

FOSTER  WHEELER

# *focus*

FOSTER WHEELER'S PHARMACEUTICALS BUSINESS MAGAZINE

ISSUE 10



**Go green with a touch  
of Foster Wheeler blue!**

## **We believe that the Foster Wheeler 'touch of blue' can really add 'green value' to our clients.**

There is an environmental aspect to just about every project that we execute, whether it's at the concept, FEED or EPC phase.

We work closely with our staff, clients, partners, suppliers and contractors to ensure that we work in an environmentally responsible way.

As well as providing a service which integrates the environmental component as part of the overall project, we also apply our environmental expertise in many other ways.

These include addressing our own environmental performance in our offices, helping to protect the natural environment, important artefacts or local wildlife around project sites, working with clients to increase energy efficiency or energy integration, providing specialist environmental consultancy or remediation services, or working with our clients on exciting new technology solutions.

Here are just a few examples of our expertise at work:

- We have leading expertise in the increasingly important areas of water management and waste water treatment
- We work with clients to increase the energy efficiency of their facilities
- We are at the forefront of the application of continuous processing in the pharma industry
- Energy Center I, the home of Foster Wheeler USA in Houston, Texas, was designed and constructed to be a LEED-certified 'Green Building'
- We're also training engineers to become LEED-accredited professionals and are supporting clients to achieve LEED certification

Our talented people and proven skills make Foster Wheeler your partner of choice for the exciting projects and emerging technologies that are changing our industry.





## From Strategic Planning to Successful Health Authority Inspection



We continue to support our pharmaceutical and healthcare clients at all stages of their investment, and to propose technical and execution solutions to guide them safely and profitably in this difficult and challenging economic climate. Always committed to understanding our clients' objectives, we share their

vision as well as their values.

This starts during the very first phases of a project, when we interpret and rationalize the logistic and manufacturing requirements, developing a range of alternative solutions and supporting our clients during the selection of the best fit in terms of strategy and investment plans. Pressure on costs is continuing and we develop every phase of a project with a cost-to-value approach, clearly separating the essential features from the optional, giving our clients the most transparent analysis possible on which to base a robust investment decision.

Continuous improvement is a must and we work hard to study, test and propose the best technologies available, with a keen eye on innovation to give that all-important cutting edge. We support our clients in designing and building their chosen solution, in getting their manufacturing license and GMP certificate, and we can even manage the inspection process with the relevant Health Authorities. And we do it all safely, working in an environmentally responsible way. Always.

Innovation, site master planning, cost-controlled project execution, safety awards and GMP certification are all in this issue of *focus*. We hope we capture your interest and we look forward to supporting you with any aspect of your forthcoming investment.

**Daniel Lachapelle (left)**  
Global Business Line Leader, Pharmaceuticals

**Franco Dindo (right)**  
Pharmaceuticals Business Line Leader - Eastern Hemisphere

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Produced by  
FW Graphics Group, Reading

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**“The strong co-operation between Foster Wheeler and Kedrion Group has become a real partnership, with both companies aiming at one single target.”**

Rodolfo Franceschini  
Global Operations Director, Kedrion Group

**Kedrion Group is a bio-pharmaceutical company specializing in the development, manufacture and distribution of plasma-derived medicinal products.**

**In 2009 our Italian operation was awarded an EPC and commissioning/qualification supervision contract by Kedrion Group and its Hungarian-controlled company Human Bioplazma LLC for the GMP upgrading and expansion of a bulk plasma fractionation manufacturing facility at Gödöllo in Hungary.**

The project's objective was to expand fractionation capacity by an additional 350,000 kg of plasma a year, with a new highly-automated production line with a dedicated process control system for almost 2,000 input/output operations.

With the integrated commissioning and qualification (C&Q) team including Kedrion and its subcontractors led by Foster Wheeler, C&Q activities required careful planning to minimize any potential impact on on-going production. Procedures were carried out every day of the week with extended shifts and even overnight execution for particularly critical activities.



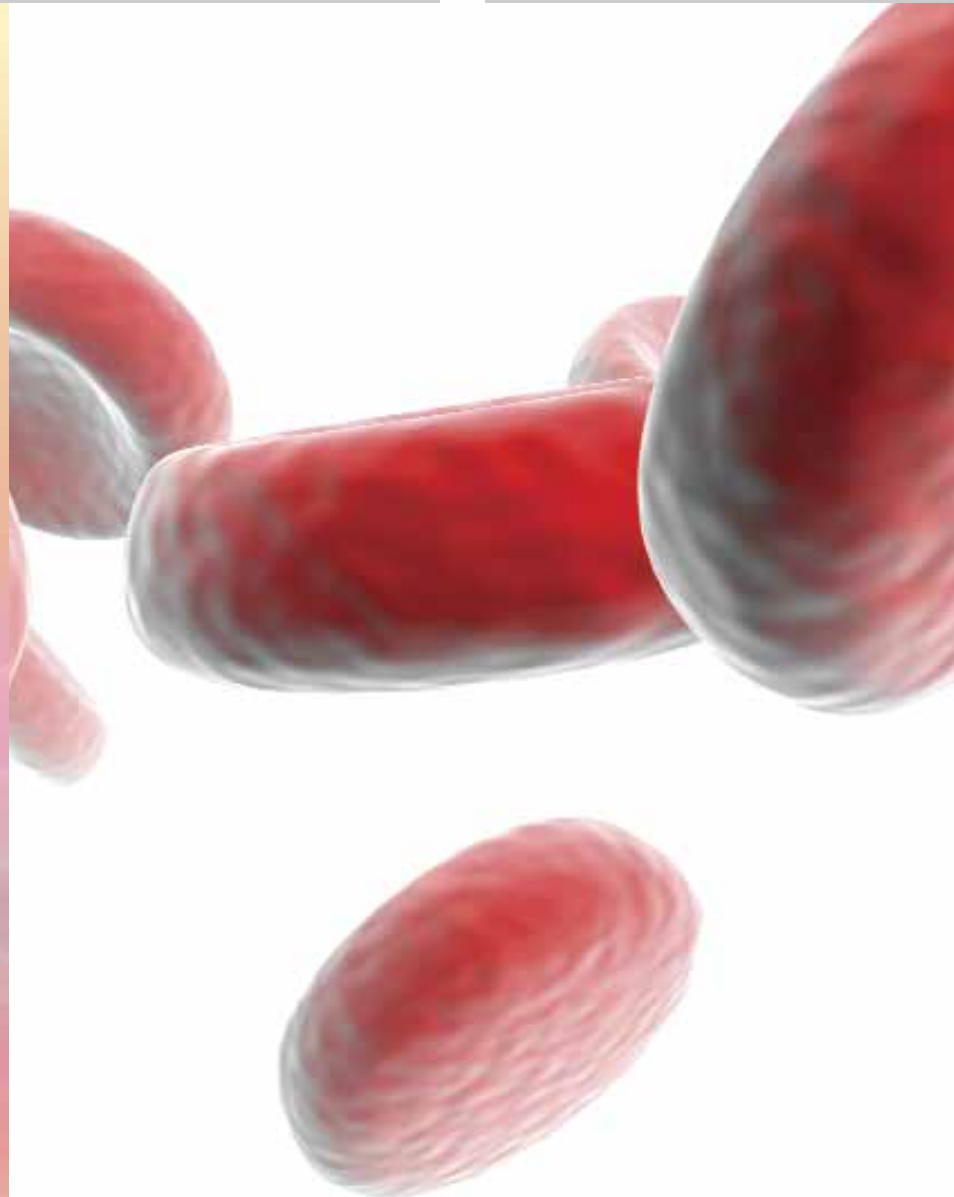
The facility achieved mechanical completion by April 2011 and commissioning and qualification was complete by June 2011, as per schedule. Production tests were carried out in July and August and stability tests are currently underway. We also supported Kedrion during its first month of production tests and our client is now manufacturing product for performance qualification by November as per plan.

