Chapter 14
Winning the "Facility of the Year" - Award with an Indian Plant

Eisai Knowledge Centre

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ISPE Judgment Criteria 2012 The judges have chosen the project as winner of the *Project Execution Category* for the following reasons:

- Outstanding safety record of no reportable safety incidents with more than five million hours worked.
- The completion of the entire complex that includes construction activities for all 14 facilities was accomplished in just 17 months.
- The ability of the project team to overcome the challenges of delivering a project of this size given the complexities of doing so in India.
- Good Japanese style and quality with a high degree of automation
- The capital efficiency of the project is commendable given such a high quality, fully integrated R&D and manufacturing complex was delivered for an investment of under US $50 million

Manufacturing in India

The Development of the Indian Manufacturing Sector

The Indian economy has undergone several structural changes in the last decades. Beginning with the 1950s, India faced excessive regulation that characterized its industrial development policy for the next four decades. These regulations, set up to govern manufacturing capacity, products, technology etc. had the objective to prevent the developing and capital-scarce economy from costly over capacity. With the opening of India's economy in the late 1980s inflows of knowledge, foreign technology, and capital has started. Local manufacturers expanded their

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production and the country became a center of interest for foreign competitors. Moreover, a lack of sufficient import regulations evoked the structural change of the Indian economy. In 1991, India introduced a new set of reforms that substantially reshaped the competitive environment for both domestic and foreign companies. Due to the abolition of India's license regime, protectionism and control measures came to an end and brought the manufacturing sector at a critical juncture (Dangayachy and Deshmukh 2001). However, although the perception of manufacturing in India as a support activity for marketing and finance rather than the vital value creation of a company is gradually changing, today's manufacturing still lacks attention of senior management (Chandra and Sastry 1998). Therefore, it's no wonder, that most companies in India are still far from practices summarized under the umbrella of world class manufacturing (Dangayachy and Deshmukh 2001). Meanwhile, international competitors improve their manufacturing functions continuously, market new products in the country, and thus increase the flexibility and responsiveness of the entire Indian manufacturing sector. As such, the domestic Indian economy experiences rising competition from both multinationals entering the market and from imported goods. This new competition is characterized by the simultaneous combination of a wider range of products – mostly coming with higher performance, reduced cost, improved quality, and better services (Chandra and Sastry 1998; Dangayachy and Deshmukh 2001).

Challenges Faced by Manufacturing in India

Although the Indian economy in general has seen numerous changes in recent years, the pharmaceutical industry, as one of the most important pillars of the industrial sector, faces several hard challenges. Many of these challenges can be traced back to the legacy of the Indian culture and traditions that have evolved over thousands of years. As such, the Indian culture – as many cultures in other emerging markets – is characterized by strong hierarchical structures (Schwartz and Shalom 2004) that carry forward into Indian organizations and thus influence behavioral patterns and thinking.

India pursues the ambitious target to rank among the major players in the global knowledge economy and higher education is seen to be a critical factor to this success. In order to remain competitive beyond the provision of low cost manufacturing, the Indian industry is heavily dependent on well-trained and skilled personnel. But recent studies reveal that the Indian higher education is currently not keeping up with developed nations and thus is severely constraining the supply of qualified manpower (Agarwal 2006). This, however, not only hampers the search and employment of people in pharmaceutical manufacturing, but also in retaining them, once they are well-trained and experienced. Scarcity of experts and plenty of emerging pharmaceutical companies, provide especially young professionals that are often willing to move across the country with rich opportunities for work. Such high turnover rate is likely to negatively impact the organization's cultures. Several

shortcomings in legal systems abet young professionals to constantly try to get the best payment fostering the "company-hopping" across the country.

In addition, the manufacturing sector in India is influenced by the existence of strong labor unions. These unions enforce to tie in workers' payment with the current productivity level i.e. an increase in productivity entails the same payment rather than resulting in an extra bonus for exceeding initially set productivity levels. Thus, there are very few incentives for employees to increase productivity.

