

# Third-Party Technology Transfer

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In all technology transfer processes, particularly when teams

have been built from companies with different cultures, certain areas of activity have the potential to cause delays in the process. **These delays can be minimized or eliminated by the correct choice of team members, strong team leadership, adequate project planning and definition, and the establishment of clear lines of communication for transmitting, recording, and reporting information.** (This article was published previously in *Pharmaceutical Technology Europe* 12 [10], 26–32 [2000].)

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**F**or projects involving the transfer of technical data between contract and pharmaceutical organizations, the transfer process starts well before any data generation.

The pharmaceutical organization, before going to a contract research organization (CRO), should define clearly the product development process and establish the technical and resource requirement for the CRO as well as the regulatory and financial implications of following this route. This must be supported fully by senior management because of the need to integrate CRO activities into the wider product development program, thus minimizing the potential for the common pitfalls of technology transfer (see sidebar “Common pitfalls”). In traditional product development situations, the correct choice of CRO can enhance the development program — major CROs are normally in a position to provide a global perspective on product or process optimization and regulatory restrictions as well as provide resources, thereby decreasing the time to market.

With new innovations such as the development of products based on biotechnology, the CRO could have a pivotal role early in the process because the technology and/or technical expertise may reside only with the CRO; therefore, it is better placed to define development timescales. Contractor–pharmaceutical organization equivalencies, in terms of equipment, processes, and raw material, probably will have to be developed. It is likely that, in this case, the technology transfer from donor to recipient also will entail significant equipment outlay for the pharmaceutical organization.

### Building the team

At an early stage in the process, it will be necessary to identify individuals within each organization who possess the necessary technical and/or managerial skills to form the technology transfer team. The team leader, and by inference the owner of the team, should be whoever, at the particular stage of the development process, has the most appropriate skills. This team will be instrumental in developing the transfer project plan. This planning will, out of necessity, have to fit into an existing overall product development plan. Within these constraints, however, development activities, milestones, and time scales can be defined.

### Defining responsibilities

Before any contractual agreement, it is necessary to define project responsibilities, and this only can be achieved by specifying



# Outsourcing Resources

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ing the ultimate objective of the transfer project, the current status of the project, and the activities that are necessary to bridge the existing gap. The first step in the process is for both the CRO and pharmaceutical organization to enter into a non-disclosure or secrecy agreement. Both partners should undertake a thorough review of the existing information, which will inevitably reveal commercially sensitive data.

A primary consideration for personnel handling the raw materials or products is personal safety, and this, together with the associated requirements, should be considered using all available data before any other evaluation. The review also should cover the technical and regulatory aspects of the project. Technical information covering the product, process, and analytical methodology should be reviewed to determine the baseline for technical activities, robustness of processes, and the technology for subsequent development, scale-up, and validation.

Subsequent activities will be facilitated if, at this initial review stage, decisions are made about documentation hierarchy and practical considerations such as document content and format. The latter is particularly important when the project will involve two organizations with different company cultures and different ideas on documentation and terminology. For example, performance qualification and process validation to some companies are the same activity, whereas to others they are different, namely equipment- and product-oriented, respectively.

Different companies also will have different interpretations of the end-point in the adequacy of their training programs. Although harmonization of both companies' training programs is not needed exactly, these must be recognized and documented.

### Signing the contract

The signed contract between the two parties should define the project objectives and deliverables and include realistic time-

lines with recognizable, achievable project milestones. The contract also should define responsibilities on a company basis, with individual responsibilities defined within the project plan. Developments, both of traditional pharmaceutical and innovative biopharmaceutical products, inevitably will give rise to patents on processes and products, and ownership of the patents involved must be defined in the contract.

Although documentation is not required by any regulation, the activities should be detailed in the form of a plan (see sidebar "Technology transfer plan — points to consider") to ensure that all the activities needed to generate the data are done and the data are recorded in a suitable format. The plan also will be used as a checklist to correlate the technical activities with the regulatory requirements. The plan can be used, not only for data compliance with regulatory requirements but also to develop commercially related activities such as an economic analysis of alternative processing stages, to plan sourcing of raw materials, to identify additional training requirements, or as a means of monitoring the development of technological innovations.