#### **Full OHSAS marks!**

As part of the overall re-certification of Foster Wheeler Italiana to OHSAS 18001, the occupational health and safety standard, the construction area was inspected by the OHSAS auditors. The project passed the audit with full marks to the great satisfaction of the Foster Wheeler and Kedrion team. The team is also delighted to report an outstanding safety performance to date, with zero incidents.

**“Maintaining high health and safety standards in our facilities is undoubtedly one of our top priorities.”**

Francesco Felicetti  
Global Engineering Director, Kedrion Group





**focusonchina**

INCREASINGLY ATTRACTIVE LOCATION



**China is poised to become the world's third largest pharmaceutical market in 2012 and will contribute around an additional \$40 billion in annual sales by 2013, comparable to the forecast for the US market in the same period.\***

With a mix of multi-national and local companies among the top ten in its highly competitive pharmaceuticals market, China represents an increasingly attractive location for investment in pharmaceuticals and healthcare.

We have been working in China since the 1970s, and have developed a strong track record. We have established operations in Shanghai and Beijing, and we have worked with many design institutes, Chinese suppliers and local construction companies.

In recent years, we have supported many projects in the pharmaceuticals sector, including:

**Shaoxing City**  
**Zhejiang province**

Comprehensive site master plan for the development of new manufacturing facilities including warehousing, utilities, solvent recovery, waste water treatment, QC/QA laboratories and infrastructure.

**Nanhui**  
**Shanghai**

Site master plan for new greenfield R&D development, part of a larger urbanisation scheme located within the New Pudong International Medical Zone.

**Jiangbei**  
**Chongqing**

Basic design for multipurpose hydrogenation workshop, including new production building interconnecting with existing facilities.

**Suzhou Novartis**  
**Jiangsu**

Project management of greenfield development of R&D and manufacturing of intermediates and APIs.

**Chengdu**  
**Sichuan**

Site master plan and concept design for the production of bulk oral pharmaceutical active ingredients on a greenfield site. Later phases of the project include proposals for four API facilities and formulation facilities.

**North China**

Conceptual design, front-end engineering design, and engineering, procurement and construction services for new grassroots fermentation and downstream processing plant including solvent recovery, mycelium treatment and waste water treatment.

**Hangzhou**  
**Zhejiang**

Quality gap analysis and site master plan for plant expansion, and concept design for fill-finish plant renovation.

**Heifei**  
**Anhui**

Conceptual design, basic design, project management, procurement and technical support for a new secondary production plant including R&D, production, utilities, QC laboratories, warehousing and administration buildings.

**Xiamen**  
**Fujian Province**

Conceptual design, front-end engineering design, and engineering, procurement and construction management for a greenfield production building, utilities and warehousing, designed to accommodate future expansion.

**Zhongshan**  
**Guangdong**

Conceptual design for expansion of an existing plant to include an aseptic filling department and revamp of existing clean rooms, cold rooms and warehousing.

\*Source: IMS



**novartisvacci**

ANOTHER SUCCESS

## medimmuneaward

TAKING FAST-TRACK TO NEW LEVELS

Last year Foster Wheeler Biokinetics, our Philadelphia-headquartered pharmaceutical and biotechnology operation in the US, was presented with the H1N1 Vaccine Supplier Recognition Award by MedImmune at a special ceremony at its facility in Gaithersburg, Maryland.

Over the last 10 years, we have executed projects for this leading manufacturer, which is the world-wide biologics unit of AstraZeneca, at a number of its facilities.

As Engineer of Record responsible for the overall design of the project for MedImmune's live attenuated influenza vaccine production facility at Gaithersburg, Foster Wheeler Biokinetics, along with other MedImmune suppliers, was able to help MedImmune achieve an increase in output of more than 700% over the previous year.

Completion of the project took fast-track to a new level; only five months from start to shipment of the first doses. Normally projects like this take 18-24 months.

MedImmune produced 10 million doses of the vaccine for the US market alone and noted that it was the first manufacturer to deliver the H1N1 vaccine to the US Department of Health & Human Services.

