Product-based planning: the importance of project and project management deliverables in the management of clinical trials

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As the cost of clinical trials continues to rise organisations are looking at ways of managing this part of the drug development process as effectively and efficiently as possible. As a tactical response, many pharmaceutical companies outsource the management of clinical trials to clinical research organisations on a fixed-price contract basis. This paper presents an alternative approach based on the concept of Product-Based Planning. Key elements of the approach are the creation of a deliverables budget and the establishment of project management-related deliverables. The conceptual developments described in the paper are supported by a telephone survey of 10 UK practitioners. The survey confirms the prevalence and limitations of fixed-price contracts while highlighting a willingness to try a deliverable-based approach – initially through small pilot studies. The key barrier to implementing a new approach is resistance from key stakeholders, such as finance departments, which can be addressed through selling of the business case.

1. Introduction

The past two decades has seen the costs associated with developing new drugs soar. An oft-cited research study of the R&D costs of 68 new drugs from 10 pharmaceutical companies estimated that it costs $802m to develop a new drug (DiMasi et al., 2003). The $802m figure compares with $231m in 1987 and $359m in 1993 (Wechsler, 2002). One stage of the drug development process that is a particular cause for concern is the clinical trial stage. The DiMasi et al. study showed acute cost increases for the clinical phase (inflation-adjusted annual growth – 11.8%) more than five times greater than for the pre-clinical research stage. Although there is some dissent regarding the accuracy of the figures from the DiMasi et al. study, see for example the review by Ezzell (2003), there is little disagreement that the sums involved have been rising at an alarming rate; and this escalation in costs is one factor driving the search to find more efficient and effective ways of managing the drug development process, while at the same time maintaining the integrity of such a risky and complex process.

This paper contributes to the search for an effective, efficient and safe process by presenting an approach to the project management of

clinical trials that aims to reduce some of the inefficiencies in, and increase the effectiveness of, the current approach. The remainder of the paper is structured as follows. Section 2 provides an overview of the management of clinical trials, with particular focus on the increasing trend to outsource this part of the drug development process to specialist clinical research organisations (CROs). Section 3 considers theoretical perspectives. Section 4 documents the current project management approach to managing a typical Phase II/III clinical trial and the limitations of the approach is discussed in Section 5. Section 6 outlines an alternative approach. Section 7 provides the results of a survey of practitioners into existing practices and opinions linked to introducing the alternative approach. The paper concludes by summarising the material presented and describing areas for further work.

2. Overview – the management of clinical trials

Given the cost escalation in the clinical trial stage of the drug development process, there is pressure on pharmaceutical (Pharma) companies to manage this stage as effectively and efficiently as possible. As both a strategic and tactical response to the pressure, companies are increasingly outsourcing this activity. While outsourcing of clinical trials by the industry is not a new phenomenon, having been employed through the 1970s and 1980s, its use has seen a steep increase since the 1990s. Quoting from various contract research surveys, Hughes (2004) estimated that the number of clinical and preclinical CROs had risen from about 100 in the United States and 100 in Europe in 1981 to approximately 380 and 650 in the United States and Europe, respectively, by 2003. Furthermore, the global value of the market increased from about $1.2b in 1987 to $3b in 1993. In terms of the level of outsourcing, Hughes estimated that by 1993 over 90% of companies engaged in some form of outsourcing, with activities currently ranging from limited outsourcing of clinical trials to extensive outsourcing of preclinical evaluations, study design, clinical trial management, data collection, biostatistical analysis and completing product regulatory requirements (LeadDiscovery, 2006).

The type of outsourcing can have implications on the nature of the relationship between the Pharma and the CRO. High-level strategic outsourcing involves forming long-term partnerships with single CROs. Such outsourcing aims to develop relationships based on trust, long-term business stability and the sharing of common and complementary objectives (Hughes, 2004). Low-level tactical outsourcing is more short term and used on a project-by-project basis. Tactical outsourcing is still by far the most common form, with Hughes suggesting that approximately 89% of companies use this approach to select CROs at some time or other (with approximately 60% of companies always using this method). Tactical outsourcing implies transactional and opportunistic relationships, with the nature of the transaction being formed by the specific contract set up for each project. As such, it involves a classic 'Principal/Agent' relationship, with the client Pharma being the Principal who sponsors the Agent, the CRO, to undertake work on their behalf.

