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When a distinguished panel of judges on the annual Facility of the Year Awards competition, sponsored by ISPE, INTERPHEX, and Pharmaceutical Processing magazine, declared Genentech’s new biologics manufacturing plant in Oceanside, CA, the winner in the 2007 Project Execution category, it was, in effect, giving the nod to a pioneering project management approach that emphasized teamwork, collaboration and partnership to reduce risk and control costs while delivering a world-class, advanced biopharmaceutical manufacturing facility.

This is the third in the annual Facility of the Year Awards, and the first year for the category awards. Five pharmaceutical manufacturing facilities emerged as winners in different categories. Along with Genentech, the other category winners were Cook Pharmica (Bloomington, Indiana) for facility integration, Shanghai Roche Pharmaceuticals (Shanghai, China), which received a regional project execution award, Taiyo Yakuhin (Takayama City, Japan), for equipment innovation, and Vetter Pharma-Fertigung (Ravensburg, Germany) for process innovation.

The winner of the overall Facility of the Year award will be announced at ISPE’s 2007 annual meeting to be held in Las Vegas, Nevada in November.

The team that was assembled for the Genentech Oceanside Product Operations project included its engineering staff headed by Johannes Roebers, PhD, Senior Director of Engineering, Facilities and Validation, project staff from the engineering company Clark, Richardson & Biskup (CRB), the architecture firm Ferguson Pape Baldwin, and DPR Construction, which served as general contractor, among others.

The partners on the team were selected more for their ‘chemistry’ or their potential to integrate and work well together to realize the vision and quality requirements of the project, rather than solely on their ability to compete on cost, according to Roebers. “For me, it was just as important how we worked together everyday as it was to get a top-notch, world-class facility at the end,” he says.

Single Company Mentality

“We found that for the most part among the key partners, and with the big players such as Emerson Process Management and Siemens Building Technologies, that companies were starving to be part of a project where the owner had a desire to collaborate and partner with
players and the owner.

"This led to decisions being made by walking four steps
down the hall rather than by flying across the country, or by
e-mail or telephone. It was all face to face, and really started
to shape us collaboratively.

"Of even greater importance, we really wanted to operate
as a single entity. We did not want to operate as a bunch of
independent firms with our own agendas," says Leopold.

Under this system, Roebers and the other Genentech en-
gineers kept their focus on the process, automation and val-
idation via direct contacts with the engineer, automation
vendor and validation contractors.

In fact, in early 2002, the entire team moved into a 20,000
square-feet office facility, in Carlsbad, CA, for the design and
early construction phase, which lasted two years. At peak
times, 120 team members, including about 30 from
Genentech, considered this their base.

For CRB’s Conrath this centralized location provided key
dividends. In essence, it removed perceived barriers around
companies and produced more of a one company mentality
while increasing communications and overall efficiency, ac-
cording to Conrath.

The project’s construction manager, DPR, readily em-
braced this approach, according to regional manager Jay
Leopold. "Johannes [Roebers] really wanted to go the other
way from what we had experienced before, and truly collab-
orate by putting everyone under one roof.

"Ultimately, this led to CRB, which was not San Diego
based, parking a part of their engineering team at the fa-
cility. Our key project staff, who were engaged in pre-con-
struction services were also stationed there with the key
Evolution of a World-Class Facility

That the Oceanside plant is also referred to as NIMO
(New IDEC Manufacturing Operation) provides a glimpse
into both the history of the facility and the vagaries of the
biopharmaceutical industry.

In 2001, Roebers was hired by the then IDEC
Pharmaceuticals to lead the design and construction of the
facility. "That year, IDEC’s
total revenue was less
Facility of the Year Award

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than $200 million, and this project was budgeted at around $400 million.

“That puts everything into perspective for me, and for the entire team — failure was not an option,” he says.

“We had a lot of engagement, support and empowerment from IDEC senior management to execute the project properly, both technically and financially. The plant was designed to manufacture the products in the pipeline of IDEC at the time. This was going to be the future of IDEC pharmaceuticals,” says Roebers.

He noted that the top management and engineering leaders at Genentech were equally supportive, and similar to the IDEC executives, made no attempt to micromanage the project once it was acquired and managed by Genentech.