Foster Wheeler Biokinetics is proud of the part it played in this crucial public health initiative.

We share our client's satisfaction with the recent successful completion of Phase 1 of the Logistic and Warehouse Upgrade Project for Novartis Vaccines and Diagnostics in Rosia, close to Siena in the heart of Tuscany, Italy. Our Milan operation executed the feasibility study and EPCm for this upgrade project.



Phase 1 of the project was focused on the reorganization of logistics flow at the site, the expansion of the receiving and shipping areas and the construction of a high-bay, fully automated warehouse able to store 8,500 pallets of bulk material, primary and secondary packaging materials for vaccines production.

Construction activities had to be carried out with the existing warehouse in full operation. Constructability studies therefore focused on minimizing any impact of construction activities on production material flows.

Novartis needed to address the constantly increasing demand for vaccines production capacity. Managing the supply and delivery chains of vaccines is particularly complex due to the need to maintain a controlled temperature for the complete cycle.

#### Key milestone

An important milestone was reached with authorisation from AIFA (the Italian Medicines Agency) for Novartis to use the newly built temperature-controlled storage system, the final part of Phase 1. This has now been granted, meaning that Novartis can proceed with Phase 2.

#### Phase 2

Phase 2 includes the reorganization of storage areas and pallet handling, with the installation of automated intermediate cold rooms and laser-guided vehicles for pallet transportation from warehouse conveyors to logistic areas. A high-bay automated warehouse for 3,500 pallet places operating at a temperature of 2-8°C will also be built.

Our Milan office designed the original facility and, following our successful performance on Phase 1, we are delighted that Novartis has awarded us the EPCm and validation work for Phase 2.

# aworldfirst!

## MULTIPRODUCT PROCESS INTENSIFIED PLANT

The Implementation of Process Intensification Technologies symposium was held in the delightful surroundings of the Prinsenhof Museum in Delft earlier this year. Nigel Fletcher, manager of speciality products in our Business Solutions Group, presented a paper entitled *Implementation of a Multiproduct Process Intensified Plant*.



Nigel Fletcher

### A world first

Nigel's presentation detailed how our team had started from a one-batch process with multiple syntheses then added several more multiple-step batch processes, working through all of these with the client's research chemists and development engineers to convert them all to continuous processes.

This all came together as the joint teams designed and built the world's first multiproduct process intensified plant.

### Britest

Significantly, the successful work was enabled thanks to both the client's and our membership of Britest, which allowed us to use the full suite of Britest tools and methodologies, pointing the way to many solutions and new routes.

Formed in 1998 via a partnership between leading pharmaceutical and fine chemical companies and academia, Britest holds a bank of intellectual property that has been developed through unique collaborative programs among members. This provides an opportunity to share knowledge and reduce risks in defining innovative process solutions that can deliver significant improvements in sustainable manufacturing. Foster Wheeler has been a key contributor to Britest's development in recent years.

### Cutting edge

The interest shown in process intensification was reflected in all the papers presented during the day, with the presenters coming from several diverse areas of industry.

Process intensification is here to stay and it will develop in the future. Thanks to our work in this area we are in a position to offer our leading expertise now and in the future to a growing group of clients at the cutting edge of process industries.

Pharma *i*

See Nigel's paper at: [www.fwc.com/publications](http://www.fwc.com/publications)

# worldclasssafety

## MORE PRESTIGIOUS AWARDS



*“Working safely in an environmentally responsible way is integral to everything we do at Foster Wheeler.”*

Kent Masters  
CEO, Foster Wheeler AG

### Super six in Singapore

We have won six Workplace Safety & Health (WSH) Awards in Singapore for outstanding safety performance in 2010. The WSH Awards are presented annually by the Workplace Safety and Health Council, in collaboration with Singapore’s Ministry of Manpower. We have been awarded a Gold WSH Performance Award (WSHPA) for our overall safety performance in Singapore. A Silver WSHPA was awarded to a Foster Wheeler-led joint venture project and a further four projects received a SHARP (Safety and Health Award Recognition for Projects) award.

### At the top in Thailand

For the second consecutive year, we have received Thailand’s National Occupational Safety and Health Award, recognising our outstanding performance in 2010 in the areas of safety, occupational health and the environment. We also received the Regional Award for our world-class record in site safety, occupational health and environmental performance during the construction of a project at Rayong, and a safety award recognising the outstanding achievement of no lost-time injuries in our Thailand office in Sriracha in 2009.



### Five stars in South Africa

Our South African operation was presented with its first NOSCAR award (National Occupational Safety Credited Awards) for health and safety performance by NOSA, the National Occupational Safety Association of South Africa. Even more noteworthy is the fact that we were awarded a NOSCAR in only our second year of being a Five-Star NOSA company. The Five-Star accolade recognizes our successful implementation of a world-class risk management system.



### Sword of Honour in UK

For the fourth year running, our UK-headquartered operation has been awarded the prestigious Order of Distinction Award for Occupational Health and Safety by RoSPA, the Royal Society for the Prevention of Accidents. We also received our eighteenth consecutive RoSPA Gold Award for outstanding health and safety performance on UK and international projects. The Order of Distinction is RoSPA’s highest achievement award and is only presented to those companies attaining at least 15 consecutive RoSPA Gold Awards.

**Our commitment to, and focus on, safety remains as strong as ever and we are delighted that our teams around the world continue to receive official recognition for their outstanding safety performance.**

“We have extensive experience in the design of pharmaceutical chemical production facilities, and our role in this project confirms our ability to bring the latest thinking and developments into our pharma plant designs.”

Richard Larkin  
Manager  
Pharmaceutical Business Development



## innovation in action

### STATE-OF-THE-ART TECHNOLOGY

Our latest project with Janssen is its new Chemical Development Pilot Plant in Geel, Belgium, which was officially opened in November 2010. The new facility represents a bridge between research and development and the production of new medicines, with a two-fold purpose:

- The chemical development, registration and launch of new medicinal substances
- The chemical production of small volumes of medicines

Our Pharmaceutical Solutions Group based in Reading, UK, assisted Janssen with the development of the project design and estimate. The design included the preparation of a 3D architectural impression which helped the team to visualise the facility and apply for the necessary permits.

