-medications, which are not in line with the European regulations, are not applicable. The national authorities and courts, in applying the provisions of domestic law, have to interpret them in the light of the wording and the purpose of the directive in order to achieve the sought result.

In response to the ECJ ruling dated April 10, 2008 (3 U 182/07), the Hanseatic Court of Appeal in Hamburg stated that a TV-advertising-spot for a herpes-simplex-infection (HSI) medication, which shows a mouth with HSI followed by the pictorial representation of a mouth without HIS, was not in violation with paragraph 11 (1) (5a) HWG. Paragraph 11 (1) (5a) HWG states that outside professional circles medicinal products may not be advertised using the pictorial representations of changes in the human body or parts thereof caused by disease, suffering or injury. With reference to the ECJ Gintec ruling, the court stated that this provision is not in line with article 90 (k) of the directive 2001/83. This provision forbids the using of pictorial changes in the human body caused by disease or injury only if it uses improper, alarming or misleading terms. The court holds that paragraph 11 (1) (5a) HWG has to be interpreted in the light of the wording of article 90 (k) directive 2001/83 and therefore, because the pictorial representation was not considered to be improper, alarming or misleading, the advertising was in line with the HWG.

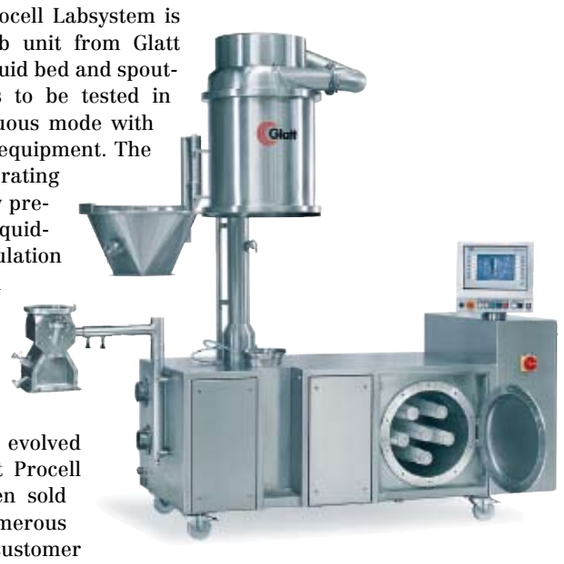
After all, the ruling leads to more legal certainty. European pharmaceutical companies can base their future advertising strategies on this ruling. Stricter national rules than those laid down in the directive 2001/83 can be disregarded, if the directive not expressly allows departing provisions. However, it remains to be seen how fast the national legislation in the various Member States will respond to this ruling by the ECJ and how fast the national courts will deviate from their previous jurisdiction and interpretation of the national regulations. Nevertheless, there will be more liberalization in the advertisement of medicinal products – particularly with regard to OTC-medications – in Europe.

Dr. Christian Tillmanns, Attorney specialised in pharmaceutical law

▶ Contact:
Dr. Christian Tillmanns
Law firm of meyer/meisterernst
Munich, Germany
Tel.: +49 89 5155 63-6
Fax: +49 89 5155 63-59
tillmanns@meyer-meisterernst.de
www.meyer-meisterernst.de

Procell Labsystem

PRODUCT The Procell Labsystem is a new mobile lab unit from Glatt which allows all fluid bed and spouted bed processes to be tested in batch and continuous mode with only one piece of equipment. The continuous operating mode is especially preferred for the liquid-only, spray granulation process. In batch mode this process can be tested only within narrow limitations.



The Procell Labsystem has evolved from the lab unit Procell 5, which has been sold and rented to numerous customers. This customer experience and satisfaction was driven by the excellent operating reliability and process flexibility of the equipment. The "new" lab unit will now offer four different process systems. Customers can select one, two, three or all four process options, based on the needs of the desired product or project, as necessary.

Using the new system, spouted bed processes can be tested. The spouted bed technology is extending the possibilities to process challenging products, like fine particles, which are difficult to fluidize in fluid beds. Particles, which are larger than 3 mm can be fluidized with much lower air volumes compared to the fluid bed. An additional advantage of the Procell is the possibility to work with small amount of bed material. In continuous mode this means short residence time, resulting in a gentle processing of temperature sensitive products.

Visit us at the Powtech 2008 in hall 5, booth no. 3.22.

▶ Glatt Ingenieurtechnik GmbH
Weimar, Germany
Tel.: +49 3643 47 1502
redaktion@glatt-weimar.de

Contract Manufacturing Avaliable in Continuous Mode

PRODUCT Fluid bed technology is used in various applications especially for agglomeration of powder or for encapsulation of tailor-made products with functional coatings. IPC, an associated company of the Glatt group, offers such technologies as contract manufacturing service since many years with growing success.

Product examples, from left to right: spray granulation enzyme – spray cooling lipid coating – spray granulation beta carotene

In addition to batch processing, IPC has installed continuous production facilities at the beginning of this year. Besides the well known agglomeration and pelletization processes, continuous fluid bed processing allows for spray granulation. With this technology, granules or pellets can be made directly from liquid raw material. The products are compact and dust free granules with a mean diameter between 100 µm and 3 mm. Thus spray granulation is an alternative to spray dryers, the conventional process to dry liquids.

The patented design of the processing chamber of the ProCell by Glatt allows to work with little material in the process, resulting in short residence times. By this means spherical, dust-free and homogeneous pellets can be formed with little thermal stress to the product. The spraying solution is layered on seed particles or powder until the required particle size is reached. The product quality depends on the process parameter as well as on the recipe of the sprayed liquid. After screening off the target fraction as product, all oversized particles are milled and returned to the process together with the undersized fraction. This recycling ensures not only a high yield. Generating seeds in the process means also that no solid raw material is needed and the granules can be made from liquid raw material only.

Visit us at Powtech 2008 in hall 5, booth no. 3.22.

▶ IPC Process Center GmbH & Co
Tel.: +49 9721 41073
gudrun.ding@ipc-dresden.de
www.ipc-dresden.de

Managing Expectations and Ongoing Communication

Keys to Successful Client – CMO Relationships

Contract Management – Pharmaceutical and Biotech industries rely heavily on Contract Manufacturing Organizations (CMO) to produce the products that are so necessary to their growth and success.

Susan Lemons
Susan Lemons Consulting, LLC

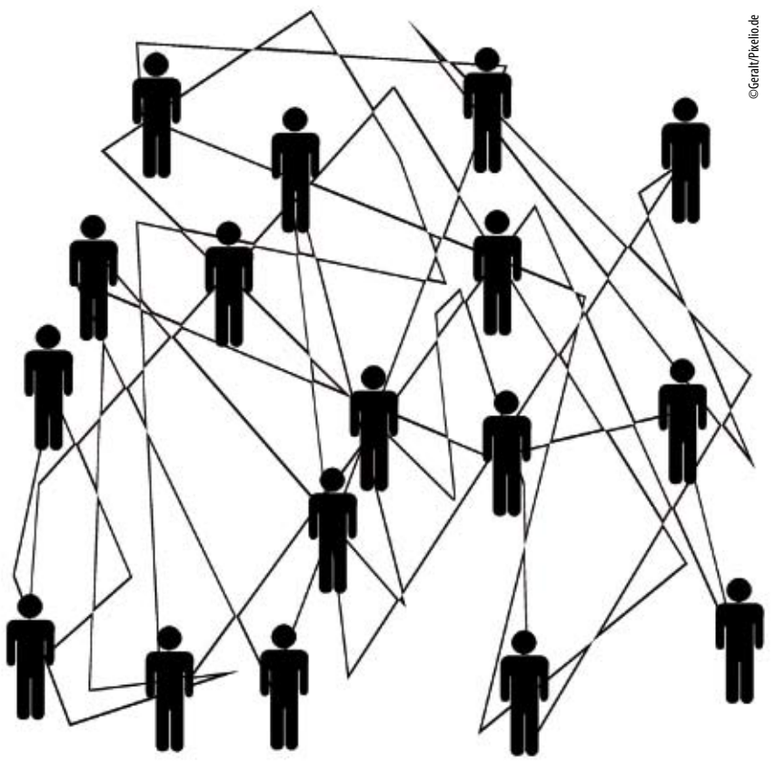
When these organizations are asked, "what is the most important element for a successful relationship?" – Managing expectations and communications make it to the top of the list. Borrowing from other contract management relationships can provide key insights into how to do this in a way that allows ongoing alignment and flexibility.

Fundamental Principles of QPM System

Utilizing Peter Drucker's principle, that you can only manage what you can measure, Susan Lemons Consulting developed a tool to allow a constructive conversation with the customer and supplier, defining expectations of quality, timeliness and cost for each performance period in the contract. Both the customer and the supplier agreed upon the definitions of these expectations and how to measure. At the end of the performance period each (the customer and the supplier) then scored performance for that period. This process may not seem any different than other contractual performance measurement systems. However, recognizing the Human Performance System, as defined by Geary Rummler, this method of measuring became a very powerful tool to communicate and foster positive performance.