An often deemphasized aspect that has yet to be taken seriously lies in the integrity of the management and the underlying failure culture. Recent quality issues having their roots in India might be an unfortunate result of such behavior. Emerging markets like India often emphasize cultural embeddedness; such culture views people as entities of collective groups that highly emphasize maintenance of a group's status quo and discourage any behavior that might disrupt in-group solidarity. Moreover, decision making in such cultures is rather autocratic and willingness to share decision making is scarce (Burgess and Steenkamp 2006). This however might lead to the non-admittance of failures rather than an open communication and bearing the consequences, e.g. scrapping bad batches. When it comes to quality, literature of a decade ago testified the Indian manufacturing sector a modest situation. Quite often, Indian companies have pursued an opportunistic approach to spur growth, lacking a consideration of their true capabilities. Consequently, Indian shop floors and their improvement have seldom been in the focus of operations managers (Chandra and Sastry 1998). Thus, Dangayach and Deshmukh (2003, p. 279) argue that such behavior has resulted "in poor quality of products, little awareness of competitiveness, [and] little integration of various functions such as marketing, sales, production". This perception currently seems to change (IBEF 2012). Despite, many studies discussing latest quality advancements of the Indian manufacturing sector neglect the fact that for many Indian companies, the reason for competing for quality prizes is image and advertisement rather than a true "excellence" philosophy.

However, especially within the pharmaceutical sector, India has seen a lot of progress in recent years. No longer are shop floors characterized by outdated technology – in fact, the industry has taken its improvement potential to heart. Today, the Indian biopharmaceutical sector has set several examples of state-of-the-art plants that provide high quality products with latest technology.

The subsequent parts of this article describe such a success story providing insights in the establishment of an award winning pharmaceutical manufacturing site.

Eisai: A Global Company

Eisai in General

Eisai Co., Ltd. is a research-based human health care (hhc) company that discovers, develops and markets products throughout the world. Eisai focuses its efforts in

three areas: Integrative neuroscience including neurology and psychiatric medicines; gastrointestinal disorders; and integrative oncology including onco therapy and supportive-care treatments. Through a global network of research facilities, manufacturing sites and marketing subsidiaries, Eisai actively participates in all aspects of the worldwide health care system. Eisai had employed 10,495 people worldwide. As such, Eisai is a human health care company seeking innovative solutions in disease prevention, cure, and care for the health and well-being of people worldwide. As a reflection of that commitment, the Company's "hhc" mission symbol is derived from the letters in Florence Nightingale's signature. Following the example set by the famed health care pioneer who devoted her life to caring for others, yet never lost sight of the importance of listening to her patients, Eisai marshals its talents to explore new therapeutic approaches that address two key goals: to meet the medical needs of patients and their families and to improve quality of life.

The traditions of genuine concern for people, dedication to excellence, and contributions to society have become hallmarks of the Company. Eisai regards patients and their families as the most important "participants" in the health care process and expects all of its employees to consider – and be responsive to – the patient perspective.

Eisai strives to promote the well-being of the patient, family and our community by discovering and developing innovative drugs in areas of unmet medical need, by raising awareness of vital issues through educational and fundraising events, and by encouraging volunteer involvement. We are determined to make a difference locally and globally.

Eisai is a responsible, focused, efficient, innovative Pharmaceutical company. This vision is designed to provide the overall direction for our company. It describes what we need to continue to succeed in the future, based on changes in the marketplace and our capabilities. Our vision helps us set goals based on the potential of our organization and what we hope it will become. Most importantly, it forms the basis for our work and business strategies.

Eisai in India

Eisai Knowledge Centre, a state-of-the-art 50-acre complex that covers the complete production cycle from research to product development, to pilot plant, to clinical manufacturing and manufacturing of drug substances and, ultimately, the final drug product in solid dosage form. The complex incorporates India's most advanced chemical synthesis technology. The Centre is located off the southeast coast of India in Visakhapatnam, the second largest city in the state of Andhra Pradesh and the third largest city on the east coast of India. Eisai made a significant investment of around more than 4 billion JPY to locate the Centre within the Ramky

Pharmacity, Special Economy Zone (SEZ) in Andhra Pradesh. The research and manufacturing complex currently occupies 33 acres with the remaining 17 acres available for future expansion.