The facility represents state-of-the-art technology and is designed for future flexibility. At every level the five-floor building is divided into a production zone and support zone, so that routine maintenance work can be carried out without requiring shutdown of the production zone. The plant was designed using a modular concept to accommodate any future expansion.

We are very pleased to have been a part of this innovative project.

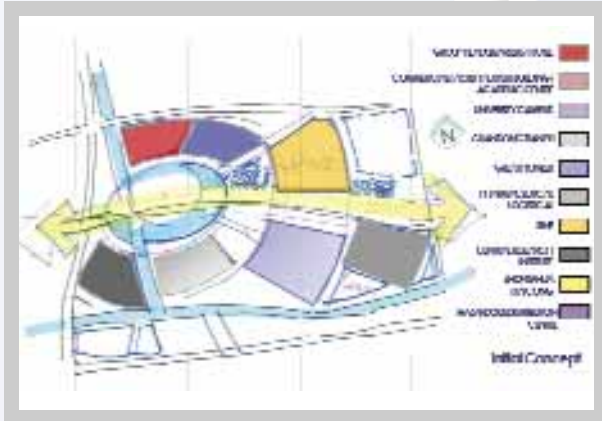




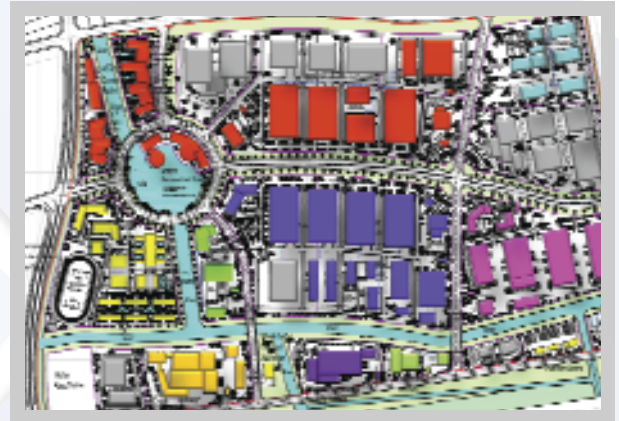
We have been working with Janssen, a member of the Johnson & Johnson family of companies, for many years. Johnson & Johnson is one of the world's largest manufacturers of healthcare products, serving the consumer, pharmaceutical and professional markets.

# changingindustry

## STRATEGIC SITE PLANNING



Strategic plan concept



Strategic plan proposal



Angus Dagnall  
Principal Design Consultant

The pharmaceutical industry is changing. As new pharmaceutical sites are developing in emerging markets such as China, India, Brazil and Russia, existing facilities are being relocated, rationalized or even closed. Clients reassessing their existing assets with a view to increasing operational effectiveness, or planning a new build, often look to an independent third party to develop a strategic site plan, also known as a site master plan.

We have been assisting clients with site master planning for many years. In fact, we reported on it in *focus* back in 2004! Today the demand for this service is stronger than ever. Angus Dagnall outlines our well-proven approach.

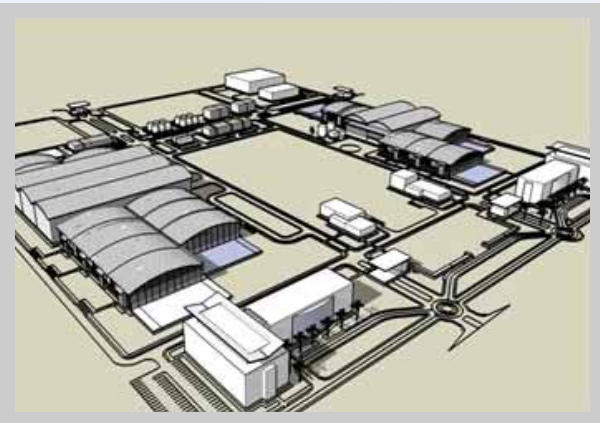
### Three-Step Approach

Time has shown our three-step approach to developing a master plan to be a consistently effective methodology.

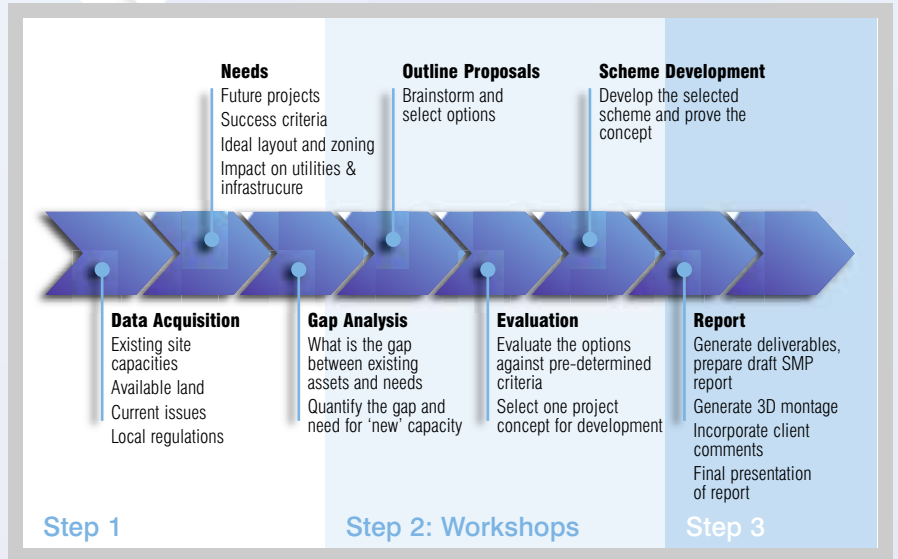
The three steps are:

- Step 1** Data gathering and gap analysis
- Step 2** Concept generation and evaluation
- Step 3** Completion of the strategic plan

We then tailor the methodology further to fit a specific plan's requirements. A good master plan relies on robust data on both current and future activities, which in turn requires a clear vision for the site.