Why the Human Performance System

In Geary Rummler's book, Improving Performance: Managing the White Space on the Organization Chart, it is clear that performance is driven by understanding requirements, timely feedback and supporting consequence systems. In the authors experience the individual's skills and knowledge are usually high and the necessary resources are often available, however it is the understanding of requirements, feedback and supporting consequence systems that drive 85 % of why people do what they do in business. The QPM System provides for requirements to be defined in advance by the client and the CMO, and for feedback to be provided against those requirements in a timely and constructive manner. Publically reporting the results also drives the consequence system for people to be recognized for achieving results, or not achieving results as the case may be. The highest impact on performance is when individuals know that the results are going to be scored at a meeting with their peers. It may seem to some that they are in their own Olympic championship series.



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How It Works

Prior to each performance period the customer and supplier, in this case the Client and CMO evaluate the work planned in the next performance period and define three elements: quality, time and cost. A total of 100 points is spread across the three elements, with no less than 10 points given to any element. This allows for flexibility for some periods when one factor is more critically important than another it can be weighted accordingly. Not only are the weights defined but so are expectations. When scoring at the end of the period, achieving expectations means a score of 50 % of assigned points, exceeding expectations is greater than 50 % and not achieving expectations is less than 50 %. An example may be that normally, quality is given 33, time is given 33 and cost is given 34. However, in a given period their may be an urgent item that is critical to final outcomes that if not in place by a certain date would drive negative performance ultimately. The weighting may be changed to give quality 30, time 40, and cost 30. This sends a clear signal that the timeliness of performance is critical. The expectations on timeliness may be the specific date and achieving prior to that date would mean exceeding expectations (>50 %), and not achieving by a window of time may mean not achieving (<50 % or severely 0 %). But quality and cost would also be assigned expectations such that there may be thresholds of requirements that must be met even though time has the highest weighting. In this example, just meeting time without cost and quality considerations would drive an overall "lower than expectations" score.

Historical Perspective

In the 1980s, Susan Lemons was part of an organization that did business contract by contract. There she developed a methodology to measure the quality of performance on a period by period basis. This quality performance measurement system (QPM) became a key communication tool to both organizations for the fulfillment of expectations. This method was then used repeatedly in other industries from research and development organizations to manufacturing organizations as well as consultant relationships, which are often characterized by missed expectations.

Ongoing Communication

The practice of establishing the QPM System, means establishing a strong communication discipline for the client and CMO. Each program review meeting is a perfect opportunity to establish the expectations and then score the performance. For most client-CMO relationships there is a quality agreement and many have begun to utilize the client services agreement. This measurement methodology becomes a way to translate the priorities of those agreements into meaningful timely expectations to both organizations. Once the weightings and expectations are defined they are published to both organizations for understanding. This helps clarify the expectations for the next performance period and gives relative weighting to those activities as well. It is amazing how people can believe they are in agreement until they have to give the elements weighting and the weightings are significantly different. Communication occurs when the gap is identified and closed with understanding.

▶ Contact:
Susan Lemons
Susan Lemons Consulting
Tempe, AZ, U.S.
Tel.: +1 480 755 0227
susanlemons@cox.net
www.SusanLemonsConsultingLLC.com

DSM Announces Closure of Wuxi Citric Acid Plant

Royal DSM has announced the closure of its citric acid manufacturing plant in Wuxi (China) by Q1 2009. The closure follows a request from the local government to relocate the plant from its current location as this location is needed for future urban developments. DSM will receive a compensation amount from the Wuxi government and does not expect to incur a book loss. A good social plan is being prepared for the several hundred people who will be affected by the closure.

According to the company, the market for citric acid has been under substantial pressure for several years, mainly due to structural overcapacity in China. As the structural overcapacity is expected to remain, DSM has decided not to rebuild the capacity elsewhere but concentrate its production at the site in Tienen (Belgium), whose competitiveness has substantially improved lately due to restructuring and process optimizations.

DSM continues on the announced track for partnership and has finalized the carve-out of the citric acid business as announced in September 2007. ■

Atlas Copco Signs Global Deal

Compressor and machinery maker Atlas Copco said it has signed a global distribution agreement with a unit of Orica. "Atlas Copco has signed a global co-operation agreement in the field of ground control and geotechnics for the mining, tunnelling and civil engineering markets with Minova International, the ground control division of the Orica group," the commpany said. "As a result of this agreement, Minova customers will have access to the Atlas Copco rockbolting products and Atlas Copco customers will benefit from the extensive Minova range of rockbolts, resins, grouts and related equipment," it said. ■

Russia's Pharma Market to Grow

Russia's pharmaceutical market is expected to grow by a third this year, ranking the country in the world's top ten pharmaceutical markets, research agency DSM Group said. It said Russia's total pharmaceutical market volume is expected to reach $18.4 billion this year compared with $14.3 billion in 2007. Sales are rising due to growing income of the population, it said in a study. The commercial segment of the market rose by 30 % in the first six months of this year to $4.55 billion because of faster price inflation than in past years, DSM said. State orders rose more quickly, by 43 % to $2.51 billion in the same six months, largely spurred by increased spending on a federal programme to provide low cost medicine to the needy. The non-medicinal segment, which includes dietary supplements, rose by 32 % year-on-year to around $72 million, while the share of non-medicinal goods made up 28 % of total drugstores' sales. ■

U.S. Drug Safety List

U.S. health officials said they are probing safety concerns with Eli Lilly and Co's antidepressant Cymbalta, GlaxoSmithKline's cancer drug Tykerb, Biogen Idec and Elan Corp's multiple sclerosis drug Tysabri and other medicines. The drugs were included among 20 products on a new quarterly list of medicines undergoing early safety probes following reports from the public of health problems.

Appearing on the list does not mean the FDA has concluded that the drug caused the problem, the agency said. The FDA is evaluating reports of urinary retention with Cymbalta, liver toxicity with Tykerb and skin melanoma with Tysabri, according to the list which can be found at: www.fda.gov ■

Umicore to Invest €45 Million

Umicore said it will invest around €45 to increase production capacity at its germanium wafer site in Quapaw, Okla., in the U.S. and two cathode materials facilities in South Korea and China. The group said its investment in capacity expansion in Quapaw will complement its existing production site in Olen, Belgium – doubling the group's current production capacity to 900,000 wafers per year. Construction at the site started in July and is slated for completion in 2010. Umicore will also expand production capacity for cathode materials for use in lithium-ion rechargeable batteries at its facilities in Cheonan (South Korea) and Jiangmen (China). Capacity will rise to around 10,000 t/y. New production lines will be installed by the end of this year and will be operational by the second quarter of 2009. ■

FDA Approval for Epzicom Generic

India's Aurobindo Pharma said it has received tentative approval from the U.S. Food and Drugs Administration (FDA) to manufacture and market Abacavir Sulfate or Lamivudine tablets, used in the treatment of AIDS. In a regulatory filing, Aurobindo added that the tablets, cleared for manufacture in strengths of 600 mg and 300 mg, are generics of SmithKline Beecham Corp.'s Epzicom. ■

Cost-effective Solution: "Plug & Fill"

PRODUCT With the "Plug & Fill" technology for the filling of cans and pails from 2.5 kg to 30 kg with liquid or pasty products, Feige presents a new solution in the field of these machines.

The concept of the Feige engineers to integrate all components of the electric and pneumatic control in one common control cabinet has well worked out. After installation and power supply has been put on, the machine is ready for use. Extensive cable laying to remotely installed control cabinet is no longer required. High output of up to 600 pails per hour is realised through the product flow control which helps to minimise the filling time in interaction with the product pump.

▶ www.feige.com

Automatic Filling into Plastic Bags

PRODUCT Haver & Boecker and Feige have succeeded in developing a fully automatic machine for now filling pasty products into plastic bags as well. The filling machine "Liffs" enables the filling of pasty products into PE plastic bags via Feige filling valve with an output of 600 bags/hour (25 kg each). It reveals new possibilities for this product range as filling in plastic bags is an attractive alternative to the commonly used packaging means in terms of economic and environmental aspects due to easier transport and low manufacturing costs of empty bags. Up to now the building industry has used pails to bring their products to the customer on site. Bags, however, are much smaller when the product is used up and can easier be disposed of.

▶ www.feige.com

Biomass To Liquid

High-Quality Synthetic Biofuel from Energy Crops and Waste

Good to Go – In the not too distant future, 15 truck loads per week of the world's most innovative diesel fuel will leave Choren's biofuel refinery in Freiberg, Germany.