The complex is a major part of the company’s strategy to transfer a portion of primary operation functions to areas with high technology standards aiming for reinforcement of global flexibility and realizing its strategic plan. Production at the site will also support global logistic infrastructure and supplement Eisai’s production plants in Japan and other countries.

This is the first time that a major Japanese pharmaceutical company has established a major production facility in India. The Eisai Knowledge Centre ensures a stable supply of high quality pharmaceutical products and supports the company’s hhc philosophy to supply high quality pharmaceutical products to meet the various needs of patients around the world. Eisai aims to benefit millions more patients around the world by entering all of the world’s top 20 markets and transforming itself into a global top-tier, high performing company by adapting to changing market conditions.

The Eisai Knowledge Centre was designed to be a global comprehensive pharmaceutical complex for the manufacturing of drug substances (Active Pharmaceutical Ingredients – API) and drug products (Oral Solid Dosage – OSD forms), as well as for process research and development of APIs. The center, Eisai’s fourth knowledge creation base, was established to generate higher efficiency and productivity by integrating production, research, global procurement and administrative functions into one site to ensure a stable supply of high quality pharmaceutical products.

This is a unique complex where all technical buildings are *integrated* from a business and production standpoint. The *Drug Substance* facility is *designed* to *produce all API* required for the *Drug Product* facility. The production capacities, operating schedules, storage capacities, etc. of the Drug Substance facility are *matched* and *integrated* with the *production capacities* of the Drug Product facility.

This flexible, fully integrated site offers Active Pharmaceutical Ingredients (API), formulation manufacturing and API process research functions, and enables advanced preparations such as technical transfer, process validation and stability testing towards full scale operations. The new complex consists of 14 buildings, including locker rooms, cafeteria, critical utilities, laboratories, administration, warehousing, research and development and both Pilot and Manufacturing Blocks.

The Drug Product facility, with an annual capacity to produce two billion tablets, and the Drug Substance facility, with an annual capacity of 30 t, will supply products to the United States, Europe, Japan and other global markets.

Eisai's innovative chemical manufacturing capabilities for cGMP API production and formulation offers greater speed, flexibility, safety and security of the supply chain and outstanding quality, meeting strategic drug development/manufacturing needs with flexibility for expansion. The facility has reserved sufficient place for expansion.

The integration of API research, support and manufacturing facilities into one flexible, state-of-the-art complex has increased the capacity and capability to research, scale-up and manufacture multiple API products simultaneously for the benefit of the patients throughout the world.

The Eisai Knowledge Centre was able to successfully manufacture cGMP commercial product immediately 7 months after facility completion. The facility is scheduled to reach full annual production capacity of two billion tablets in fiscal year 2014–2015.

The Drug Substance and Drug Product facilities were fully validated to Japanese, US and European regulations. Construction activities, involving one project team, have been run simultaneously and in parallel, successfully completed within 17 months and were below the released budget of around more than 4 billion JPY.

Establishment of the Site

Construction Type

The project to establish the multi-functional complex followed a greenfield approach that combined a unique design, seamless quality, innovation, and facility integration. During the peak of construction the project team counted nearly 2,000 people working on site. Moreover, about 70 different vendors, contractors and subcontractors had been coordinated on simultaneous and paralleled construction project that altogether contributed to complete the entire complex within 17 months.

Building structures and ceilings are made of reinforced cement concrete and walls have been built of a brick masonry that is plastered with cement. Additionally, the walls are coated with polyurethane paint to provide a hard, smooth finish. All floor, wall and ceiling joints in the manufacturing area are coved with epoxy to avoid dust accumulation and to facilitate ease of cleaning. Also from a cleaning aspect and to support housekeeping, all manufacturing area floors have an easy-to-clean self-leveling epoxy that provides a smooth, impervious, hard surface. Double glass view panels (free of joints and crevices) have been installed at doors and walls to facilitate viewing and supervision of activities on either side. Since finishing requirements were different in each building, manufacturing areas were finished according to cGMP requirements whereas at administration and offices attention has been paid to aesthetics and modern finishing requirements. Thus, friendly and pleasing offices are located in beautifully landscaped open areas. Besides, the complex offers night catering and company vehicle transportation to support the three shift production schedule.

