

Chapter 2

Overall Perspective of Due Diligence Investigations and Processes

1 Experience of Risk-Based Transactions

Risk-based transactions are rapidly becoming more popular methods of delivering innovative partnering solutions to customers. As a result, CROs and CSOs now add partnering solutions to their list of client options in addition to the more traditional, contract-awarded business transactions such as study start-up, site management, safety surveillance, data management, biostatistics, regulatory, medical writing, commercial consulting, brand solutions, and sales forces. Partnering solutions have evolved from simple fee-for-service transactions. They are offered to pharmaceutical companies and start-up biotechnology companies and represent a growing trend that includes straightforward arrangements such as milestone payments (as products increase their net present value along the drug development value chain), royalty payments (usually as a return mechanism for a partner taking risk on co-development/registration), sales force dedication (e.g., sales representatives, nurse educators, or those who manage sales forces), and co-development (expertise, capital, or a combination of each) solutions or more complicated solutions such as “fixed price” contracting. Fixed price contracting involves a relationship between a sponsor and a contracting entity—such as a CRO—that offers services based on factors such as recruitment or other operational milestones (e.g., last patient enrolled) tied to a particular time point (e.g., number of months or even to a particular date). These solutions can be attractive to sponsors, but must be carefully evaluated in order to make sure that the supplier can deliver and manage the contract in order to make the relationship a “win-win” for each party.

These opportunities represent a paradigm shift from the historical sponsor/client/CRO/CSO relationship to a partnering relationship based around a product or portfolio at various stages of development. Such solutions are a response to pressures on the pharmaceutical industry—some of which are caused by increased scrutiny on health care costs, country specific risk/benefit analyses [e.g., assessments by bodies such as the UK National Institute for Health and Clinical Excellence (NICE)], and

patent cliffs. Many larger companies, due in part to mergers, find themselves with too many products to advance and not enough capital or other resources to move them forward effectively. Partnering opportunities for strategic (or “the right”) products can offer a powerful incentive to develop creative solutions to maximize their value—or just as appropriately, abandon (e.g., “no-go”) the drug in the most efficient manner.

Each solution can be tailored towards the unique needs of a particular client and should be crafted in an objective manner in order to eliminate business conflicts of interest. Although beyond the scope of this brief, it is just as important to effectively manage each relationship after a deal is signed. This is usually under the direction of an Alliance Manager, who takes into account the ever changing CI environment and potentially re-negotiates the deal, as needed.

The key difference between the more traditional fee-for-service construct and the new partnering solution is that both parties now have a material stake in the performance of the product. Therefore, a thorough review of the product by the CRO/CSO is a critical step in evaluating the partnership, identifying risks, defining the terms of agreement, and managing the partnership (to the satisfaction of each party) until completion of the contract.

2 The Process of Due Diligence

Due diligence is the process of investigating an investment or partnering opportunity to mitigate risk. Due diligence includes a thorough investigation of all available data—both proprietary and nonproprietary—by a team of experts with the intention of predicting future events, such as the probability of success and a forecast of sales, in order to equip a deal team to manage risk and execute a financial transaction. All VCs and investment arms of companies perform due diligence prior to investing money in a deal or getting involved in a partnership arrangement.

A pleader is identified for the due diligence (DD) team (which assimilates CI throughout the investigation) and this person—with guidance from upper management—determines the budget and sets timelines for the due diligence process. Nonproprietary materials are reviewed, and a CDA is signed in order to obtain access to proprietary materials. During internal meetings, specific key team members work to identify potential weaknesses that might develop into deal-breaking problems.

Timelines for the due diligence process typically proceed along the following course:

- After a potential partner is identified, preliminary due diligence team members develop a forecast to generate discussion around deal terms.
- The outline deal terms are agreed.
- An information requirement list is sent to the potential partner.
- A core due diligence team is assembled (external consultants can be utilized, if necessary).

- Information is generated from internal sources (e.g., data mining sources such as ADIS, confidential source files) or primary research (e.g., opinion or thought leader interviews).
- A detailed functional review is then completed which often includes one or more on-site meetings to review the following areas: (1) regulatory; (2) sales; (3) marketing; (4) preclinical; (5) biopharmaceutics; (6) clinical; (7) medical; (8) chemistry, manufacturing, and controls (CMC); (9) commercial manufacturing and distribution; (10) finance; and (11) legal issues.
- This input leads to a refined sales forecast and risk assessment.

3 Outcomes of Due Diligence

Possible outcomes of due diligence rely on a thorough knowledge of national and global regulatory requirements and can include the following:

- Confirmation that the proposed strategy is appropriate.
- Re-evaluation of investment, price, or return.
- Re-negotiation of key terms/contractual language or introduction of new terms.
- Amendment of regulatory strategy.
- Abandonment of the transaction.

Although teams generally consist of a team lead with members from other multifunctional areas and may vary with each potential deal, regulatory professionals should always be included in the DD process. Knowledge of the regulations, combined with a thorough knowledge of clinical drug development and the competitive environment, is essential for every partnering solution.

For the purpose of this brief, we will focus on the regulatory portion of the detailed functional review from a US perspective.

Reference

1. Huml, RA. 2003, The Process of Due Diligence from a Regulatory Perspective. RAPS Focus Vol. 8, Issue 11, pp 50–53.

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