Joint efforts of Choren, Shell, Daimler and Volkswagen have been concentrated to develop and improve a process which is capable to produce a novel biofuel with superior quality as well as an excellent CO_2-balance. The fuel is called Biomass to Liquids (BTL) and is considered one of the most promising candidates of the so called "second generation of biofuels."

Biomass To Liquids

BTL is a biosynthetic high-purity fuel, completely free of sulphur and aromatics. BTL emissions are extremely low in pollutants and almost CO_2 neutral, because its combustion releases only the same quantity of CO_2 to the atmosphere as the biomass originally absorbed while growing. Transport and storage of BTL requires no adaptation of the existing infrastructure. BTL is completely compatible with the diesel engine technology of today and tomorrow.

The feedstock consists of a variety of non-food biomass – wood residue from forests, recycled wood, fast-growing energy crops or agricultural residues such as straw. Also the BTL fuel yield from agricultural energy crops per hectare is considerably greater than from conventional biofuels such as plant oil based biodiesel or ethanol produced out of grain. The Choren technology utilizes the entire plant, not only plant components containing starch, sugar or oil.

The core innovation of Choren lies in the fist process stage, the patented Carbo-V-gasification process. This is an innovative globally unique multi-stage gasification process to convert solid biomass and other feed materials containing carbon into a high quality synthesis gas, which can be used to generate power or produce second generation biofuel.

In the second process stage, a high quality synthetic fuel is produced from the synthesis gas using the Fischer-Tropsch synthesis process. The Fischer-Tropsch process know-how came from Shell.

The synthetic biofuel has a number of major advantages over fossil fuels or plant oil based biodiesel:

- Compared to fossil diesel, BTL reduces life cycle CO_2 emissions by up to 90%.
- BTL is virtually free of aromatics and sulphur, with significantly lower emission of carbon monoxide and hydrocarbons, as well as nitrogen oxides and particulates.
- BTL is a designer fuel that can be used in any past, current or future diesel engine, without the need for modifications.

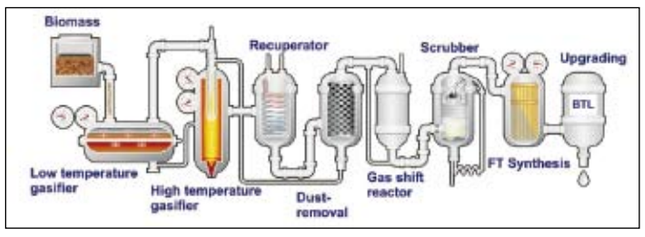
The BTL Plant in Freiberg

At the Choren site in Freiberg, Germany, the building phase of the world's first commercial-scale pilot plant for producing synthetic diesel from biomass was completed in April, 2008. The so called Beta plant is expected to produce close to 18,000 litres of synthetic biofuel annually. This is equivalent to the requirement for about 15,000 cars per year.

In the coming months, the plant will be commissioned: 113 sub-systems in 26 main operating units will be started up individually then in sequence. Around 1,200 steps will be needed for the commissioning of these systems, which in themselves consist of several sub-steps. This will take 8 to 12 months which is a common and realistic time frame for such a highly-complex process.

Looking ahead, Choren is working on a concept for the first BTL plant on an industrial scale, with an annual biomass demand of 1 million tons of dry matter and an output of 270 million litres of synthetic biofuel, to be built at Schwedt, in Brandenburg, Germany. Once the Beta plant has proven its viability, and provided the final investment decision for Schwedt is made in 2009, production of the industrial scale BTL plant could commence in 2012/2013.

Unfortunately the current German legal framework for biofuels has only been defined until 2015. A time horizon that is not long enough for investors to plan for the first Sigma plant with any certainty. However, the company remains confident that the politicians will shortly introduce an economic policy framework enabling second-generation biofuels, and thus the synthetic biofuel made by Choren, to be a key contributor towards achieving the ambitious CO_2 reduction targets of the future.



The Biomass Procurement Strategy

Annually 65,000 t dry matter biomass will be needed to keep the already technically completed Beta-plant in Freiberg running at full pace. This amount can still be procured in a rather regional context. Large scale BTL facilities with a demand of 1 million t dry matter and more, however, will also develop strong impacts on supra-regional biomass markets. The proactive development of a long term biomass supply strategy is therefore inevitable.

Generally all kinds of biomass can be used for BTL production provided that they are inflammable. But in the first step, Choren is concentrating on woody biomass only, to minimize complexity for storage, handling and preconditioning as well as to reduce variation in feedstock qualities affecting gasification parameters. Besides recovered wood from the recycling industry especially low quality logwood, forest residues and by products of the sawmill industry are feedstocks of choice for Choren's BTL process. In the future fast growing short rotation plantations will subsequently play an increasing role for the biomass supply of most large scale bioenergy consumers.

In awareness of the necessity to enlarge the feedstock base of woody biomass Choren itself planted the first 20 hectares of fast growing willow trees three years ago. This year another 20 hectares were established for testing and demonstration purposes close to Schwedt, where the first large scale BTL plant is planned to be built. Twenty two different poplar and willow species have been selected and three different planting techniques have been tested. Provided the BTL-plant in Schwedt is built, several thousand hectares of fast growing trees will be planted in the coming years.

Once established, fast growing tree plantations can be harvested for the first time after three years with a modified forage harvester. Shortly after harvest the trees re-grow from the roots requiring no further activities or treatments until the next harvest is scheduled. Depending on soil quality and climate, fast growing trees yield 8 to 20 t of dry matter/hectare/year in Germany, resulting in 2,000 to 5,000 litres BTL. Roughly 4 kg of dry biomass is needed to produce one litre of BTL-fuel. However, due to the lower calorific value of biomass in comparison to liquid fuels the conversion rate in terms of energy is approximately 50%.

In the long run Choren is confident about supplying at least 50% of the required biomass demand for its German BTL projects from woody energy crops. As the fossil energy prices carry on rising and incentives to reduce CO_2 emissions increase, the currently available biomass quantities are not sufficient to satisfy the growing demand from all biomass users. Fortunately the perspective for the production of fast growing trees on excess crop land within the EU is looking encouraging for the years to come: The Biomass Action Plan of the EU Commission estimates the raw material availability from energy crops to be up to 330 million tons of dry matter per year in 2030 – without harming the environment or endangering food supply. Theoretically this would be sufficient to substitute roughly 40% of the diesel demand within the EU through BTL.

Authors: Michael Dentmeyer, Michael Weitz, Dr. Ines Bilas

Contact:
Choren Industries
Freiberg, Germany
+49 37 31 2662-0
info@choren.com
www.choren.com

CO_2 Emissions Reduction

Energy Efficiency and What Else?

A Refiner's View – In the frame of the European Union (EU) strategy against climate change, the European Union Refining sector is concerned by an important package of EU legislation aimed at reducing industry CO_2 emissions. The major one is the Emission Trading Scheme (ETS) directive now currently under review.

For the post 2012 period, the European Commission's proposal is setting a scene where CO_2 constraints will be much tougher for the refining sector: the global industry cap will be significantly reduced in comparison with the present ETS period (2008–2012) and auctioning might become the predominant allocation mode.

Some other pieces of legislation have an adverse impact on CO_2 balance: they indirectly cause an increase of refining CO_2 emissions. Environmentally driven measures focused on reducing the sulphur content of petroleum products are part of these. Upward impacts on CO_2 emissions are also expected from changes in crude supply and in product demand, particularly the increasing imbalance between gasoline and diesel. Both driving forces, legislation and market, will call for significant adaptation of the existing refining tool. The implied increase in conversion and thus complexity of the sites will be inevitably translated in an absolute rise of energy consumption and therefore CO_2 emissions.

The upward trend of crude oil prices clearly influences the refiners' approach in the field of energy management: The ratio of energy expenses to total operational costs has been rising steadily in recent years. Energy saving has always been a concern for refiners but the present price context is making this issue all the more acute. They now have to cope with the challenge of adapting their tool to market changes in a way that minimizes the energy consumption and CO_2 impacts. Total group is actively working on this challenge and Total refining is handling this most important issue by:

- Reviewing and reinforcing its on going energy efficiency improvement plan.
- Re-evaluating the required adaptation of its European sites at the 2020 horizon to meet future product demand patterns, in the context of high energy prices and more severe carbon constraints in the EU.
- Studying opportunities for carbon capture and storage (CCS) and initiating R&D projects on the "low CO_2 emission" refining site.

ETS Impact on Refinery CO_2 Emissions

The ETS directive review proposal gives an indication of the effort which is requested from the ETS sector at the 2020 horizon: 21% green house gases (GHG) emission reduction in comparison with the 2005 real emissions. This target will be managed at EU level: Member states (MSs) no longer need to establish ETS National Allocation Plans. On an EU level, the non ETS sector has a 14% reduction target. Contrary to the ETS perimeter, this target will be individualized by MSs through a reviewed burden sharing agreement.