The technology transfer plan also must cover activities that need special attention during third-party transfer. These almost entirely are related to the differing philosophies and management styles of the two companies and include equivalency issues relating to facilities, processes, equipment, raw materials, and personnel.

### The technology transfer process

CRO facilities tend to be designed to handle development-scale batches rather than the larger industrial-scale batches found at mainstream manufacturers. Therefore, many of the manufacturing processes and associated activities within the CRO environment are performed under non-CGMP conditions, whereas mainstream manufacturing never is performed outside CGMP requirements. This means that, in transfer, consideration must be given to the quality of the services and utilities and their effect on the process.

During the development of the manufacturing process, scale-up will take place and, should it occur during transfer, steps must be implemented to demonstrate process equivalency at both sites in terms of scale, testing schemes, and methodology. Regardless of the sampling or testing schemes adopted, the acceptance criteria must be identical.

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in scale of equipment but also in mode of action. For example, if gradient high-performance liquid chromatography is used for assay or impurity determination at the CRO, it must be used initially at the transfer site.

One of the most common causes of intersite process inequivalency is that of raw materials from different sources. On

Common pitfalls	
Poor communication	verbal or written
Inconsistent documentation	hierarchy content format/style
Nonequivalence	equipment process raw materials analytical methods personnel
Poor management	poor training poor project definition inappropriate staffing
Different company cultures	



## Technology transfer plan — points to consider

Complete process development history	analytical development stability data validation studies
Defined documentation and its management	standard operating procedures batch manufacturing records process flow diagrams technology transfer report
Documentation presentation that is appropriate for a regulatory body	
Correlation of technical, marketing, and regulatory requirements	
Economic analysis of process stages	
Sourcing of raw materials (supply chain management)	
Use of training for regulatory inspections	
Monitor technological innovation	
Issues specific to third-party transfers	facilities (air and water quality, CGMPs) process (testing methods, sampling) equipment (equivalence, maintenance) materials (supplier, homogeneity) personnel (experience, training)

process transfer, a change of raw material supplier may give rise to a material that meets the specification of the original material but has critical characteristics not included in the specification. This can be caused because some specifications that

in the recipient company must be minimized by retraining all affected personnel.

### The technology transfer team

The technology transfer plan is converted into action by the members of the technology transfer team. In technology transfer, as in any process, the people are the most difficult to validate. The same training principles apply to this activity as to any other, namely, the technology transfer capability of each member must be assessed and any shortfalls covered by additional training. The issue is more difficult to handle in intercompany teams, where different training requirements are available from each company and a degree of harmonization will be necessary.

Once the team is established, clear lines of communication must be established within the team, between the team and other involved parties, and between the companies. This is facilitated if the flow of information is channeled between a designated person from each company and records are kept of documentation and data transfer.

People manage the technology transfer process and, regardless of their experience, there inevitably will be first-time failures. The plan must contain fall-back positions to allow for these incidents.

The experience requirements of team members for a CRO-manufacturing company transfer are no different from any other type of transfer. Team members must be hands-on specialists in the various aspects of the development process under review. The team must be led by a person with both the necessary managerial skill to coordinate activities and the technical expertise to be able to prioritize the numerous concurrent ones. It is essential that this team is provided with adequate resources to perform its activities and the necessary authority from the senior management of both companies. **PT**

are chemically stringent, for example, pharmacopeial specifications, do not include critical physical attributes. In the case of powders used in the manufacture of tablets, batches of powders from different sources, all of which meet pharmacopeial specification (they are chemically equivalent), may still have different physical characteristics that can have subsequent disastrous effects on processing or in the biological response of the patient.

No two companies will have the same level of personnel experience. This is true particularly in many biotechnology companies where the only experience of a product or process may be held within the biotechnology company itself. This lack of expertise