Construction Safety Statistics

From the very beginning, safety during the construction period was seen as mandatory by Eisai's management. Everybody agreed that it is not only to establish a new state-of-the-art facility complex that in the future will supply millions of people with high quality medicine and helping them to enjoy a healthier life but also to treat and value high every single individual that contributes to this ambitious vision. These safety aspects were also requested from and enforced at all vendors that supplied the construction site at an initial vendor meeting through the finalization of the contract. Therefore, all workers and supervisors were conscientiously trained in several safety aspects like tool box talks and electrical and grounding safety. Beyond training safety techniques on site like barricading, staging, edge protection, safety belts and nets have been employed. Supervisors additionally trained in project management skills ensured safety for on-site personnel and substantially

contributed to the construction site's record of zero accidents at the total construction time of more than five million man-hours.

Environmental Impact and Sustainability

The Eisai Knowledge Center was established as a place for all employees to share knowledge and information in modern and aesthetic biopharmaceutical complex. Therefore, the center on the one hand provides a bright staff cafeteria, a fitness center, a reading area and other cozy spaces for employees to relax and collaborate. On the other hand the center has no constraints for employees with disabilities as all buildings are accessible via ramps, upper floors via lift, and every building has disabled friendly restrooms.

Cafeteria

The entire complex features environmentally responsible technologies. A natural ventilation system is used for office acclimatization and brings in fresh outside air. Besides, the air handling system is equipped with a heat recovery wheel for efficient energy use. High intensity incident solar radiation is damped by high-insulation, double glazing, light shielding screens and skylights. Inside the office spaces high-efficiency lighting with presence sensors foster a comfortable atmosphere.

Cafeteria

Corporate Environmental Protection Policy was extended to the site that entails the minimization of environmental impact through protection measures for water, air and effluent. Overall energy usage reduction results in lower CO_2 emissions. The reduction and gradually removal of chemical substances that cause pollutant emission is promoted. All data that give information about environmental impact such as energy, water, paper consumption, waste volume, discharge, contamination, vehicle exhaust and atmospheric emissions are measured and assessed routinely.

The Facilities

Drug Substance (API)

The building was sized to allow the production of up to 30 t of API per annum that is used for on-site formulation as well as exported to the West and Japan. The design involves the vertical configuration of the drug product facility. Hence, process operations maintain a vertical flow in clean areas for the product to follow progression from final crystallization process to finished product. Dispensing of raw materials occurs within contained dispensing booths under laminar air flow to avoid cross-contamination. Three segregated booths facilitate dispensing of powders, liquids and corrosive powders and liquids. Powder Transfer Systems (PTS) are applied to avoid cross-contamination and minimize oxygen content in the reactors by creating nitrogen blanketing. Dispensing of solvents through a distributed control system minimizes manual errors and avoids direct exposure to the solvents. The integrated Powder Handling System (PHS) facilitates contamination free manufacturing of final operations e.g. milling, sifting, metal detection and predefined weighing with online sampling. For the first time in India a drug substance building used clean classifications similar to drug product operations.

API Pilot Plant

The API pilot plant enables verification of process improvement studies of all intermediates performed in the API laboratory through scale up, it serves as a multi-purpose plant to produce intermediates.

Bulk Product Storage/HazMat Storage

Raw materials for production and products from drug substances are stored within a controlled environment. The effective use of space and insect/pest control measures was incorporated into the design of the storage building.

Administration Buildings

The design offers Japanese open-style layout in administration and cafeteria to support better a communication while considering unique Indian customs. Open courtyards provide with natural lighting creating a comfortable atmosphere.

Drug Product (Formulation)

With a capacity to produce approx. Two billion tablets the OSD formulation facility supplies the global market. At the two-floor building the ground floor is used for warehousing, manufacturing and packing operations. The second floor is the technical area, including air handling and purified water systems. In order to ease and

facilitate a smooth material handling, storages for raw and packaging materials are adjacent to the production area. Also designed to encourage lean operations, warehousing and shipping is located next to formulation and thus improve traffic direction of the finished products and their shipping processes.


