

## Ingelheim's new RESOMER® building makes rapid progress

Dr Volker Trach, Head of Resomer Product Unit / BI Pharma GmbH & Co. KG

Construction work on Pharma Chemicals' new, dedicated RESOMER® building at our Ingelheim site in Germany, which will bring together most of our biodegradable polymer activities at the site under a single roof, is on schedule to be operational by next April.

Since the groundbreaking ceremony on the 15th of February this year, construction of the three-storey building, with its planned 1,000 m<sup>2</sup> of floorspace, has made rapid progress. Our RESOMER® staff, at present spread between various premises at the Ingelheim site, are also busily preparing to join their colleagues for the first time in one and the same building.

With its two RESOMER® product lines of resorbable polymers for medical and pharmaceutical applications, RESOMER® is firmly established as a world leader in its niche market. And we are determined to stay ahead of the competition by our customer-driven business approach supported by the new building.

The consolidation of our RESOMER® activities in Ingelheim in one building is primarily aimed at improving operational efficiency. It will also raise production capacity substantially. The flexible design of the new facility, which will house Development and Production and Quality Control, furthermore allows easy expansion whenever

needed in the future. Importantly, the new building will also enhance the company's GMP compliance.

Labso Chimie Fine, the Pharma Chemicals unit located at Blanquefort, near Bordeaux in southwest France, will continue to produce lactide and glycolide as the feedstock for the polymerisation processes undertaken in Ingelheim.

The RESOMER® business, now in its third decade, is very much customer-driven. We are widely recognised by companies searching for novel applications for biodegradable polymers as an extremely reliable supplier of the highest quality polymer. That we are part of the Boehringer Ingelheim group of companies, a research-driven organisation, is also seen as a particular advantage.

Currently, the bulk of our RESOMER® output is used in the production by our customer companies of screws and plates for surgical applications, largely replacing previously employed metal implants. Use in surgical membranes is also growing. In the pharmaceuticals industry, the polymers are at present used mainly for slow release delivery of cancer drugs and growth hormones. But demand for slow release applications is increasing for other therapies, too, including, for example, vaccines and regenerative medicine.



The architect's model of the new building.

Our customers are constantly looking for innovative new applications to benefit from the distinct advantages biodegradable polymers can offer.

And our consolidated new RESOMER® operation in Ingelheim will from next spring on be ready and able to provide customers with improved support.

# Ingelheim successfully introduces Value Stream Mapping

By Dr Andreas Ikker, Certified Chemist, Project Manager Six Sigma / Boehringer Ingelheim Pharma GmbH & Co. KG and Stefan Bertram, International Account Manager / Boehringer Ingelheim Pharma GmbH & Co. KG

Value Stream Mapping (VSM), originally developed by Toyota, today the world's leading carmaker, has been successfully introduced by Pharma Chemicals at our Ingelheim site in Germany to provide valuable analysis for our customers. Two projects for APIs for external customers have already been completed and a third is now planned for a captive API.

VSM is commonly used in lean environments to identify opportunities for improving lead times. The technique analyses the flow of materials and information across the whole value chain required to bring a product or service to the end-consumer. Generally associated with manufacturing, VSM is nowadays also applied far more widely, e.g. in logistics, supply chain, software and product development.

- Improved production and communication
- Waste at each step of production process identified
- Streamlining of work processes enabled to eliminate waste
- Lead times and work in process reduced
- Security of business processes enabled from beginning to end
- An improved supply reliability