The contracts associated with tactical outsourcing are variations on fixed price and variable (fee-for-service), with the most common form of contract being fixed (Hughes, 2004). From a Pharma and CRO perspective each contract type has potential advantages and disadvantages (see Table 1). Regardless of contract type, there is also an inherent limitation associated with all Principal/Agent relationships. Namely, that the relationship is vulnerable to the 'Principal/Agent problem', where the interests of the Principal (in this case the Pharma) and Agent (CRO) may be misaligned and they will each then act in their own best interest (Lovallo and Sibomy, 2006).

A survey of 28 professionals engaged in outsourcing identified the range of services contracted out by Pharma during clinical trials (Parrett et al., 2003). Clinical monitoring was the most commonly outsourced activity, cited by 96% of respondents, followed by data management (92%) and project management (81%). Despite the high levels of project management outsourcing the survey found relatively low levels of satisfaction with the project management service provided by CROs. Of 24 respondents returning usable data, project management recorded an average rating of 5.9 (scale of 0 – lowest to 10 – highest). Only protocol development (5.3) and case report form (CRF) design (5.8) scored lower satisfaction ratings. Of course, low levels of satisfaction with project management are by no means limited to clinical trials, being reported across all types of business sectors (KPMG, 2006). One factor that has been identified as being important in explaining some

Table 1. Pharma/CRO contract types – advantages and risks

Type of contract	Advantages		Risks
	Client (Pharma)	CRO	
Fixed price	Predicable costs (though pass-through costs are usually variable) Pressure on the CRO to work within budget Competitive bidding can drive the price downwards	Easy to forecast revenue and resource Working more efficiently than the contract will lead to greater margin	Renegotiation is common. Not only is the original price increased by there are increased transaction costs associated with the renegotiation and there is the risk of confrontation unless the renegotiation is part of a clearly defined scope change Competitive bidding can result in deliberate under pricing by the CRO to win the business. Renegotiation would be a high priority following the award of the contract. If the strategy was unsuccessful then the contract may well lose money. This is a risk for the Client as well as the CRO as the contract may become a low priority for the CRO The requirement for the CRO to make a profit will also result in the project team being subjected to and responsible for the financial health of the project. This can compromise the other key performance indicators of timeline and quality The initial contract required a great deal of up front work e.g. in defining the scope of work. This can lead to delays in starting the project. The CRO is also vulnerable to 'Scope Creep' i.e. small changes that individually are not significant but when total across the whole project can have a seriously adverse effect on the margin Payment schedule may not be neutral resulting in either cash flow problems for the CRO or overpayment by the Client
Variable (Fee-for-service)	Only pays for the hours worked and will benefit from any CRO efficiencies Sub-contractors can be picked on quality not price Scope change is easy Start-up can be rapid CRO team will not be distracted by the need to make a profit	Guaranteed margin Neutral payment schedule	Perception that there is no financial constraint on the CRO, the proverbial blank cheque No incentive for the CRO to work more efficiently, in fact there is a financial disincentive It is difficult for the Client and the CRO to predict cost/revenue and resource needs

Pharma, Pharmaceutical company; CRO, clinical research organisation.

instances of low levels of satisfaction is the use of fixed-price contracts as part of the contracting strategy for outsourced projects that have typical Principal/Agent relationships. Muller and Turner (2005) describe how mistrust arises in such situations due to the Principal not being party to, or being properly communicated of, all the decisions made by the Agent on the Principal's behalf. While caution needs to be exercised in drawing any conclusions from the Parrett et al. study, due to its exploratory nature, it does suggest that there are shortcomings in the project management on clinical trials. Such a conclusion, though, would be entirely consistent with research of other project arenas that have similar tactical outsourcing methods based on fixed-price contracts.

3. Conceptual thinking

3.1. Managing inputs, work or deliverables?

In the lexicon of contemporary management enquiry the term 'deliverables' is increasingly present. A search for the term deliverable in the title, abstract or key words of academic journal articles published in a 5-year period, covering 2001–2005, by one particular publisher (Elsevier), produced

84 articles (ScienceDirect, 2006). This is a 323% increase in the number of articles with the term present compared with the preceding 5-year period (1996–2000), which produced 26 articles. Although comparisons of different time periods are dangerous given the continued growth in the number of papers published, this increase is striking if one considers that the term 'planning' witnessed only a 29% increase in its use over the same periods: 7547 (1996–2000) and 9800 (2001–2006).