Typical overall strategic site plan



Overall strategic planning methodology - example

## Success Stories

We have used our methodology very successfully for many clients. A recent example is a site in the UK where we have been responsible for master planning for the last few years, adapting the plan as our client's requirements change.

A second example is an existing secondary manufacturing site in the USA, where our client sought to optimize and reduce the number of manufacturing blow-fill-seal lines.

## Thinking Big

At the other end of the spectrum is the type of strategic plan that we prepare for clients planning a brand new site, even a huge pharmaceutical business park.

We apply the same overall methodology, but focus on major building massing and orientation. For example, we have successfully delivered strategic site plans to a number of clients investing in China using this approach.

## Broad-based Skills

We believe there is no substitute for in-depth experience. These studies are demanding and require a thorough knowledge of the industry coupled with both pharmaceutical engineering and architectural planning skills.

Our global experience, our knowledge of local requirements, and our flair for innovative and sustainable solutions, mean we can provide a robust site master plan to support our clients' investment planning.

## Pharma *i*

For more information, see our pharma-focussed brochures, including site master planning, at: <http://www.fwc.com/GlobalEC/Pharmaceuticals/pharmaceuticals.cfm> or e-mail us at: [fw\\_pharma@fwc.com](mailto:fw_pharma@fwc.com)



# findingtomorrow'scures

BIOMEDICAL RESEARCH & INNOVATION CENTER

**The UK Center for Medical Research & Innovation (UKCMRI) is a new UK biomedical research and innovation center to be located in central London.**

Founded by four of the UK's most prominent scientific and academic institutions – the Medical Research Council, Cancer Research UK, the Wellcome Trust and University College London – UKCMRI will be one of the most significant developments in UK biomedical science for a generation. Its goal will be to understand the basic biology underlying human health, finding ways to prevent and treat the most significant diseases affecting people today.

We were delighted to be a part of this exciting project as, based on our extensive experience of bio-containment technology, and in particular our previous experience in providing similar HAZOP services to other medical research institutions, project managers Arup selected us to provide HAZOP review services for the bio-containment laboratories, with particular focus on the building service systems. Luca Arrighi, head of HVAC in our Milan office, provided consultancy on high containment requirements for HVAC systems, and the HAZOP reviews were chaired by Joanne McCallum, principal process safety engineer based in our Reading, UK, operation.

The basic design of the UKCMRI is now complete, with a fully operational center scheduled for completion by 2015, by which time it will be renamed the Francis Crick Institute, after the scientist who discovered the DNA double helix.

# shinpoong

A KOREAN FIRST



Thomas Bischof  
Manager, Qualification  
& Validation



Our team based in Basel, Switzerland, was as proud as our client Shin Poong Pharmaceutical Co., Ltd., when it received a manufacturing licence and Good Manufacturing Practice (GMP) certificate without any restrictions, the first company in South Korea to achieve this.

We supported Shin Poong by managing the whole inspection process by the European Medicines Agency (EMA), together with our local partner, Sartorius Korea Biotech Co., Ltd.

Shin Poong, a mid-size pharmaceutical company located in South Korea, has developed an antimalarial drug in partnership with the non-profit Medicines for Malaria Venture. To support this initiative, Shin Poong built two new manufacturing facilities, one for active pharmaceutical ingredient (API) manufacturing and one for finished dosage forms.

The scope of our project was a little different from usual. The manufacturing facilities had already been completed and the commissioning phase was underway. At this stage, Shin Poong required support and advice on how to meet European Union GMP regulations ready for start-up of production. Our consultancy included:

- Set-up of a quality management system
- Providing templates of umbrella standard operating procedures
- Design review of manufacturing facilities for API and drug product
- Review of equipment qualification
- Process validation program
- Cleaning validation program
- Training
- General GMP consulting
- Mock inspection
- Support during EMA inspection

Being awarded the manufacturing licence and GMP certificate is just reward for an extraordinary achievement by the three partners and their project teams.



# experts in clean utilities

## MULTIPRODUCT PROCESS INTENSIFIED PLANT

Clean utility systems, that is, utilities with a bacteriological specification, are commonly encountered in pharmaceutical and biotechnology plants, and in plants that manufacture silicon wafers and microelectronics. We have a great deal of experience and an in-depth understanding of the challenges involved in clean utility system design.

“Designers of clean utilities have to be fully conversant not only with the process design, but also the commissioning and handover of the operational system, providing the owner with the highest levels of assurance that manufacturing is safe to commence.”

**Paul Frey**  
Process Consultant



## Stringent standards

The quality standards for clean utilities are strictly regulated within the pharmaceutical industry by the US Food and Drug Administration, the European Medicines Agency, and other national or regional agencies. Stringent quality standards apply to various categories of clean utilities:

- Potable water
- Purified water
- Highly purified water
- Water for injection
- Clean steam
- Pure gases (e.g. nitrogen, CO<sub>2</sub> and laboratory gases)

## Infectious microbes

Clean utilities are fundamentally different from plant steam, cooling water and boiler feed waters in that all of the clean utilities come into direct contact with the drug product or the patient. The microbial quality of each utility must be strictly controlled to ensure that harmful bacteria are not added, even when just washing and cleaning equipment.

The water used in any drug manufacture, even though it may have been subsequently removed in the final form of the drug by drying, leaves a risk of bacterial contamination. What makes removing bacteria from clean utilities so difficult is that they are living organisms which are able to protect themselves. Their size makes detection possible only under the microscope. Even when destroyed, the cell wall of bacteria ruptures, releasing cell material known as endotoxin, which is responsible for febrile/shock reactions and can be fatal to patients under intensive care.