In addition to 5% of the global cap being put aside in the new entrants' reserve, the global ETS cap will decrease linearly (1.74% per annum) from 2013 to 2020. If applied to the refining sector, prorata its 2005 verified emissions, it would mean going from a 2013 cap equal to 90% of its 2008–2012 average allocation to a 2020 cap equal to 78% of its 2008–2012 allocation. The current proposal distinguishes three groups of industrial sectors:

- Sectors in group A are deemed to be able to pass through CO_2 costs and not to be subject to international competition. As such they will not receive any free allowances and will be subject to 100% auctioning. Group A includes the electricity production sector, and CCS installations. Electricity production installations within refineries are also in group A.
- Sectors in group C are energy intensive and subject to carbon leakage. Allocation for group C might be up to 100% free for the whole period.
- The remaining sectors are classified as group B, 80% of their allocation will be free in 2013 dropping to zero in 2020. The refining sector is at present located in group B.

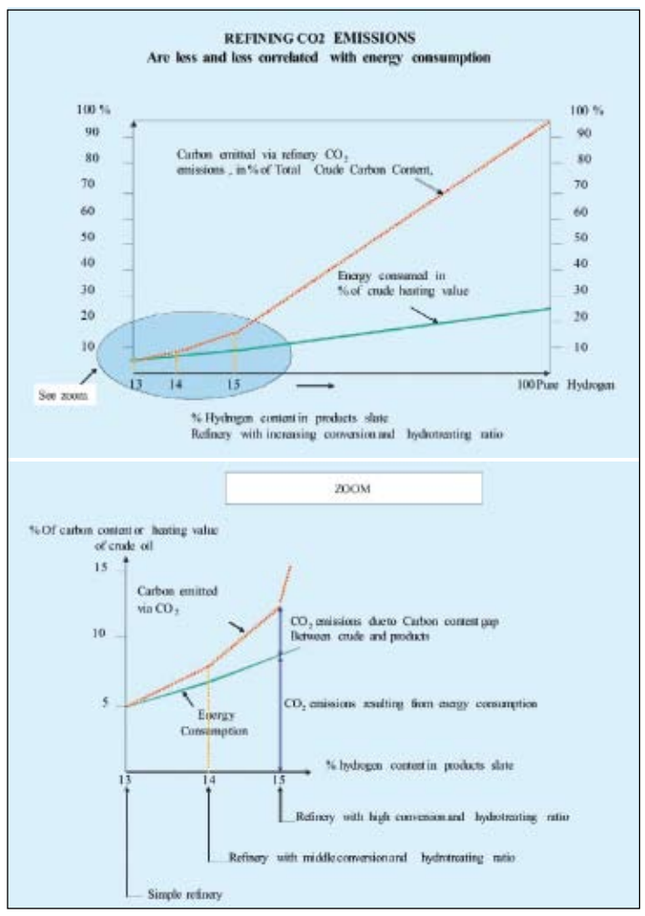


Fig. 1: Refining CO_2 Emissions (Sigaud, IFP)

External Drivers

Current and forecast changes in products' quality and demand induce significant CO_2 emissions increase. In regard to demand change, one main parameter impacting EU refining CO_2 emissions is the diesel growth at the expense of gasoline consumption. This diesel growth is a consequence of the EU legislative pressure on car makers to decrease the ratio of CO_2/km. Tax or fiscal incentives, either on the diesel itself or on low CO_2 emitting engines, favour on average the development of the diesel car fleet.

The other main parameter influencing EU refining CO_2 emissions is the erosion of gasoline and heavy fuel oil markets. These changes in products' quality and quantity will require considerable adaptations of the refining tool:

- Increase need for products hydrotreatments and for hydrocracking units, both implying new hydrogen plants.
- New units for desulphurisation or, most probably, conversion of heavy residue.

These new units, even built at the best available technology standards, increase the absolute and specific consumption of energy and CO_2 emissions (fig. 1).

Energy and CO_2 Weight in Refineries' Economics

In this current oil price context, energy costs of an average European refinery, including self consumed primary energy, represent probably over 60% of its global operating expenses. Energy efficiency improvement has always been a concern for the refining industry. The incentives to pursue efforts in that field have never been so high; All the more that saving energy also implies a reduction of CO_2. Auctioning is not at all necessary to create incentive: when free allocations are granted within a cap scarcity, a CO_2 opportunity cost is created by the stringency of this initial cap. The stringency of the proposed post 2012 ETS cap is significant and its impact on CO_2 price will come along with fuel prices to further motivate refiners in their efforts.

Total's EU Refining Tool

Energy performance of a refinery is very much correlated to the investments decided in the design stage. Most important energy efficiency gains in recent years have been achieved when implementing major new projects such as Residue Desulphurization, cogeneration and Hydrocracking. Consequently Total sets ambitious energy goals when designing its new projects.

Higher energy prices and tougher carbon constraints play a critical role in Total's ongoing analysis upon its ideal EU refining tool at the 2020 horizon. This holistic analysis takes into account the shift in product quality and quantity and the international competitiveness issue induced by the EU stance on environment translated in the last ETS and integrated pollution prevention and control (IPPC) review proposals.

GHG Balance

The current draft fuels quality directive review includes a proposal for a 10% GHG emissions reduction target for road transport fuels in a Well to Tank approach. As underlined by Europia, apart from being unachievable in practice, this target is inconsistent and overlapping with the ETS directive and the Renewable directives proposal. This issue is an opportunity to underline the actual contribution of refining operations in the total GHG emissions linked to motor fuels.

This illustrates the low refining share in the motor fuels total GHG balance and puts the potential to reduce it in its proper context. For fossil fuels the bulk of the emissions are incurred upon combustion. Only the production chain can be influenced and mostly through improved energy efficiency. In the case of biofuels the potential for improvement is much higher as fossil carbon is substituted for renewable carbon: this is credited to the combustion part.

Apart from energy efficiency improvement, burning biomass, developing CCS and using hydrogen produced by low carbon emitting process, are the most often quoted routes for reducing the refining part of the GHG balance.

Burning biomass could be envisaged only for utilities and for the portion of refinery fuel that is not self produced (approx. 25%). But biomass available for energy production would be better used in some dedicated power/heat plant or co-fired in large coal power plants according to appropriate logistical context.

CCS is probably a more promising route but it will not deliver significant contribution in the short/medium term: Capture of CO_2 in refineries is technically achievable when addressing units such as POX (Partial Oxidation Unit), where CO_2 is highly concentrated in exhaust gas, or SMR (Steam Methane Reformer). But, in most cases, these CO_2 concentrated streams represent a minor part of the refineries emissions. The major part originates from combustion which emits flue gases at much lower CO_2 concentration (below 15 %) and these sources are generally spread over the whole site. Adapting technologies initially developed for big power plants to a standard refinery is a real techno-economic challenge.

Contact:
Jean-Yves Touboulic
Total S.A.
Paris, France
Tel.: 33 (0)1 41 35 69 89
Fax: 33 (0)1 41 35 31 65
www.total.com

Opportunities to Promote Biofuels Production

Central And Eastern Europe

CEEC – Since the 1990s, the new EU member states from Central and Eastern Europe are in constant economical development. This development can be directly linked to the quantity of carbon emissions in those countries due to industrial activity.

Giuliano Grassi
EUBIA

Stéphane Sénéchal
EUBIA

During the '90s, total emissions declined in almost all Central and Eastern European Countries (CEECs) due to their introduction into the economic market and the reconversion or closure of heavily polluting and energy intensive industries. However, in 2004, after being 23% below the '90s level, economical development grew again and projections estimate a level 12% below the '90s level even with implementation of additional domestic measures. For example, transport sector greenhouse gas (GHG) emissions decreased by 6% between 1990 and 1995, but increased sharply from 1995 onwards. By 2004 these emissions exceeded the 1990 levels by 28% (fig. 1).

All new member states, except Slovenia, were on track in 2004 to meet their Kyoto targets using existing domestic policies and measures. Slovenia projects that it will meet its Kyoto target with additional policies and measures which also include CO_2 removals via land use change and forestry. Bulgaria and Romania project that they will over achieve their targets.

Energy Consumption and Renewable Energy Share in Europe

Despite energy efficiency improvements, the EU continues to release increasing amounts of GHGs. Around 80% of energy consumed in the European Union comes from fossils fuels, with over 85% in Central Europe and 90% in Eastern Europe. These fuels are expected to dominate Europe's energy sources in coming decades. In addition, Europe's coal reserves are abundant, readily accessible and prices are stable. So, coal remains an important fuel for electricity generation and heavy industries despite the high level of GHG emissions.

The share of renewable energy in the electricity generation of EU 25, averages at 12.8%, but nine countries get less than 3% including Belgium, UK, Poland and Hungary. Each country still has much to do in order to comply with the 2010 objectives and little time to do so.