Deliverables are the 'end products of a project or the measurable results of intermediate activities within the project organisations' (Association of Project Management, 2000). If one takes a 'hard systems' perspective, the increasingly widespread adoption of the concept of managing deliverables recognises the importance of managing outputs from the system; and is a feature of 'Product-Based Planning' (Office of Government Commerce, 2005). A 'Hard' system thinking approach is illustrated in Figure 1, which applies the concept of the operations management system (Krajewski and Ritzman, 1999, pp. 3–4) to project management. Here the inputs to the system are the resources required to complete the project. Resources include: the people, capital, facilities, materials, information – such as a business case, and project management tools and methods. The outputs are the deliverables, which can take the form of products, services or a changed state. The project work itself takes place in the middle box, 'operations and processes', through which the inputs pass and where activities are carried out to transform these inputs into outputs. Client participation is an output from the system that also forms an input. For example, the client may participate in activities to define the scope of work and the resultant output, in the form of a scope document, is information that is input to subsequent stages of the project life cycle. A second form of input is feedback that is received through information on project management performance,

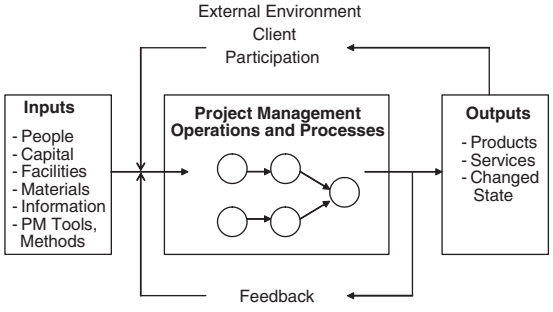

Figure 1. The project management system.

such as adherence to budgets and schedules. The final element is the wider environment. Projects are not managed in isolation. From an internal perspective they may be one of a group of projects that make up an organisation's programme or portfolio and they will be subject to external environmental forces, such as the actions of external sub-contractors, politics and legislation.

Various project management-related tools have been developed to help structure, and hence manage and control, the inputs, the work and the outputs. These include: the Product Breakdown Structure (PBS), which establishes a hierarchy of deliverable products required to be produced on the project; the Work Breakdown Structure (WBS), which divides the work into discrete groups; and the Organisation Breakdown Structure (OBS), which divides the organisation into management levels and groups (Association of Project Management, 2000). Useful illustrations of each of these three structures are provided by Field and Keller (1998). If one relates these structures to the Project Management Systems diagram (Figure 1), the PBS focuses on the deliverables, the OBS on the inputs, in terms of the people, and the WBS on the operations and processes.

While the PBS, WBS and OBS are precisely defined, there is some debate as to the emphasis to be placed on each and the inter-relationships. Turner (2000) asserted that the key focus ought to be on the PBS and OBS, on the basis that it is not the management of work that is important but the deliverables in the PBS and the input of resources in the OBS. In Turner's words 'People manage people and products' (p. 83). In response to this assertion, Lamers (2000) argues that, while the OBS and PBS are undoubtedly important, the WBS is an integral element as, rather than 'people managing people', a more accurate expression is, in Lamers' words 'people manage working people' (p. 326). As such the WBS, which defines the work to be done by people, becomes a key tool for integrating the management of outputs, using the PBS, and of resources, using the OBS. The key is not applying the tools in isolation, but in understanding how they interact in relation to the holistic project management system (as shown in Figure 1).

3.2. *Project management and systems thinking*

The need to look beyond the individual elements in the system and take a holistic perspective is at

the root of 'soft' systems thinking. The application of systems thinking to understand how organisations work and to solve management problems has evolved over time (Steele, 2003). In the 1950s/1960s there was a focus on a 'hard' structured, systematic and mechanistic approach, whereby understanding was sought by reducing larger systems into smaller parts and by developing methods that have their conceptual basis in this 'hard' systems thinking. Analysis of project management is traditionally rooted in this hard systems thinking. The 1970/1980s witnessed the development of a 'soft' systemic approach, typified by the work of Checkland (1981). This approach sees the system as more than the sum of the parts and understanding is sought by studying the whole system and the interactions between the various sub-systems. Soft system methods, i.e. Soft Systems Methodology (SSM) (Checkland and Scholes, 1990), pay particular attention to ill-structured problem situations and multiple perspectives of the problem, seeking to understand how issues such as culture, values, attitudes, perceptions and behaviour of people impact on organisations and people.