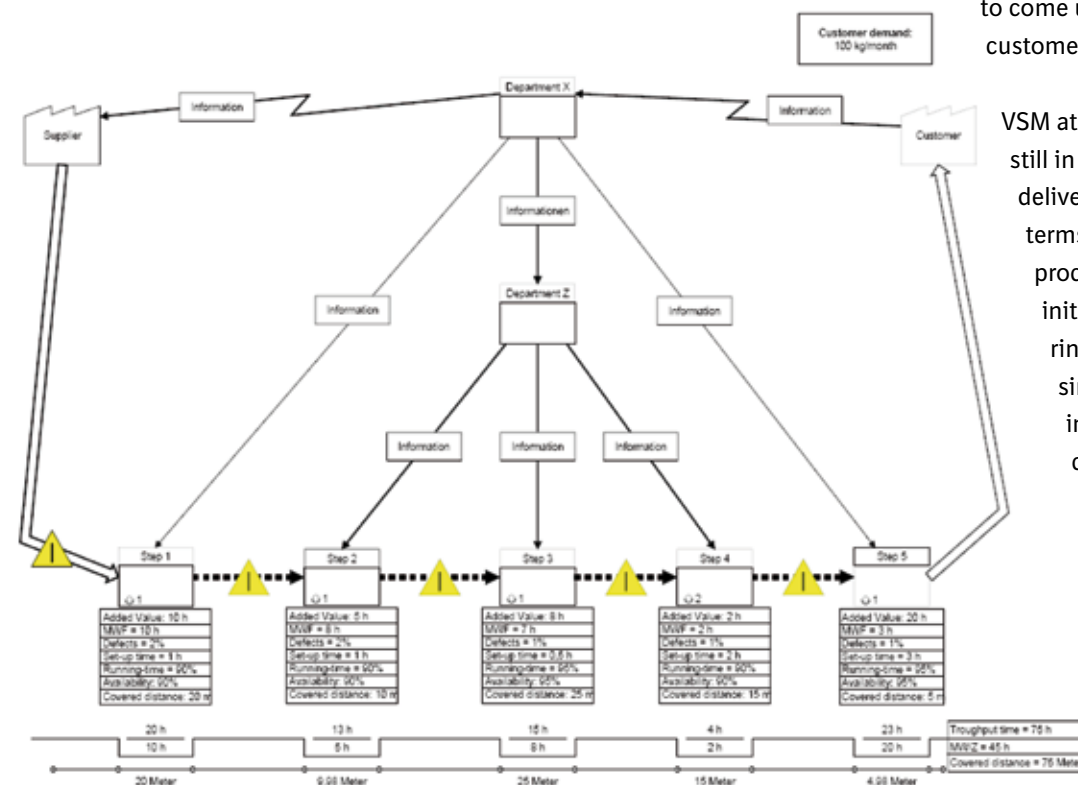
followed up by a project on digoxin, a phytopharmaceutical derived from foxglove (digitalis). The latter had its special challenges because of the uncertainties in cultivating and harvesting the plant material. Our VSM projects are led by people from our Business Process Excellence unit and involve departmental representatives of each of the stages covered by the analysis. While finding time to participate in the VSM sessions has proven difficult for participants, the projects have had a very positive impact on teambuilding, have improved communication between the departments involved and made it easier to come up with solutions with customer need in focus.

## The benefits of the VSM tool are:

- A visual representation of every process involved in the material and information flow

## Our experience so far

At Ingelheim we implemented our pilot VSM project for the API trosipium chloride in 2007. This was



An example of a value stream map.

# Pharma Chemicals to the rescue - a success story

By Bernhard Rausch, Corporate Senior New Business Development Manager / Boehringer Ingelheim GmbH

Success comes in many different ways. Sometimes you have a clean run at it. Other times it is more complicated. When, in 2005, Pharma Chemicals was called in by a key customer in serious trouble with a new API for treating urinary incontinence, things looked bleak. Having opted for a quick and dirty supply of material, and unable to upscale the API, the customer was desperately looking for someone to rescue the company from its own mistakes. And that is exactly what we succeeded in doing.

The Pharma Chemicals team sent in to solve the problems quickly found out that poor sourcing of raw material had not only made the customer use an unnecessarily long 7-step synthesis process, but had also led to the production of additional impurities and generated a catalyst poison in the hydrogenation stage. And this was no simple chemical, but the company's first-ever organic compound and an amorphous API. That made it that much harder to isolate. In truth, the company had no real method of isolating its new API.