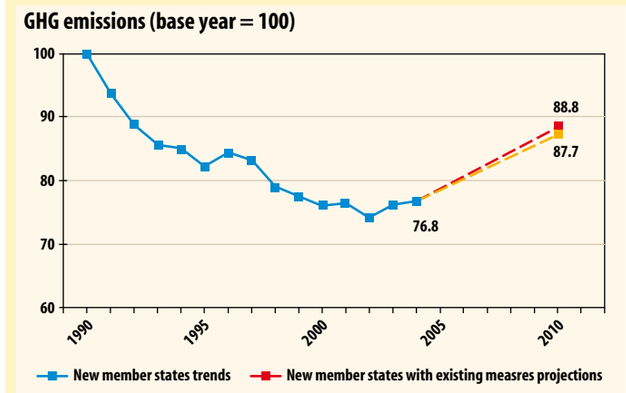
Regarding biomass potential, even if it is the main resource used today for renewable energy production, we can note that biomass could be used and valorized in a more efficient way, despite bioenergy already being well developed in some countries such as Latvia. However, this use and exploitation has to be made very carefully, ensuring biomass is used in an environmentally compatibility way. Some studies promote, as better use in medium term, the production of ethanol, biogas and short rotation forestry. The lignocellulosic ethanol development is expected in the long-term.

Opportunities of Bioenergy to be Promoted

In view of this situation, Eubia already promotes some activities for the limitation of GHG emissions in a sustainable way, at short and medium term, promoting the use of solid biomass. One of the main market opportunities in new member states is the stabilization of humid biomass for large scale supply and trading, and the co-firing (coal-biomass) in large power-plants by agro pellets.

The stabilization of humid biomass has various positive effects. A positive chemical effect is that fresh biomass is submitted to biological degradation with emission of GHG. Furthermore, a logistical positive effect, in the case of large scale supply, is that all year around quantity and volume of biomass is very important. This biomass should be dried and densified in order to facilitate the handing and limit the storage requirements.

The new "Agro-pellets technology" is a basic refining (pretreatment) technology, for stabilisation of humid biomasses and compaction to eliminate its biodegradation and for increasing its specific energy content. Taking into account its innovative performance, its high energy efficiency and relative low cost, this new technology is opening broad perspectives for large-scale modern exploitation of all types of cellulosic biomasses (agroforestry residues, organic wastes, energy crops) and for all sectorial energy markets (heat, power, transport). The most peculiar characteristic is that it is able to process humid biomasses (moisture level of 25–30%) directly in one step, avoiding thermal predrying.



Note: Data exclude emissions and removals, from land-use change and forestry. Due to lack of data, Cyprus and Malta are not included.

Source: EEA, based on new Member States greenhouse gas inventories and projections.

Fig. 1: Greenhouse gas emissions in new member states actual and projected

The use of agropellets for bioelectricity production present benefits for efficient cogeneration plants, for co-combustion of coal-agropellets and provides a homogeneous high-energy biomass product important for avoiding major operational problems with boilers. As said before, coal will still provide a large contribution to the total world energy needs (2.6 billion Toe in 2010 – 3 billion Toe in 2020) with a typical emission of 3.3 kg CO_2/kg coal. Co-firing of biomass in efficient coal power plants is the most effective way to utilise renewable biomass with great benefits for CO_2 reduction. Biomass (CO_2 neutral renewable fuel) can be co-fired with coal in large boilers. In general, biomass can be blended directly with coal at low percentages (5–7% heat input) and milled and fired in existing combustion plants. The performance of the mills can limit the proportion of biomass utilised. The biomass can be co-fired in higher percentages (up to 20%) with coal. However, the amounts of biomass required for co-firing seem compatible with the estimated future available biomass scenario; 1.5 billion d t/y of which 600 Mdt/y as agricultural residues in Europe and 14 billion d t/y in the world. Up to now more than 150 coal-fired plants have experienced some co-firing activity (U.S.: 40, Sweden: 15, Germany: 27, Finland: 14). About 40% of these plants were co-firing biomass on commercial basis, most in Sweden and Finland.

The two main liquid biofuels with concrete market opportunity for Central and Eastern Europe are bioethanol and biodiesel, which are now in development in those countries. The EU has excellent potential for biofuel production in its newest member states and this should be exploited, especially since demand for energy is increasing and fuel is becoming more expensive than ever. The role of these CEECs will be pivotal in the EUs overall biofuel production, as they have the most feedstock potential. CEECs will play a decisive role in the EUs fulfilment of renewable energy targets by 2020. With increased efficiency in agricultural production in these countries, this will lead to more efficient biomass production. Although CEECs have a higher share of good arable land per capita than Western European countries, they have only average yields in comparison. Thus, improvements can, and should, be made as the agricultural sector in CEECs still needs to be reformed to achieve increased production efficiency.

The EU27 bioethanol production in 2007 was around 5,900 Toe and biodiesel around 1,300 Toe, but production is still very low in CEECs. Bioethanol production seems to be more promising than biodiesel in term of sustainability, volume and economic production in CEECs. Bioethanol production through an integrated approach offers better commercial competitiveness in a more sustainable way. This commercial production of bioethanol can be based on sweet sorghum and benefits from integrated processing. Sweet sorghum is a multi-functional crop, thus not a competitor for the food market. Furthermore, it grows in low quality soil with lower water inputs (1/3 of sugar cane). Its productivity is very high (~100 fresh ton/ha) thereby enabling the production of low cost sugars and lignocellulosic residues (i.e. sugars ~50€/ton; residues: ~20€/ton), making viable co-production of bioethanol and bioelectricity. The optimised sweet sorghum biorefinery presents a high energy ratio (outputs/inputs). Therefore, it is very efficient for atmospheric CO_2 absorption and has the potential for gaining substantial carbon credit benefits. This ratio is obtained thanks to integrated bio-energy complex, utilizing all crop components to obtain several products (animal feed, power, agro-pellets and bio ethanol), and keeping the priority product bioethanol at minimum cost.

Conclusions

We can observe high potential for biomass use in CEECs by changing the actual use of biomass for bioenergy production and exploiting marginal lands and new areas available not suitable for food production. The co-firing of biomass (using agropellet technology) in coal power plants can be carried out at high levels and presents high CO_2 reduction benefits. Sweet sorghum appears to be a promising viable multifunctional crop for large scale production of bioethanol and power in Central and Eastern Europe.

▶ Contact:
Stéphane Sénéchal and Giuliano Grassi
Eubie European Biomass Industry Association
Brussels, Belgium
Tel.: +32 2 4001020
Fax: +32 2 4001021
eubia@eubia.org
www.eubia.org
www.refuel.eu

Institutional Needs for Industrial Biorefineries

Thoughts From The UK

Clearing the Ambiguity – The age of integrated biorefineries is not yet here. In fact, given the vagueness of biorefinery definitions, how will we know when it has arrived? Cross-sector participation, clear environmental goals and flexible definitions could be central to getting on the right path and enabling biorefineries to evolve naturally.

These pages have chronicled numerous recent developments and discussions relating to the use of agricultural products as new raw materials for fuels and chemicals. A confluence of pressures arising from climate awareness, enduring high oil prices, heavier crudes, and consumer interest in renewables, is being felt by the chemical industry. In June's edition of this publication we heard from McKinsey & Company about some of the prospects for white biotechnology.

That article highlighted some of the difficult choices between molecular targets for biotech processes; it gave an optimistic prescription for JVs between well-endowed raw material suppliers and chemical companies in familiar fields such as ethanol dehydration, lactic acid and 1,3 propanediol (PDO). The enthusiasm was slightly tempered however by an acknowledgement of the fickle nature of biofuels investments, which can potentially drain resources away from bio-based chemicals and towards the vast and subsidised green energy markets. Oleochemical producers, whose feedstock supplies have suffered from competition with biodiesel, can testify to this.

Integrated Biorefineries: Pipedreams or Blueprints?

Competition for raw materials between food, feed, fuels and chemicals serves to exacerbate an already risky investment environment. Yet one widely acclaimed idea offers a solution. The integrated biorefinery has captured the imagination of industrialists, European policy-makers and an expanding network of researchers. It is a simple and alluring idea: biomass feedstock is separated into its constituent elements, which are then processed locally into an array of products for which they are most suited, generating high value specialty chemicals, high functionality building blocks, high volume fuels from cellulosics, and where feasible heat, power and feed too. It is generally presented as analogous to an oil refinery and petrochemical cluster.

A number of potential biorefinery designs, or concepts, exist on the drawing board. But in the absence of any firms leaping into action to construct such a facility today – indeed, in the absence of many of the component technologies – how might we get from here to there? And what is the role for institutional guidance in the process?

