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Planning ahead: How to move smoothly and quickly into Asian markets?

Biopharmaceutical companies looking to manufacture in the Middle East or India may find they can't simply transfer the plant they've been using successfully in Europe, for logistic as well as regulatory reasons. An expert in integrated process technology and engineering, Glatt Ingenieurtechnik (Engineering & Consultancy Division) outlines the potential pitfalls and solutions

Training staff early on helped Julphar Gulf Pharmaceuticals to achieve speedy commissioning and operation start at its new biotech plant in the UAE. (© Julphar)

TRANSFERRING production of any pharmaceutical that contains biotechnologically produced active ingredients such as insulin, vaccines or antibodies using micro-organisms to a new country – especially one on a different continent – creates a number of challenges. Not only do technical documentation and technology have to be considered, but regulatory guidelines, which vary from country to country, and compliance issues must be addressed. The technology and engineering experts at German company Glatt Engineering know how to tackle these issues and have helped several companies to set up manufacturing facilities successfully and smoothly across the Middle East and India.

Fundamental questions

For many pharma projects, early availability is important and fast time-to-market are imperative for the manufacturer. Effective project management and scheduling are therefore crucial. Working to a clearly defined structure based on sound experience, when it receives an initial enquiry from a pharma manufacturer, Glatt asks two fundamental questions: does a suitable biotechnological production process already exist within the company? Or will it need to be purchased from a technology provider or licensor? As soon as these points are clarified, the Glatt engineering team will begin to evaluate and compare the relevant technologies, in line with the pharma company's specific criteria.

It is important that a defined and stable micro-organism or a high yield cell line exists, and that the scale and status of the biotechnological process has been assessed to attain regulatory approval for the pharma production in the Middle East, in India or other process technology receiving regions. If the procedure only exists in a laboratory, scale-up may be available at a pilot plant or – better still – a proven and commercial-scale process may have already been established at a potential process technology donor location.

This status report determines the schedule of the entire project. Additional evaluation criteria include, among other things, secured patent status, any royalties to be paid, material requirements, expected turnover rate and yield. It is also important to know whether guarantees can be given regarding process parameters such as yield and product purity.

The right choice of technology

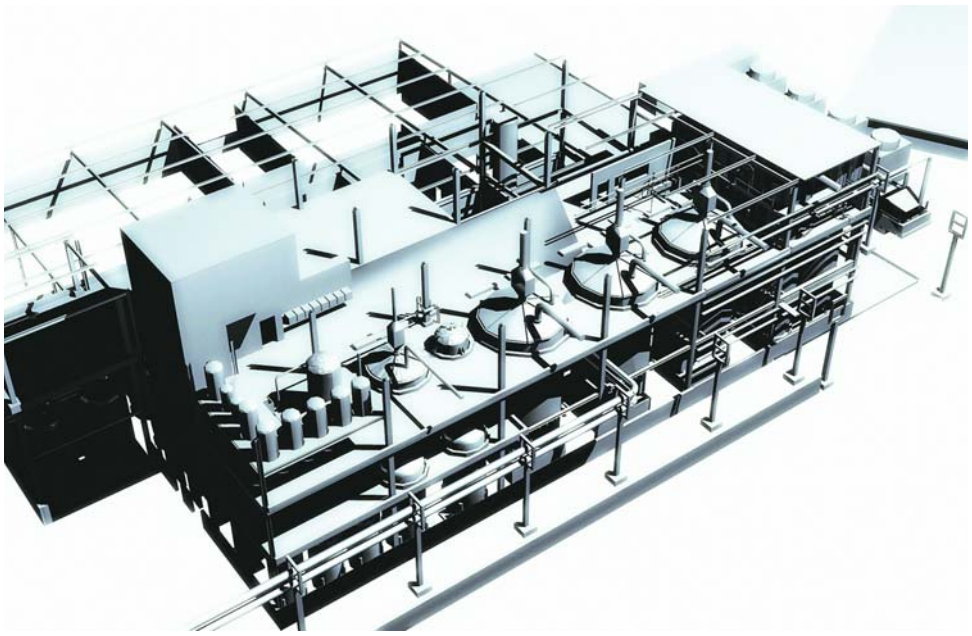
The next milestone is technology comparison, which will result in the selection of pre-