Drug Product (Formulation)

The innovative design of the facility involves a “one room – one unit operation” concept that clearly separates various unit operations to avoid cross-contamination. Furthermore, closed loop granulation and drying equipment is applied to prevent any contamination and exposure to operators in the drug product building. For an effective prevention of cross-contamination either by personnel or by material a pressure cascade system with H13 high efficiency particulate air (HEPA) filtration and various airlocks for both personnel and material to avoid dust circulation between rooms has been installed.

The facility is provided with full automatic granulation, compression and coating equipment. A state-of-the-art laser based tablet inspection equipment is used to check any defects to the level of 40 μm – a valuable device when it comes to the supply of the challenging Japanese market.

R&D/Laboratories/QA

The building houses R&D and Laboratories for API producing processes on the ground floor. The architecture incorporates key concepts like the possibility for future expansion and common facilities for both API and formulation laboratories. Chemical R&D is focused on complex synthetic and organic chemical compounds, including process research at kilo lab level and scale up to pilot scale. In contrast, analytical R&D delivers feasible, cost effective, eco-friendly & commercially viable analytical and validation methods for identified products.

R&D / Laboratories / QA

Quality Assurance (QA) and Quality Control (QC) for the entire complex are located in the upper floor. The Quality Control lab has in-house testing facility for incoming materials, raw and packaging, in-process materials and finished product. Besides, the lab is self-contained and has separate labs to cater to the needs of various kinds of analysis.

Energy Centre/Pump House

External electric power is transformed in the energy center and supplied to each zone throughout the campus. In order to cope with unstable power supply, emergency generators for each zone have been installed to provide 100 % power back up. Moreover, each zone is supplied with WHO standard drinking water and medium pressure steam that is generated in the Utility Zone.

Energy Centre

The site’s waste water plan segregates the effluent on site in low total dissolved solids (TDS) and high TDS streams. Both streams are sent out for final treatment. The ISO 14644 conform HVAC system is equipped with H13 HEPA filters in the supply air stream to remove contaminants and prevent cross-contamination in the process areas. The motors for supply and return air blowers have variable frequency drives to maintain the desired air flow and help in energy conservation.

On site infrastructure also comes with access roads around each building. However, material and vehicle movement is restricted to one gate only. Flows of people, material and equipment have been optimized from scratch. As mentioned earlier already, the process flow for the drug product is designed to maintain linear whereas drug substance flows are arranged vertically, such that the product follows a natural progression from incoming starting material to finished product. The campus master plan has provision for expansion for each building adjacent to the existing building. To also meet future requirements and developments of the complex, critical utilities are located within the Energy Centre in the middle of the complex and effectively fulfill the utility requirements of the R&D, API and Formulation buildings. Latest fiber optics-based communication links enable data integration between all building operations.

Advances in Design, Commissioning/Validation Technology

At the planning phase, a validation master plan has been developed. The defined approach and methodology was applied for commissioning and qualification of all technical buildings, equipment, systems, utilities and processes. A risk-based approach was adopted for equipment and facility at the design stage to look at the possible risks and their mitigation built into the design. The risk analysis also comprised systems and processes that establish and maintain environmental control and provide a harmonized environmental standard. Based on the ISPE baseline guide, impact assessments were carried out by evaluating the impact of operating, controlling, alarming and failure conditions of a system on the quality of a product. Direct impact systems were subjected to installation, operational and performance qualification (IQ/OQ/PQ) testing; indirect impact systems were subjected to IQ/OQ (only functional testing) and periodic calibrations and no impact systems were installed as per Good Engineering Practices (GEP). For immediate corrective actions on-site vendor support during IQ/OQ execution was guaranteed. Only validated methods were transferred to the site and revalidated to ensure comparable results.

Pollution Control

As mentioned above, liquid effluent is segregated at each facility level as low TDS and high TDS. The Low TDS effluents are collected and transferred into a common collection pit where it is neutralized prior to disposal for further treatment. In case of high TDS, apart from separating low TDS, the streams are further segregated as acidic, solvent, and aqueous & solvent. These streams are separately collected in above ground tanks and disposed of through a common effluent treatment plant.