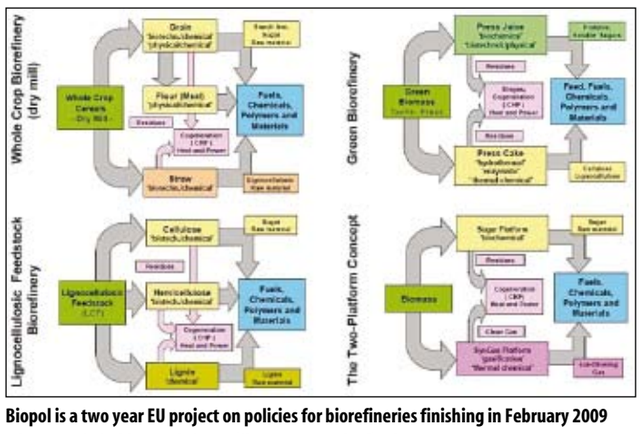
Deep technological transitions are long-term processes. Making biorefineries into attractive propositions thus requires harmonised advances in agronomy, biomass treatment, biotechnology, bioprocess engineering, but also inter-industry relationships, government policies and societal attitudes. Such transformations have been termed system innovations. They are the realm of visionaries such as Thomas Edison with an entrepreneurial approach to the whole system of production and consumption. Yet for all the roadmaps and visions that have been produced in recent years, change rarely follows the prescribed path, especially where political decisions are central. This is highly relevant for clean technologies.

Lessons From The Past

The petrochemical revolution arrived in the UK in 1951 with the construction of the first large ethylene crackers for refinery by-product naphtha. But the transition from coal-based aromatic feedstocks towards aliphatics began some 30 years earlier. In 1921, following a drop in consumer demand for potable spirits, heavy subsidies were introduced to support the whisky makers' diversification into new uses for ethanol. New uses included blending with gasoline, for security of fuel supply and as industrial solvents for the struggling dyestuffs industry.

This government policy response to a change in public opinion against drinking led to the distillers company becoming the leading UK producer of ethylene products. Having been pioneered in the U.S. where cheap petroleum gases were available, products such as ethylene glycol were adopted in the UK over the next 10 years using a cheaper – subsidised – dehydrated ethanol feedstock. Hence, when ICI first scaled-up production of their new polyethylene polymer in 1938 the feedstock of choice was dehydrated ethanol; and when BP needed a partner for its first petrochemicals venture it was the Distillers Company that had the skills and knowledge of olefins and their derivatives. ICIs pride in its reliance on coal and refusal to become reliant on the oil majors almost caused its downfall.

Reading the history of how petrochemicals were adopted by users of a subsidised alcohol feedstock it is apparent how the British chemical industry was shaped as much by institutions as it was by the science. Protectionist ties between government, ICI and BP made them slow to respond to new challenges in synthetic materials. British oil policy in the 1930s was concentrated on retaining concessions in the Middle East to supply wartime needs, but neglected the benefits of home refining and higher value co-products. Not until there was an alignment between strategic objectives in both gasoline production and organic chemicals, did petrochemical complexes start to assemble around oil refineries, which had chosen their locations decades earlier and have not moved much since.



Biopol is a two year EU project on policies for biorefineries finishing in February 2009 when a stakeholder workshop will accompany the final report. http://www.biorefinery.nl/biopol.

The complicated dynamics of technological evolution mean that things rarely turn out as planned. Policy interventions in one sector can influence developments in another if the interactions are not well understood.

Common Stories Are Needed

A sample of UK policymakers for bioenergy and chemicals was surveyed this year for the EU Biopol project. Preliminary results indicate that amongst civil service and government bodies a working knowledge of the biorefinery concept exists, but confusion over definitions is apparent. Clear answers were absent for questions such as what is a bio-plastic? Or which industry will drive biorefinery development?

Without institutional agreement regarding the way forward, stylised models of green or two-platform biorefineries appear a long way off. Aligning the various interests in this exciting new industrial field needs to overcome a number of barriers, including disharmony over the objectives of supporting bioproducts. A common story needs to emerge regarding whether they are aimed at avoiding fossil fuel depletion, increasing security of supply, hedging against oil prices, being more environmentally benign, or reducing carbon emissions. The story may be different for different product families, but ought to be consistent.

The development of white biotechnology in the UK is likely to be dominated by the following institutional pressures:

- National security of supply strategy – The biofuels markets much larger than that for bio-based chemicals and is arguably closer to take-off; if security of supply drives biofuels production then availability of renewables for chemicals may be constrained to that of a fuel by-product.
- Climate policy – Pricing carbon globally is crucial to advance second generation biofuels and develop pretreatment and fractionation processes for biorefineries.
- Facilitation of new alliances – government ministries and trade associations are organised around present supply chains. New processes need engagement of industries that could bring new skills and resources. In the UK the Integrated Biorefining Technologies Initiative (IBTI) is taking steps in this direction.
- Lead markets – The first products to reach markets have been concentrated in bio-plastics (e.g. PLA) and bio-detergents. Initial successes or failures could easily determine subsequent developments yet LCA tools and standards are not well advanced for assessing environmental performance. Initiatives such as the EU's lead market initiative and the UK's from renewable platform chemicals to high value products (Froptop) are welcome; but must resist picking winners.

The idea of integrated biorefineries is a powerful reminder of how far renewables can still progress. But if we learn anything from history it should be that technological change is a meandering and manipulable process. Policies contributing to biorefinery development need to appreciate the importance of timing; some products will be brought to market before others, possibly altering the options for co-location of facilities. Governments can, and should, protect market niches where experience with LCA tools and standards can be gained.

▶ Contact:
Simon Bennett
Centre for Energy Policy and Technology (ICEPT)
Imperial College London
London, UK
Tel. +44 20 759 47314
simon.bennett04@imperial.ac.uk.


Andy Piers

Clariant Appoints Andy Piers Head of Group Technology and Member of the Board Clariant has appointed Andy Piers as head of Group Technology. He is now also a member of the board of management. Andy Piers, a British and Zambian citizen holds a Ph.D in chemistry and engineering from the University of Dundee, Scotland. He worked at inorganic chemical producer Brunner Mond & Co, a division of ICI, and Union Camp Corporation that became part of Arizona Chemical, a subsidiary of International Paper, in 1999. He held several important management positions in R&D as well as commercial operations functions. Piers joins Clariant from Englefield Capital, a private equity firm, where he was working as an independent advisor. ■


Ravi Uppal

Ravi Uppal to Leave ABB Ravi Uppal, president of Global Markets and a member of the ABB Group executive committee since July 2007, has decided to relinquish his position for personal reasons and plans to return to India to pursue a career outside ABB. He will remain non-executive chairman of ABB in India, to help ensure continuity in the business in this market. A successor for his Zurich-based role as head of Global Markets will be announced in due course.

Uppal joined ABB in 1980 and, after a five-year spell at Volvo, returned to the company as ABB country manager in India in 2001. Uppal steered a period of very profitable growth in the country and, as the regional manager for South Asia from 2005 until his appointment to the executive committee, contributed to ABB's development in the region. ■

Unilever: CEO Cescau to Retire, Nestle's Polman New CEO Anglo-Dutch consumer goods producer Unilever said that chief executive Patrick Cescau will retire at the end of the year to be replaced by Paul Polman, the current executive vice president and Americas regional head at Swiss Nestle.
The maker of products such as Dove skin and hair products, Hellmann's mayonnaise and Ben & Jerry's ice cream said that Polman will be proposed for appointment to the Board at an Extraordinary General Meeting to be convened during the autumn. He will take over as group chief executive following an orderly transition, Unilever said.

Cescau, who turns 60 next year, had been expected to step down at Unilever's next annual meeting, to be held in May 2009.

"Four years ago we set out to transform Unilever and to get the business back on track," Cescau said. "I believe that phase of work is largely complete, so now is exactly the right time to pass on the baton." ■


Lars Rasmussen

Coloplast Appoints Lars Rasmussen as New CEO Danish healthcare products maker Coloplast said it has appointed Lars Rasmussen as its new chief executive and president, replacing Sten Scheibye from Oct. 1. Rasmussen has been with Coloplast since 1988 and a member of its executive management since 2001, most recently as chief commercial officer with the responsibility for sales, marketing and product development, the company said in a statement. ■


Erich Brunn

New CEO for Takeda Pharmaceuticals Europe Takeda Pharmaceutical Company, a Japan-based pharmaceutical company, has appointed Erich Brunn as CEO of Takeda Pharmaceuticals Europe, its wholly owned subsidiary for oversight of pan-European sales and marketing.

Brunn has a doctorate in chemistry and, since 2001, has been president of Takeda Pharma, a wholly owned subsidiary of Takeda in Germany. He previously worked at Upjohn, Pharmacia & Upjohn and Pharmacia in various functions.