But plans had to be adjusted following IDEC’s merger with Biogen, a top-tier biopharmaceutical company. This led to a decision to produce the potentially blockbuster Tysabri (natalizumab), a monoclonal antibody for the management of multiple sclerosis at the Oceanside plant. In February 2005, however, Biogen Idc and its Irish collaborator Elan withdrew Tysabri from the market because of a reported association with progressive multifocal leukoencephalopathy (PML), a grave nervous system condition. With Tysabri off the production roster, the new plant quickly became excess capacity, with a $100 million annual running cost to boot.

Genentech acquired the facility, which is located on a 60-acre site 35 miles north of San Diego for $408 million. The current facility, which is one of the most advanced of its class in the world, boasts a six-building, 500,000 square-feet, master planned campus complete with manufacturing, laboratory, office, warehouse, central utilities, operations space, and a versatile ‘spine’ to facilitate rapid adjustments and expansion, a capability that gets tested every time there is a product change.

While the central spine was included to facilitate future expansion, it has immediate utility in streamlining the flow of goods and facilitating the movement of people, says Sean Eickhoff, Associate and Project Manager, with Clark, Richardson & Biskup Consulting Engineers.

Once it is fully operational, the large-scale mammalian cell culture plant, which was approved by the FDA in late April, will provide 90,000 liters of manufacturing capacity to be

Valve array
dedicated to the production of the therapeutic antibody bevacizumab (Avastin), which has been approved for the treatment of colon or rectum cancer and non-squamous non-small cell lung cancer (NSCLC).

Key Contributions to Pharmaceutical Manufacturing

Even though the players seem proudest of their ability to partner with each other throughout this project, the fruits of their collaborations, such as process design and automation, were taken to new levels at the facility.

The idea behind the automation was to reduce cycle time, boost operational efficiency, slash manual work and operator errors, raise product quality and consistency and enable controlled and immediate access to process data.

Emerson Process Management provided the manufacturing control system (MCS) for the facility. The MCS coordinates manufacturing operations by managing resources and executing operations in areas such as primary manufacturing functions like media preparation, fermentation and harvest, buffer preparation and hold and purification and formulation.

Furthermore utilities and support operations such as CIP, SIP, AWFI/HWFI distribution and usage management and clean steam distribution are controlled by the MCS.

Advancements in manufacturing technology at the facility are defined by three elements: the high degree of automation and system integration, a high degree of integration of process, CIP and SIP design, and a high degree of process design flexibility.

The manufacturing facility design hewed closely to the process flow of a large scale mammalian cell culture facility with buffer and media preparations located on the third floor, buffer hold and fermentation on the second floor and harvest, purification and bulk formulation on the ground floor.

The “top down” design combined with clean, cGMP compliant people and material flows dictated the design of the facility’s manufacturing building. The design team maximized the use of “grey space” (unclassified areas) for process tanks, according to Sean Eickhoff of CRB.

“The process design implemented the ‘closed tank operation’ concept extensively, which allowed many tanks to be located in ‘grey space’ and minimizing classified clean room space as a result,” says Eickhoff.

“This approach to grey space utilization, resulted in the reduction of classified space to 25% of the total floor plan of the manufacturing facility,” says Jim Ferguson, vice president, Ferguson Pape Baldwin Architects, who was at the forefront of the energy efficient and environmentally friendly attributes the facility now boasts.

Ferguson says that the optimal use of grey space versus classified clean room space has several operational advantages and considerable cost savings in both the construction and operational sides of the facility.

The project team believes that the manufacturing building at the Oceanside facility is one of the first to use the concept of large modular equipment design, that is super skids. Quite likely one of the most innovative aspects of the plant, super skids were used in the buffer preparation, buffer hold, media preparation, fermentation, harvest, purification and formulation areas.

Overall, more than 70 process tanks and 18 fermenters were integrated into 17 modules or super skids, which provide three key advantages: overall construction time savings, reduced on-site labor and the highest construction quality.

Such innovations no doubt contributed to the decision of the judges. Roebers says that because of the award and the attention, there are now a number of requests for tours of the facility and speaking invitations for him to talk about their execution philosophy, which he puts in a nutshell: “The idea was to extend the collaboration and teamwork beyond the company’s borders to our partners. In turn, this provided great value to our company, which empowered us to do what we accomplished.”