All corrosive gaseous emissions are scrubbed prior to venting into atmosphere. A point exhaust system is provided for fugitive emissions, which are separately collected and scrubbed. Besides, all vacuum pump exhaust that is connected to the scrubber, also exhaust from the reverse laminar air flow (RLAF) charging booth is connected to the scrubber. Hydrogenator exhaust is processed through a specialized exhaust tower, then scrubbed with low pressure steam. In order to control fugitive emissions, all solvent storage tanks are kept under nitrogen blanketing and solvent transfer pumps are provided with mechanical seals.

Success Factors

The project planning and execution was centered on the need for "total backward integration", as India is a key Eisai location for supplying all global markets at affordable price, as well as for developing new processes. This, however, put considerable pressure on the entire project that was condemned to success from the start.

The main reasons this project was successful and accomplished its intended goals can be summarized as follow:

- Senior management oversight of project with a close monitoring
- Excellent project management and communication with the teams
- Use of risk assessment and mitigation strategy right in the design stage to look at the possible failure probabilities and its solutions
- Elaborate commissioning and qualification activities through an experienced team
- Small close knit team for enhanced decision making and choosing alternate course of actions
- Blank dry runs in the beginning of the trials to prevent any wastages
- Good training both for operational and regulatory compliance
- Sound procurement practices and negotiation to keep costs in control
- Vendor development activities started before the construction started to give sufficient trials for search, evaluation, audit and certifications
- Culture of safety and compliance throughout the whole project including regular training and inspiring the teams to follow a compliance driven decision making.

Project Management

A decisive success factor was indeed a sound project management. Influenced by several observed projects of launching global manufacturing facilities in the US and UK, along with the following concepts of existing formulation facilities in Japan, lessons learned were derived, optimized, adapted, and implemented into the complex.

To start very early with all planning procedures was key to coordinating a project of this magnitude and not to waste time while get bogged down in details or needless micro-management. The construction activities for all 14 facilities began simultaneously and were run in parallel and constituted a daily challenge for the project management team. The entire project was based on an aggressive timeline that at the end was exceeded as the facility complex was constructed in 17 months only and its inauguration date was scheduled earlier as intended at project onset.

An integrated project team was established at project inception and continually collaborated with all stakeholders. The entire project was handled by one project team whose members brought in sound knowledge of manufacturing operations along with execution of large projects. During project peak, the entire workforce counted nearly 2,000 people. Daily meetings with a highly effective project team communication offered a tight coordination; pre-planning and execution of several activities and "to dos" were discussed, and critical issues were addressed in a timely and proactive manner.

The tight team collaboration facilitated to continuously monitor and forecast deliverables and to address all potential issues in advance. Tracking of the project implementation, planning and execution was supported by several tools e.g. MS Projects, S-curve etc. Such outstanding teamwork with cohesive relationships, communication and the team's commitment to safety and quality resulted in increased efficiency and productivity.

Budget Control

Budget control of such a large project requires sensitive management skills. It is important to remain always consistent when it comes to business, but fair and friendly when it comes to people. This approach, however, was meaningful for successful negotiations with key vendors.

As there are worldwide many examples available of how the management team of large construction projects has lost control on cost, regular review meetings on how to leverage cost were held; unnecessary expenditures have been identified and if possible they have been removed.

Finally, speed in decision-making was the key to keep the project on its tough schedule which resulted in the project being under budget.

Eisai's Performance

After having won the Facility of the Year Award 2012 for Project execution and having run production successfully for more than 1 year, the leadership team of the site was looking for a meaningful industry comparison of the Visakhapatnam site with other successful industry practices. The leadership team was looking for a benchmarking not only based on single Key Performance Indicators (KPIs) but rather for a management cockpit like visualization of a broad summary of KPIs. The St.Gallen OPEX Benchmarking provides such a holistic consideration of a multitude of KPIs that need to be taken into account and continually measured. This goes with the leadership team's pursue of excellence and was considered as beneficial for a target setting, future tracking of the site's improvement progress, and beyond.

Eisai Knowledge Centre as part of Eisai's global manufacturing network is a corporate center for R&D and supplies several sites within the network with high quality OSD products. The site's manufacturing strategy is in line with corporate and is primarily focused on achieving highest quality. A balanced network approach allows the complex to focus on its existing product portfolio – there is no need to provide the company with a high manufacturing flexibility and a broad product mix.