Yasuchika Hasegawa, president of Takeda, said, "Dr. Brunn has a proven track record of success and excellence, which is apparent through the remarkable growth achieved by Takeda Pharma under his leadership. We are confident that he will provide Takeda Pharmaceuticals Europe (TPEU) with the same level of success as he takes on this pivotal role as CEO of TPEU."

Dystar Appoints New President and CEO Dystar's owner, Platinum Equity, has appointed J. Mark Allan as Dystar 's new president and chief executive officer. He replaces Phil Norment. Allan was previously serving as the COO and acting CEO. Norment will remain a member of the board of general managers and continue to oversee Dystar in his capacity as president of portfolio operations for Platinum Equity. Most recently, Allan was senior vice president for Platinum Equity where he was responsible for the European portfolio company operations.

▶ www.dystar.com

SAFC Appoints New Vice President of Quality and Regulatory Affairs SAFC, a member of the Sigma-Aldrich Group, has announced the appointment of Tom Beil as vice president of Quality and Regulatory Affairs. Beil, a quality systems and operations professional with nearly 25 years experience, will lead SAFC's quality assurance team and oversee all aspects of the company's regulatory and quality assurance programs. He will report to SAFC President Dr. Frank Wicks, and to Rich Keffer, general counsel and secretary for Sigma-Aldrich. This is Beil's second tenure with Sigma-Aldrich, having spent 13 years as Quality Systems Manager from 1986 to 1999.

▶ www.sigmaaldrich.com


Dr. Günter von Au

Süd-Chemie Renews von Au Contract The supervisory board of Süd-Chemie has reappointed Dr. Günter von Au as chairman of the managing board. A contract running from Jan. 1, 2009–Dec. 31, 2013 has now been signed.

Von Au has been chairman of the managing board of Süd-Chemie since mid 2004. Between 1980 and 2001 he worked for Wacker Chemie holding various management positions including director of the company's Brazilian subsidiary, head of the group's polymer and chemicals division and managing director of the joint ventures Wacker Polymer Systems. Upon joining Süd-Chemie Group in 2001, von Au took over the management of its U.S.-subsidiary, Süd-Chemie Inc. in Louisville, Ky. At the beginning of 2004, he was appointed deputy chairman of the Süd-Chemie managing board. He took over as chairman of the managing board in mid 2004.

▶ www.sud-chemie.com

Chemical Society Honor 'Heroes of Chemistry' During National Meeting

Bruce Roth's name may not be on the tip of many tongues, but his invention has been on more than 26 million in the U.S. alone. Inventor of Lipitor, the cholesterol-lowering pill that is the world's largest selling drug, Roth is among 25 unsung scientific heroes who are being inducted into an American Chemical Society (ACS) hall of fame called the Heroes of Chemistry.

The other new Heroes include Karen E. Lackey, Glaxo Smithkline Pharmaceuticals, for work on discovery of a new breast cancer drug; a team from Pfizer Global Research & Development that discovered a new drug for HIV infection; a team from Wyeth Research that discovered and developed a new drug for renal cell carcinoma; and scientists from Exxon Mobil Corporation. and Albemarle Corporation who discovered a way to make cleaner diesel fuel.

"Heroes of Chemistry strives for greater recognition of scientists like these who, like chemistry itself, often wear a cloak of invisibility so far as public awareness is concerned," said Bruce E. Bursten, Ph.D., president of the American Chemical Society and Dean of the College of Arts and Sciences at the University of Tennessee, Knoxville. "Their dedication and scientific contributions save lives and make life healthier and happier for billions of people around the world."

The other 2008 Heroes of Chemistry have made extraordinary contributions, according to the review panel. They are:

Karen E. Lackey, vice president of discovery medicinal chemistry, Glaxo SmithKline Pharmaceuticals, Research Triangle Park, NC. Lackey's chemistry team was involved in discovering the lapatinib molecule, which became the anti-cancer drug Tykerb. First marketed in 2007 for advanced breast cancer, Tykerb is among a new family of "targeted" anti-cancer medicines. It targets the 20–25 % of breast cancers that produce too much of a substance that enables tumors to grow quickly. In doing so, Tykerb may prevent these cancer cells from growing, dividing, and surviving.

Anthony Wood, Ph.D., David Price, Ph.D., Blanda Stammen, Ph.D., and Duncan Armour, of Pfizer Global Research & Development for research on the discovery of maraviroc. In 2007, that molecule went into medical use as Selzentry (Celsentri in Europe), the first of a new class of drugs for infection with the HIV, the virus that causes AIDS.

Magid Abou-Gharbia, Ph.D., Jerauld Skotnicki, Ph.D., James Gibbons, Ph.D., Ker Yu, Ph.D., Warren Chew, Ph.D., Joseph Camardo, M.D., and Gary Dukart, M.D., of Wyeth Research for contributions to the discovery and development of a molecule called temsirolimus that became an innovative new treatment for renal cell carcinoma. In 2007, Torisel (temsirolimus) was approved for the treatment of advanced renal cell carcinoma. Renal cell carcinoma accounts for about 85 % of the 51,000 cases of kidney cancer diagnosed each year.

Sonja Eijsbouts, Ph.D., M.B. Cerfontain, Ph.D., Hans W. Homan Free, Michael C. Kerby, Ph.D., Bob Leliveld, Ph.D., Ernie Lewis, Ph.D., Stephen J. McCarthy, Sabato Miseo, Bob Oogjen, Frans L. Plantenga, Ph.D., Kenneth Lloyd Riley, Ph.D., Stuart L. Soled, Ph.D., of Albemarle Corporation and Exxon Mobil Corporation. Responding to more stringent air pollution regulations for diesel fuel sulfur content, the scientists developed and commercialized a new type of catalyst, called Nebula, that allows refineries to produce cleaner diesel fuel. ■

Pharma, Supply Chain Meetings in London

PharmaIQ is again hosting the 5th Annual Pharma Secure Chain and End-to-End Supply Chain Optimization industry meetings Oct. 21–22 in London.

Event A: Pharma Secure Chain 2008 is lock down security against counterfeit medicines: Protecting revenue and reputation, and above all patient safety. Topics: Mass serializations; Distribution channels; EU GMP regulation; 2D and RFID; EFPIA; track and trace; authentication; parallel trades; derogation; regulation; and brand protection.

Event B: End-to-End Supply Chain Optimization 2008 is a comprehensive program that will allow you to design your global supply chain into a controlled, viable and compliant process.

Topics: Supply chain integration; direct to patient or pharmacy (DTP); reduce lead times and inventory levels; sourcing apis; legal challenges; operational excellence and optimization; pull planning; final miles visibility.

For access to both meetings, CHEManager Europe guest list prices and further information call: Tel: +44 (0)207 368 9518 IQPC, PharmaIQ registration direct line.

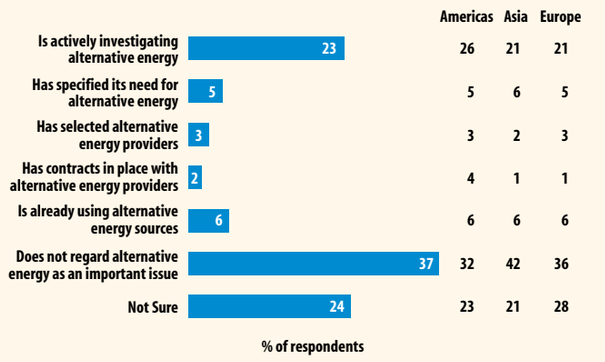
▶ www.iqpc.com

Please send your event information to chemanager-europe@gitverlag.com

Alternative Energy

Company Approach to Alternative Energy

Which of the following comes closest to your company's current approach with regard to alternative energy?

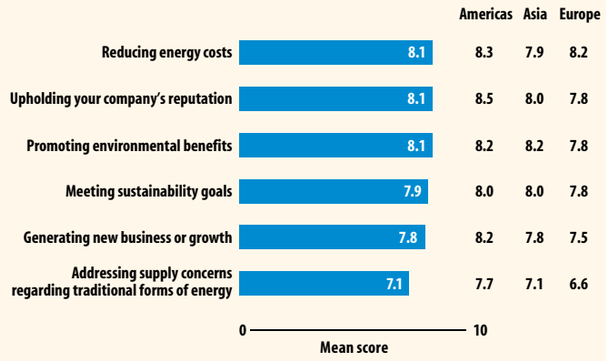


Source: Dow Corning © GIT VERLAG

Overall Americas, Asia and Europe show great resemblance in regard to company's approach to alternative energy. While all three regions say their company's are actively investigating alternative energy, 37 % also say that it is not an important issue. Despite public pressure only 6 % of survey respondents say their company is utilizing alternative energy sources.

Decision Driving Factors

How important are the following factors in influencing your company's decisions about alternative energy?