## Design criteria

The risk to drug manufacture is of microbial contamination, rendering sterile products non-sterile, causing loss of medicinal efficacy or, in extreme cases, adding pathogenic organisms. Therefore specific design criteria apply to equipment and systems producing and distributing clean utilities for drug manufacture. The engineer has to be aware of all relevant methods for the elimination and control of bacteria and their by-products, and techniques include:

- Design and maintenance of feed water supplies to ensure potable quality
- Removal of contaminants by reverse osmosis and ultrafiltration membranes
- Filtration using very fine filters with pore size of 0.22 microns (liquids) or 0.01 microns (gases)
- Use of sterilizing agents such as steam, ozone, ultraviolet radiation and chemicals
- Designing equipment to meet minimum hygienic standards which include smooth, polished surfaces and materials approved for use by the regulatory authorities
- Designing piping and equipment to be free of traps or deadlegs and able to be cleaned and sterilised in situ
- Lifecycle validation, including closer scrutiny of fabrications and construction, and extensive postinstallation testing

## Clean bill of health

Ensuring clean utility systems in pharmaceutical facilities are correctly designed protects the health of any patient who is administered drugs, is in intensive care, wearing contact lenses, or even just wearing a sticking plaster.

We have the expertise to help our clients address these stringent requirements.

**Pharma** *i*

For more information, please contact us at:  
[pharma@fwc.com](mailto:pharma@fwc.com)

# bio-xcell

## DEVELOPING MALAYSIA'S BIOTECH SECTOR



Ray Mikrut  
Head of Pharmaceutical Group  
Foster Wheeler Asia

**A new biotechnology park is being created in Nusajaya, Wilayah Iskander, Malaysia as part of an initiative by the Malaysian Government to develop its healthcare and industrial biotech facilities. It is owned and developed by Malaysian Bio-XCell Sdn Bhd, a joint venture company between Malaysian Biotechnology Corporation Sdn Bhd and UEM Land Holdings Bhd.**

As well as attracting pharmaceutical and biotechnology companies from within the healthcare sector, Bio-XCell is committed to facilitating the development of a vibrant agro-based industry through biotechnology, as well as industrial biotechnology which is used for the processing and production of chemicals, materials and fuels.

The 150-acre park features green initiatives such as natural lighting, passive cooling, solar energy and rain water harvesting and will hold a central hub consisting of offices, laboratories, canteen, 22 standard building shells, and larger land plots for custom-built facilities. All facilities will be supplied with chilled water and steam from a central utility facility (CUF) which will also treat all wastewater.

Planned to be built in phases, the initial design includes a 30-ton package boiler and a 40-ton biomass boiler which will use palm waste as its fuel. The chilled water will be produced by three 750 KW chillers.

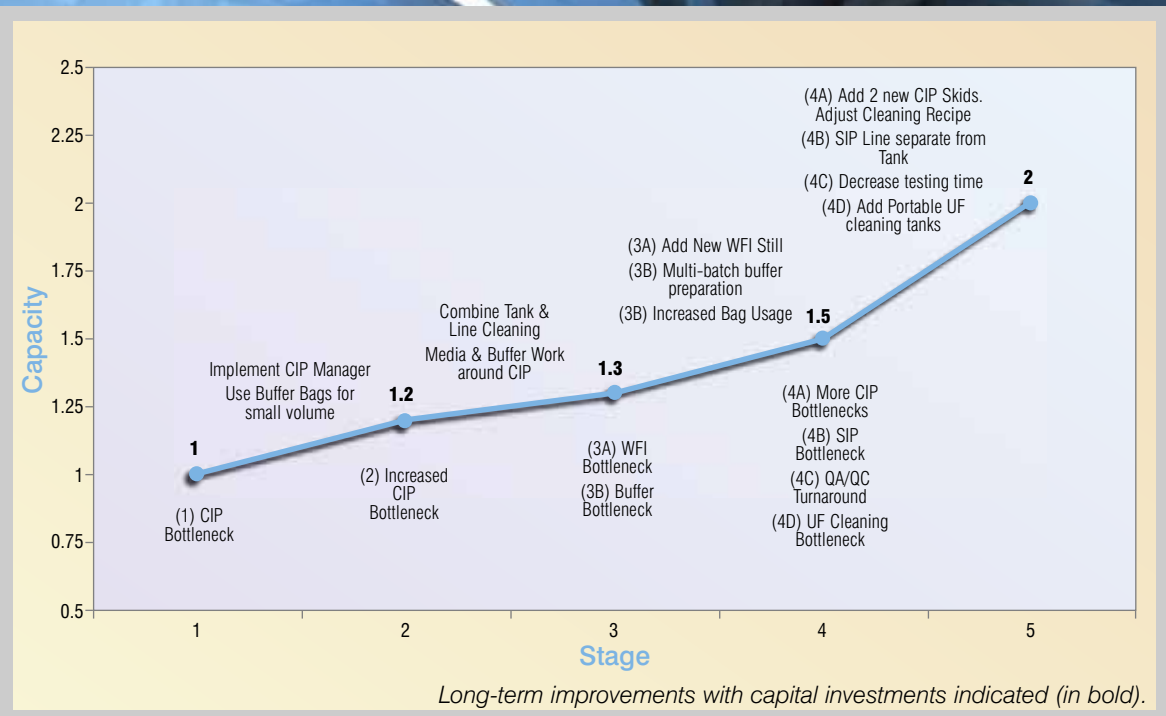
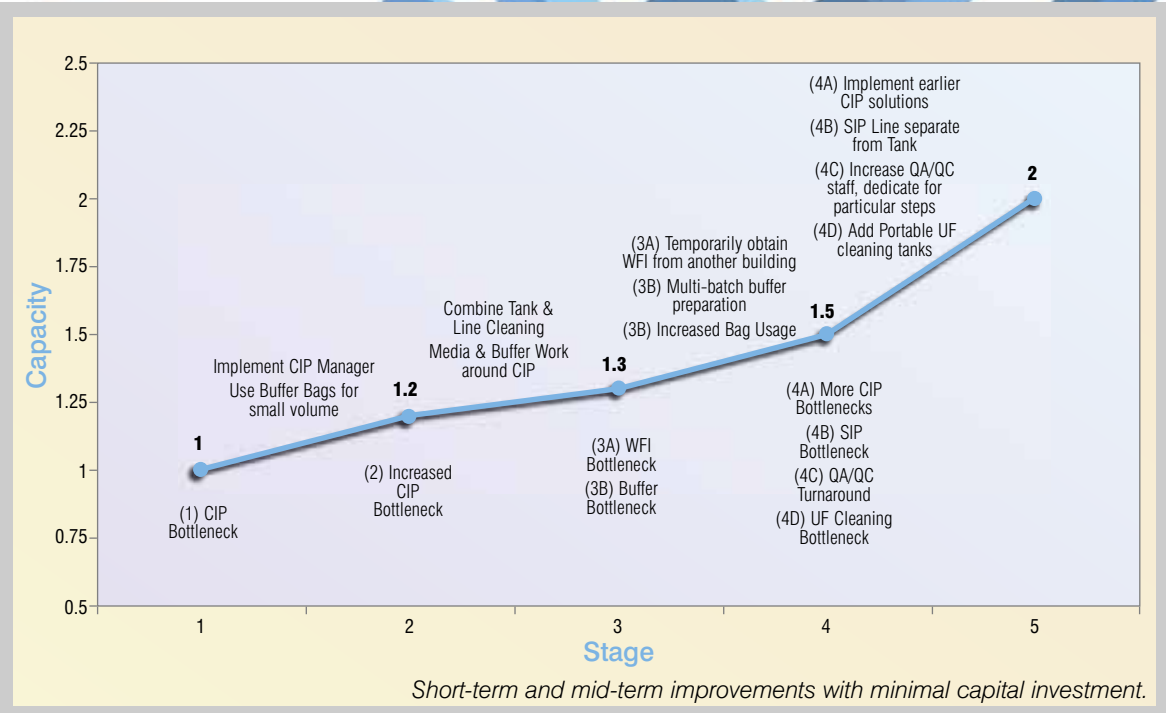
The CUF is being designed to accommodate two more 40 ton biomass boilers and four more 750 KW chillers.