Invited in at phase IIa of the development project, our team faced the challenge of establishing an effective synthesis. At that point, the customer had not even been able to produce more than a kilo of the API. But with its wide-ranging expertise in development, our team was at a definite advantage. The problems confronting it were to some extent familiar from other projects over the years. It conducted a feasibility study in just two months and developed the process in another two months. After only six months, the team had increased batch production to 15 kilos, reached 40 kilos in 2006 and was up to some 80 kilos in 2007.

The target for the amorphous API is an output at the low multi-ton level by the early part of the next decade. And the Pharma Chemicals team has not focused solely on volume output. It



## From the first stone to launch.

Pharma Chemicals – the innovation and launch partner with a wide range of offers:

- Process Development and Scale-up
- Analytical Development
- Cutting-edge Technology
- Registration Services and Compliance
- Supply Chain
- Successful Launch History

has also succeeded in telescoping the original 7-step process into a 5-step version. In addition, it has managed to improve the yield from 35% to 75%, reducing waste substantially.

A challenging project like this not only makes good business sense for Boehringer Ingelheim, but keeps us close to the latest developments in

pharmaceuticals, gives us greater experience and keeps our Pharma Chemicals teams at the cutting edge of the industry. We can make a real difference for our customers who range from small start-ups to Big Pharma. In some cases, as explained above, we can even help ensure that the new medicine they have already flagged for launch stays on schedule.

# Phyto-competence - a key strength for Pharma Chemicals

By Dennis Seagle, International Marketing Manager / Boehringer Ingelheim GmbH

The foxglove, familiar to people around the world as a wild or garden flower, is also the natural source of the active ingredient digoxin, one of Boehringer Ingelheim Pharma Chemicals' API classics. Digoxin, a cardiac glycoside used in the management of congestive heart failure, perfectly demonstrates our well-established competence in phytochemical production. And, importantly, we have full control over the whole supply chain for digoxin and other phytochemicals - from plant breeding and selection to extraction and purification of the active ingredient.

## One-stop shop

Our world leadership in phytochemicals gives an extra dimension and key strength to what we can deliver to our customers as a full-service provider. We can offer them with a one-stop shop with the options of either chemical synthesis or extraction and refining from medicinal plants to produce the required active ingredients. Phy-



The foxglove is the natural source of the ingredient digoxin.

tochemicals are widely used today in both medicines and cosmetics. Major companies with well-known brands are among our clients.

## Green chemistry

Our green chemistry experts are available worldwide to customers considering the phytochemical route. But developing an actual phytochemical is not an overnight process. Nature takes its time. The plant breeding specialists at our Ingelheim site in Germany typically breed and select initial elite plants in year one of a project. Seed production follows in year two, cultivation, harvesting and processing in year three and extraction and purification of the active ingredient in year four.

The foxgloves for digoxin are currently grown on our plantations in various European sites. We also have large plantations in Australia and South America for growing other medicinal plants. The latter was in fact expanded in 2007 to meet rising demand.

## Security at every step

Our Pharma Chemicals production sites in the USA, Germany, Italy, Spain and France offer state-of-the-art chemical development facilities, experienced chemists, analytical expertise, highly flexible, multi-purpose production plants and the highest quality stan-



Purification by counter current distribution.

dards. The large scale of our phytochemicals facilities also guarantees customers that we have sufficient production capacity to meet their needs. Our commitment to cGMP ensures compliance with regulatory authorities. Successful inspections by the US Food and Drug Administration provide powerful guarantees. And with all production steps firmly in Boehringer Ingelheim's hands, our customers are ensured of the utmost security throughout - from the rights to crops in the field to the ultimate patent-protected API.

# Staying ahead of the curve with key account customers

By Thorsten Biermann, International Account Manager / Boehringer Ingelheim Chemicals Inc.

Pharma Chemicals' strong customer focus has this year intensified with the introduction of an innovation-promoting initiative aimed at offering key global accounts access to Boehringer Ingelheim's wealth of pharma expertise and innovation.