ferred technology candidates. Subsequent negotiations will hopefully lead to a Tech Transfer Agreement (TTA); and, with the signed TTA or a licence agreement in place, the technology supplier will provide the planning input. Alongside a process description, characteristic flow diagrams, quality and measurement parameters and Standard Operating Performances (SOPs) from reference systems should also be available.

Local authority requirements for the approval of the technology required to manufacture the products must also be considered. For instance, the reference authority for all Arabian Gulf Co-operation Council (GCC) countries is the Saudi Food and Drug Authority (SFDA), which is oriented towards biopharmaceutical products at the European EMA.

For customers on the Arabian Peninsula, a European regulatory consultant can accompany the entire approval dossier according to European standards. The regulatory compliance of an active biological substance (ABS) and final dosage form plays an important role. Technology transfer is usually carried out by an established pharma company, which, in turn, has specific standards as well its own constraints.

It is therefore advisable for the manufacturer to define their specific requirements or design basis documents clearly. General requirements such as "all our operational standards must be taken into account as well as the company standards of the licensor" simply lead to duplication and don't necessarily fit the project and this can sometimes render a clear design solution impossible. By comparing Tech Transfer Packages and applied practices, user requirements and SOPs can often be used as a future design base for projects in countries with similar requirements.



Holistic engineering from Glatt's point of view: a three-dimensional CAD model of a fermentation plant in the Middle East. (Source: Glatt Ingenieurtechnik)

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Cross-country partnerships deliver cost benefits

Biopharmaceutical projects in Asia and the Middle East are under pressure from Indian manufacturers with low-cost production capabilities. Thus, when procuring equipment components, it is vital to conduct a global search and to source the most cost-effective solution. Finding a partner who can assist with both engineering and process development is also crucial.

GMP reviews regarding process planning, zoning and layout should be implemented at an early stage – during the concept phase. They should involve the technology providers, the engineering service team and the future operator. Regular design review meetings are also essential. A previous project, for example, involved several meetings between a biotech company from the Arab GCC region and technology licensors from the United States at the Glatt engineering offices in Germany. Part of the technology transfer involved increasing the scale of production, so Glatt's biotech team conducted a series of tests with appropriate equipment manufacturers. The results of the multi-week trials were included in the project plan, as were the additional transport, time and costs involved.

To reduce production costs, it is important to involve regional specialist planners and suppliers. Another crucial project management strategy is to procure equipment components in "Best Cost Countries". Glatt Engineering's procurement strategy remains independent of its own portfolio of equipment, and takes into account the best manufacturers, suppliers, references and fulfilment requirements for the task in question. In addition to production facilities in Germany, Switzerland and the United States, the Glatt Group has manufacturing plants in Eastern Europe and in India. Stainless steel equipment and containers are manufactured to comply with Western European standards. While components are being produced for the plant, it is vital to keep track of suppliers. Clearly structured project management and central data systems should serve as a cockpit for this. At the very least, acceptance tests for complex units should include the future operator.

Staff training ensures easy commissioning

It is Glatt's policy to ensure that key staff from the client company is given a proper training at the Licensors plant in Europe to prepare for technology transfer. In all cases, Glatt's biotechnologists recommend early sourcing of key staff, joint training with the technology provider and the engineering team, and the participation of key personnel during Factory Acceptance Tests (FATs) and Site Acceptance Tests (SATs), commissioning and Installation Qualification (IQ) and Operational Qualification (OQ). This way, and by expanding the team in a step-by-step manner, full operational efficiency can be achieved more quickly than might be imagined.