We were delighted when Bio-XCell selected us to be part of this state-of-the-art development as project management consultant. In addition to participating in contractor selection for the detailed design and construction of the CUF, we are monitoring the project during the design, construction and commissioning phases.

With Ray Mikrut as project manager, our Singapore office will execute the design review while our Malaysian personnel overlook site operations. The project is scheduled for completion in June 2012.



Examples of both the quick-hitting and longer-term advantages provided for a client by our experts using K-TOPS®, identifying bottlenecks and providing solutions to overcome them.



# K-TOPS®

TWICE THE DETAIL IN HALF THE TIME



Joe Weiss  
Plant Simulation Leader

When it comes to providing high value to our clients, we believe we have a significant extra advantage: our K-TOPS® process simulation and optimization tool.

Evaluation of facilities and campuses is a challenge, balancing cost, flexibility and operability, with key areas of uncertainty in support systems and root utilities. Our goal, on behalf of our clients, is to maximize capacity at fixed capital costs while designing in easy flexibility - to identify opportunities to increase production capacity with small cost increases.

K-TOPS® is our award-winning\* dynamic process simulation and optimization tool. Its power lies in the delivery of alternative scenarios and ideas for staged implementation, which allows clients to do a truly in-depth evaluation of the alternatives as part of a robust decision-making process.

The alternatives can be deployed, visually, at the push of a button. A multi-layered view with multiple scenarios is automatic. And it's fast: K-TOPS® deploys solutions with twice the detail, in half the time.

K-TOPS® has saved our customers millions of dollars:

- By optimizing existing equipment, we saved a client \$30 million on a proposed expansion and reduced total cost by over 60%
- We realised a 50% production capacity increase for 7% increase in capital cost for a client's bioprocessing facility

Key benefits:

- Easily adapted to any process
- Delivers results quickly without complicated data entry
- Rapidly produces biopharm-specific solutions

K-TOPS® adds visible value at all levels, whether it's addressing a CFO's concerns over supply chain issues, supporting the plant manager with anticipated capacity increases and a shortage of clean water, or just to evaluate the possible bottlenecks in a unit operation.

K-TOPS® can be used to simulate any process and can be used worldwide. A dedicated Foster Wheeler team, along with our dynamic K-TOPS® software, working in partnership with you, is the best recipe for optimizing success.

\* *Pharmatex Product Innovation Award, voted by a panel of judges for a product that showed significant innovation in both engineering and excellence towards pharmaceutical applications.*

# asepticfilling

## INNOVATION IN FILLING MACHINE CONCEPT



Germana Molinari  
Manager of Fill/Finish  
Process Design



Fabiana Stoppa  
Pharmaceutical Process  
Engineer

Over the last few years, regulatory requirements for aseptic filling of injectable drugs have become even more stringent, demanding increased environmental safety in critical areas where the sterile product is exposed.

The design of filling equipment is responding to the challenge by providing better air quality control inside the filling area and removing maintenance operations from the clean room by the use of wall-mounted equipment.

Germana Molinari and Fabiana Stoppa have been working closely with the Marchesini Group and supporting their development of one innovative design which includes a balcony structure and vertical plate concept offering two major advantages:

- The critical area for vial filling and transit at the front of the machine is clearly separated from the mechanical control and drive parts to the rear by installing the critical area inside the clean room and the mechanical area outside
- Air distribution at the vial filling and transit level is optimized by increasing the distance between the vial conveyor and the bottom plate of the filler and providing air extraction on the lower part; vials are transported without any friction, in dedicated pockets mounted on a stainless steel conveyor, flushed by a unidirectional air flow in line with GMP requirements

A clean and smooth design, rotating motion and optimized component dislocation improves air distribution and minimizes turbulence, protecting the product from contamination. Additional enhancements include better distribution of vial holder plates when installed in isolation technology. The slim design of the filler - only 800 mm - is more ergonomic, allowing easy access to machine parts with gloves from the operations side and reducing operator movements inside the clean room.