The initiative, recognition of an accelerating trend among major pharmaceutical companies keen on filling their product pipelines, enables an innovative full-service provider, like Pharma Chemicals, to leverage its breadth of technologies, products and overall expertise across several Boehringer Ingelheim business units. This competitive advantage, while creating exceptional added value for key customers, provides the foundation for the building of even stronger and more successful customer relationships in the future. By tapping into their strategic supplier

our Ingelheim site in Germany in 2005 and upgraded to a Global Key Account strategy in 2007 throughout the remaining Pharma Chemicals network. Our innovation-promoting initiative takes our long-standing customer focus an important step forward and helps ensure that we stay ahead of the curve in this fast-changing business environment.

Although the initiative is still only in its early days at Pharma Chemicals, projects are already being discussed with key account customers on the

In the USA, home to many of the world's Big Pharma groups, programmes are already being offered which bring together cross-functional audiences, ranging from R&D people to marketing support, to learn about the latest innovative ideas of their suppliers. Following the supplier presentations, the host company quizzes the suppliers about their ideas to see if there is a basis for taking them forward. Pharma Chemicals plans to participate in such a programme in the coming months as part of its rapid learning process.

Currently, our dedicated international account managers are based in the USA and Germany serving key customers on a global basis. If and when the need arises, this network could be expanded to other emerging markets where other major pharmaceutical entities may be based.

While our intensively customer-focused initiative might at first glance appear to offer a one-sided benefit for key customers, it is very much a two-way street. For Pharma Chemicals it can provide new and wider opportunities to supply our APIs to major users.

For Boehringer Ingelheim's other Industrial Customer business units, such as Resomer, Pharma Manufacturing and Biopharmaceuticals, the initiative may in fact be able to open up entirely new markets and opportunities, aiding their quest in targeting new growth areas. Definitely a win-win situation.



base, companies often are, among other advantages, able to cut costs out of certain business processes, often resulting in plant capacity optimisation and streamlining of their respective facilities.

Our initiative represents a natural progression of our key account approach, a concept introduced on a local level in

joint development of innovative new products. As they are commercially confidential, it is not possible at this stage to disclose any project specific details. However, as we progress our initiative with our established customers over time, and as projects materialise, we hope to be able to provide further updates.

# InformEx - the market place for New Business Development

By Cornelia Wissenbach-Heel, Communication Manager Pharma Chemicals/Boehringer Ingelheim GmbH

After having experienced great success with our new booth last year in New Orleans, we are determined to write another chapter in effective networking and co-operation within our Pharma Chemicals Business.

Representatives from the US and Europe will be in San Francisco to meet attendees in our comfortable exhibit area at booth No. 520.

Our pharmaceutical network combines expertise, experience and service quality and offers added value to customers ranging from research-led start-ups to the major pharmaceutical groups.

InformEx, this year taking place in San Francisco, gives us an excellent opportunity to bring our specialists from the most important areas and countries together, so that effective communication during the meetings is guaranteed.



San Francisco, one of the most international venues in the US is a perfect place to make new business contacts.

Further on, we take the opportunity to present our business in more detail on January, 27, 2009 at the:

For appointments with Boehringer Ingelheim representatives, please contact:

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**TECHNOLOGY SHOWCASE**  
“Source your API through our phytochemical expertise”  
10.00 a. m. / Room 300



Speaker: Dr. Friedrich Bischoff,  
NBD Manager Phyto-Chemicals,  
Boehringer Ingelheim GmbH

**EXHIBITOR SHOWCASE**  
“The NCE launch factory”  
2.00 p.m. / Room 303



Speaker: Dr. Bernhard Rausch,  
NBD Manager,  
Boehringer Ingelheim GmbH

Join us at InformEx in San Francisco, California from January 27 - 30, 2009  
Chemistry you won't find anywhere else! Boehringer Ingelheim, Booth 520.

Event details are posted at [www.informex.com](http://www.informex.com)