Before the site's very first SOP, all employees attended several trainings. Especially for shop floor employees, Eisai Knowledge Centre run several maintenance and machine setup & cleaning workshops and trainings to get a proper machine handling and understanding of necessary maintenance work. Workshops on the mindset of continuous improvement (CI) laid the foundation for all value-creating processes and CI mindset is encouraged by management and evolves step by step ever since. These trainings, however, contributed to the site's TPM performance that is apparent in lower setup and cleaning times as well as a lower proportion of unplanned maintenance compared to other OSD manufacturers in the St.Gallen database.

One of the site's main markets is Japan, a highly demanding market when it comes to product quality. Several constraints of pharmaceutical manufacturing in India have been discusses in section "Manufacturing in India" of this article. However, corporate and the site leadership team are aware of the challenges but also of the rich opportunities of manufacturing in India. In order not to challenge luck, quality was handled with utmost care and is meticulously supervised. Such persistence on quality became evident while participating at the St.Gallen OPEX Benchmarking. The significantly higher proportion of the Visakhapatnam complex' indirect QC and QA compared with an industry average of approx. 100 pharmaceutical manufacturing sites underlines the focus on quality. Moreover it symbolizes the awareness of India's quality issues in the past and the efforts never to be mentioned with those in the same breath. Additionally, benchmarking certified the site to put above-averagely high emphasize on customer involvement, cross-functional product development, and supplier quality management in order to achieve its high quality products. High quality performance, however, is reflected

by less process deviations per batch, zero rejected batches, a significantly shorter release time, and zero customer complaints. On a quality cost perspective, the site utilizes its advantage of manufacturing in a low wage country and realizes a pleasant input–output ratio.

As mentioned above the Eisai Knowledge Centre was designed to facilitate smooth flow of people, material, and equipment at the entire area. Optimization of layout thus comprises both infrastructures like roads and material supply, and shop floor layout facilitating low inventories, fast throughput and highly synchronized process steps. High employee involvement and cross-functional teams support the site’s implementation of the Just-in-Time philosophy. A higher JIT performance than most of the sites in the St.Gallen database is demonstrated in e.g. high turns of finished goods, shorter cycle and lead times, and surpassingly short changeovers.

Although the St.Gallen OPEX Benchmarking testified the site an already high performance, based on the assessment of the St.Gallen Model’s technical system (Chap. 2) the benchmarking also revealed potential for further improvements. The potential and how to utilize it has been discussed by the site leadership team, and an agenda list with distinctive initiatives for future improvement has been drafted. In accordance with daily business management will work thorough the prioritized list of initiatives and start them little by little. A repeated participation at the St.Gallen Benchmarking will reveal the site’s progress not only based on Eisai’s own KPIs but also in comparison with the entire industry’s movement.

Outstanding pharmaceutical manufacturing is a tough challenge in India and many companies struggle to get their manufacturing function in line to cope with the country’s volatile environment. Against all criticism, the example described is evidence of the possibility to achieve very high performance from the start – even in a country that is yet in its development stage. But facing the challenge and taking the advantage of the situation will pay off in the future and strengthens the position in one of the world’s fastest growing markets.

Future Challenges for the Site

At present the facility acts as a supply hub for the Japanese market. The site is also approved by US FDA, MHRA, WHO and Korean FDA for supply of APIs and drug products. In the future a number of additional products for different markets will be supplied from this site making it more complex both from a stable supply and a regulatory compliance perspective. The number of SKUs will increase considerably leading to challenges in operational excellence. The process research and development needs will increase further having to deal with additional scale up requirements and the need for the development of new vendors and new materials. We will approach this situation with the following measures:

- Kaizen for continuous improvement.
- Quality by design approach for greater reliance on compliance by design and not relying on quality by testing.
- Six sigma approach for sustainability in supply to stringent pharmaceutical markets.
- Training of employees at various levels for their skill development.
- Building a culture of openness, transparency and professional conduct.
- Benchmarking of operational excellence parameters and improving them continuously.

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