As the pharmaceutical industry becomes ever more regulated, and space becomes ever more at a premium, our engineers keep an eye on the cutting edge of new technologies. This new filling machine concept is one of several options to consider as we continue to develop even more compact layouts and to meet regulatory requirements.



Luca Arrighi  
Head of HVAC Department



Images courtesy Marchesini Group

# ispegoodpractice

## COLD CHAIN MANAGEMENT

**Cold chain management describes the manufacture, supply and distribution of commodities that must be kept within a defined temperature range throughout the entire cycle. If, at any time in the chain, a temperature-sensitive commodity is exposed to temperatures outside its defined range, irreversible damage can occur, with consequential product and profit loss.**

Increasing volumes of cold products, the complexity of these products, and the complexity of the associated supply chain are causes for concern, and organizations need adequate control over the cold chain element of pharmaceutical and biopharmaceutical distribution systems.

Recognising the need for guidance in this area, ISPE's dedicated team of subject matter experts from across the industry developed the ISPE Good Practice Guide: Cold Chain Management. Luca Arrighi, head of HVAC in our Italian operation, was very pleased to be part of this team. The guide is intended to provide practical guidance to assist in the specification, design, commissioning and verification of fixed and passive systems within the cold chain.

Cold chain management is vital to the success of a regulated company and understanding it will help to ensure that solutions are based on robust science and undergo appropriate risk assessment to meet regulatory standards and ultimately provide protection to the patient.

# continuous processing

## TEN REASONS TO CHOOSE FOSTER WHEELER



In recent years the pharmaceutical industry has been undergoing a quiet revolution. For a long time, batch manufacture dominated pharmaceutical production.

Today, there's a new way - **continuous processing.**

Those companies who have invested in this new technology have seen a radical change, with batch reactors disappearing and being replaced by small continuous reactors. We have been at the vanguard of this development, working with our clients to design and deliver ground-breaking new continuous processing facilities, or to convert batch processing facilities to continuous processing. Even clients who want to retain batch manufacturing can benefit by the selective addition of continuous processing and create hybrid processing by mixing batch with continuous processing.

Here are ten reasons to talk to us about how continuous processing could revolutionize your operations!

### 1. Improve product

All of the continuous processing projects in which we have been involved have chosen designs based on Britest methodologies. These designs have delivered higher quality products than our clients were achieving with their existing batch plants. This has even been the case during proof-of-concept laboratory trials where significant reductions in impurity levels have delivered this higher quality.

### 2. Reduce work-in-progress

One of the great benefits of continuous process is the ability to generate product or intermediates quickly, allowing the next stage of processing to proceed more quickly, leading to reduced work-in-progress (WIP). Where processing has gone from raw materials to finished product in one continuous stream, the reduction in WIP is highly significant, delivering real financial benefits.

### 3. Improve environmental performance

Continuous processing means very few vessels are filled and emptied so emissions from the process are significantly reduced and utility demand is lower. Where gases are emitted in the continuous plant, they are not diluted with blanket gas and so are concentrated and more easily treated, in line with regulations.

### 4. Reduce utility demand

A batch plant generally has large utility supply systems to satisfy the sudden peaks in demand for cooling and heating. Our continuous plant designs have small, compact utility generation systems providing steady low-level utility supplies. Our experience is that continuous processing can deliver a ten-fold reduction in utility demand, with lower carbon emissions and a more sustainable energy position. This translates into reduced cost of manufacture – a significant benefit when manufacturers are seeking to reduce costs.



### 5. Reduce waste

With continuous processing, the focussed process means that raw materials are used close to their stoichiometric levels. We've used Britest methods to help our clients modify their processes to optimize the use of raw materials and so to reduce waste. Less raw material waste, together with a purer product, delivers clear financial and environmental benefits!

### 6. Reduce capital cost

Size is important where continuous processing is concerned and our designs are compact as well as ergonomically efficient. Smaller equipment means that the capital cost of implementing continuous processing is lower than the equivalent process using conventional batch designs. This reduced size, allied with the ability to use modular designs, means that installation is easier, so reducing construction cost and schedule.

### 7. Reduced plot space

Small equipment only needs a small plot space. The benefits from this are immediately obvious; reduced cost of buildings, the ability to use an existing space without major modifications, reduced HVAC, and easier operation. Where our clients need a hybridised plant in which continuous and batch processing are mixed, then the smaller equipment can be fitted into the existing plant areas.

### 8. Optimize the process

Whatever method is used to make a process continuous, any improvement in process knowledge helps to optimize the process and delivers a benefit to the manufacturer. Britest comes in to play again here: we use the Britest methodologies, which employ a series of tools to generate questions and challenge the project team. Together with laboratory trials, this gives the manufacturer the opportunity to optimize the process and realise reduced costs, improved environmental position and improved safety.

### 9. Continuous or hybrid?

We agree that not all processes can be made continuous. With our experience, and with a completely objective viewpoint, we can help you take continuous processing as far as it makes sense for your own circumstances and objectives. We've developed designs in which continuous process steps are interleaved with batch processing. This often works particularly well where there is a hazardous process. Continuous units are so small that they contain little hazardous material or reaction mix and can provide a viable containment solution.

### 10. Multipurpose design

Often a reason given for not using continuous processing is that it is fixed on one process. Our experience is just the opposite. We have designed and implemented a multipurpose pharmaceutical API plant based on continuous processing, which realised huge benefits to our client.

#### Pharma *i*

We have the skills and experience to help you find the right continuous processing solution. To arrange to talk with our experts or for more information, please contact us at: [fw\\_pharma@fwc.com](mailto:fw_pharma@fwc.com)



the right people with a  
'can do' attitude and the  
commitment to deliver

Technical consultancy  
Feasibility studies  
Concept design  
Site selection  
Site master planning  
Permitting  
Environmental consultancy  
Process simulation  
Basic design  
Detailed engineering  
Project management  
Procurement  
Construction management  
Commissioning  
Validation  
Plant operation  
Maintenance  
Site remediation



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