Source: Dow Corning © GIT VERLAG

The top reasons companies consider alternative energy are cost reduction, company reputation and environmental benefits. The reputation aspects scored the highest for Americas. In Europe the primary reason is the need for cost reduction whereas in Asia, it is the environmental benefits that influence decisions on alternative energy.

Carbon Footprinting

Familiarity

How familiar are you with the term carbon footprint?

Global

Familiarity	%
Very familiar	11
Somewhat familiar	21
Not at all familiar	68

Americas

Familiarity	%
Very familiar	18
Somewhat familiar	35
Not at all familiar	48

Asia

Familiarity	%
Very familiar	2
Somewhat familiar	8
Not at all familiar	90

Europe

Familiarity	%
Very familiar	18
Somewhat familiar	26
Not at all familiar	56

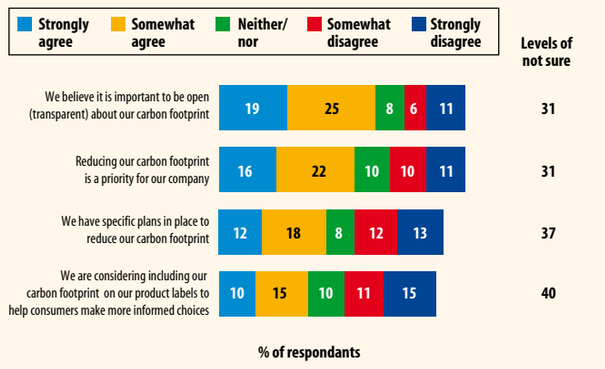
The question was asked first without a definition – if the respondent was unable to answer, the following definition was provided: the amount of greenhouse gases produced, measured in units of carbon dioxide.

Source: Dow Corning © GIT VERLAG

The term "carbon footprint" is not widely recognized. Globally 68 % of respondents were not familiar at all with the term. Particular Asia has the lowest level of recognition with only 2 % of respondents being very familiar with the term compared to 18 % for both Europe and Americas.

Attitudes to Carbon Footprinting

To what extent do you agree or disagree with the following statements about your company?



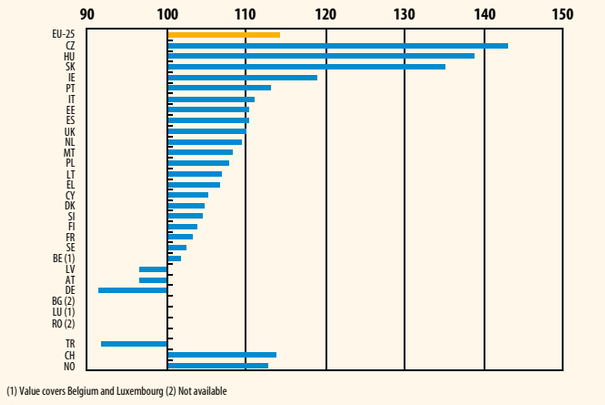
Source: Dow Corning © GIT VERLAG

Asia and Europe responded significantly different across the board from the Americas on attitudes toward carbon footprinting. In Europe, 57 % place importance on transparency of their carbon footprint and 46 % indicated that reducing their carbon footprint was a priority.

Economy and Finance

Price Convergence and Competitiveness

(real effective exchange rate), 2006 (1999 = 100)



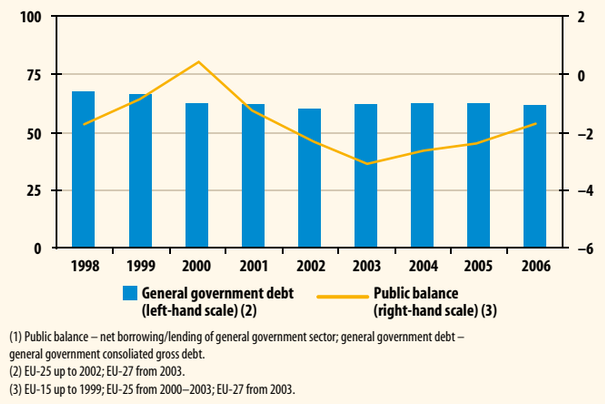
(1) Value covers Belgium and Luxembourg (2) Not available

Source: Eurostat © GIT VERLAG

Comparisons of price changes between countries depend not only on movements in price levels, but also exchange rates, and together these impact on price and cost competitiveness. The real effective exchange rate aims to assess a country's price or cost competitiveness relative to its principal competitors in international markets. A rise in the index means a loss of competitiveness. The real effective exchange rate shown here is deflated by nominal unit labour costs and is based on an aggregate of 34 industrial countries.

Government Debt

EU (% of GDP) (1)



(1) Public balance – net borrowing/lending of general government sector; general government debt – general government consoliated gross debt.
(2) EU-25 up to 2002; EU-27 from 2003.
(3) EU-15 up to 1999; EU-25 from 2000–2003; EU-27 from 2003.

Source: Eurostat © GIT VERLAG

Government debt is a key element when assessing the government sector's financial position. Both the general government public balance and general government debt are reported on April 1 and October 1 of each year to the European Commission within the framework of the excessive deficit procedure. Under the convergence criteria, the debt ratio of general government consolidated gross debt to GDP, should generally be no more than 60 % and the ratio of planned or actual government deficit (net borrowing) to GDP should be no more than 3 %.

World Drug Manufacturing Summit 2008

The 7th Annual WDM Summit took place on Sep. 9–11 in Düsseldorf, Germany. Many attendees said they were pleased with the high caliber of speakers, who presented a number of engaging topics. Jean-Francois Ricard, supply chain director at UCB Pharma, at one point even had the entire conference on their feet, though it was by his request for attendees to join him in a "virtual" walk through the plant.

The World Trade Group, organizers of the event, utilized technology to facilitate easier networking. Throughout the three-day event, the most common sight was people walking around with their hand held "Spot Me" devices. These enabled attendees to locate people they wished to network with, send them messages and exchange electronic business cards. Furthermore, a virtual conference can be obtained by those who were unable to attend.

▶ www.wdsmsummit.com

Coming up in CHEManager Europe 11/2008:

- Interview with Jack Bolick, president of Honeywell Process Solutions
- The concluding part of principles of heterogeneous catalysis
- Chemical investment clusters
- The future of wireless solutions in industrial automation

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Publisher:
GIT VERLAG GmbH & Co. KG
Roesslerstr. 90
64293 Darmstadt
Tel.: +49 6151 8090 0
Fax: +49 6151 8090 168
info@gitverlag.com
www.gitverlag.com

Managing & Publishing Director
Dr. Michael Schön

Product Management
Dr. Michael Klinge
Tel.: +49 6151 8090 165
michael.klinge@wiley.com

Editor-in-Chief
Brandi Schuster
Tel.: +49 6151 8090 166
brandi.schuster@wiley.com

Managing Editor
Ana Wood
Tel.: +49 6151 8090 255
ana.wood@wiley.com

Editorial
Dr. Michael Klinge
Tel.: +49 6151 8090 165
michael.klinge@wiley.com

Dr. Michael Reubold
Tel.: +49 6151 8090 236
michael.reubold@wiley.com

Dr. Roy Fox
Tel.: +49 6151 8090 128
roy.fox@wiley.com

Wolfgang Sieß
Tel.: +49 6151 8090 240
wolfgang.siess@wiley.com

Dr. Dieter Wirth
Tel.: +49 6151 8090 160
dieter.wirth@wiley.com

Dr. Birgit Megges
birgit.megges@wiley.com

Media Consultants
Thorsten Kritzer
Tel.: +49 6151 8090 246
thorsten.kritzer@wiley.com

Miryam Preußer
Tel.: +49 6151 8090 134
miryam.preusser@wiley.com

Ronny Schumann
Tel.: +49 6151 8090 164
ronny.schumann@wiley.com

Roland Thomé
Tel.: +49 6151 8090 238
roland.thome@wiley.com

Corinna Matz-Grund
Tel.: +49 6151 8090 217
corinna.matz-grund@wiley.com

Team Assistants
Lisa Rausch
Tel.: +49 6151 8090 263
lisa.rausch@wiley.com

Christiane Rothermel
Tel.: +49 6151 8090 150
christiane.rothermel@wiley.com

Intern
Linda Tonn
Tel.: +49 6151 8090 203
linda.tonn@wiley.com

Freelancers
Dr. Sonja Andres
Anja Szerdi

Production Managers
GIT VERLAG GmbH & Co. KG
Dietmar Edhofer (Management)
Sandra Rauch (Deputy)
Claudia Vogel (Advertising)
Mattias Funk (Layout)
Elke Palzer, Ramona Rehbein (Litho)

Reprints
Christine Mühl
Tel.: +49 6151 8090 169
christine.muehl@wiley.com

Subscription/Reader Service:
Tel.: +49 6151 8090 115
readerservice@gitverlag.com

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Dresdner Bank Darmstadt, Germany
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