Since the early 1980s the project management literature has examples of the use of systems thinking – see, for example, Knoepfel (1983), Walker and Hughes (1984), Davies and Saunders (1988), Barnett (1992), Walker and Kalinowski (1994), Metcalfe (1997), Chapman (1998), and Lefley (2004) – to both understand and conceptualise project management, with a growing call to augment hard systems thinking with ideas and approaches from soft systems (Winter, 2003).

3.3. Project management as a deliverable?

The use of the term 'deliverable' views the main outputs of the project management system as being the new products, services or changed state that the project was set up to deliver. An additional view is that project management is a service and that the quality of project management is based not only on what is delivered but also on how it is delivered (British Standards Institute, 2003). This leads to a distinction between 'project management' success and 'project' success (De Wit, 1988). Project deliverables are linked to ensuring the project is successful, for example, it does what it says it would do and it provides some benefit to the client. Project management success encompasses elements such as delivering the project within time and cost constraints and satisfying the key parties to the project in terms of the way in which the project is managed. This might include being focused on the client during the project implementation, by responding quickly to requests for changes and keeping the client informed of project progress (Winch et al., 1998). As was the case with project deliverables, there is a need to manage both the outputs and the inputs of project management. The input has traditionally been defined in terms of the resources devoted to project management, particularly the time spent on managing the project by the project manager and team members. However, while not explicitly using the term 'project management deliverable' – and a search of academic journals for the term will produce little if any instances of its use – practitioner-led project management methods recognise the importance of managing not just the project management time (input) but also the outputs of the project management service. For example, a widely adopted project management method, PRINCE2 (Office of Government Commerce, 2005), requires the production of management products, such as plans, risk logs and lessons learnt reports. While not naming them as such, these are all examples of project management-related deliverables.

3.4. Summary

To summarise, the salient points of this review of pertinent project management concepts are as follows:

- Viewing the project management system as an input–output-transformation process model (hard systems thinking) shows the importance of managing the outputs from the system (the deliverables).
- 'Soft' systems thinking highlight other complexities, including the need to consider the whole project management system and to consider multiple perspectives.
- While the general concept of project deliverables is widely understood, that of project management-related deliverables is less well-known; although it is implicit in specific project management methods.

4. Case study – project management of a Phase II/III clinical trial

A Pharma has contracted out a Phase II/III clinical trial to a CRO on a fixed-price contract

basis. In Phase II the drug is tested for safety/efficacy in a population of patients (several 100). This may last up to 2 years. Most are randomised, double blind studies. In this manner, the trial can provide the pharmaceutical company and the regulatory authorities with comparative information about the relative safety of the new drug, and its effectiveness. Only about one-third of experimental drugs successfully complete Phase II studies. In Phase III the trial involves a larger test population (sometimes several 1,000s) of patients with the new drug in comparison with the standard therapy or a placebo. The results provide the information that is included in the package insert and labelling. This testing provides a more thorough understanding of the drug's effectiveness, benefits, and the range of possible adverse reactions. The Phase III is a randomised and blinded study lasting several years. Seventy percent to 90% of drugs entering the phase successfully complete it. The Pharma will then request approval for marketing the drug.

In many industries it is difficult to scope the work involved in a project. For example in software development it can be hard to predict how many person-hours will be required to design and implement a new system. Life is more straightforward for the pharmaceutical industry, where good clinical practice (GCP) and the International Conference on Harmonisation (ICH) have made the process of running Phase II/III clinical trials fairly prescriptive. So the CRO has a detailed costing model that produces a list of tasks with the hours required to complete the task and the associated costs. Then a margin is added to allow for profit, which is a typical cost plus pricing solution. An extract from an example activity schedule is shown in Table 2. The table shows example activities for the first three project phases. The actual activity costs and hours are for illustrative purposes only. The cost of project management is a significant part of the budget, in some cases up to 40% of the total budget. Factored into project management are such

Table 2. Extract from phase II/III clinical trial activity schedule

Activity schedule (Part of)		
Activity	€	Hours
Project Set-up		
1 Investigator training	2,723	18
2 Protocol design	5,658	52
3 Protocol familiarisation	474	4
4 Review of protocol translations	756	8
5 CRF design	2,069	25
6 Patient informed consent		
7 Project planning	3,885	33
8 Analysis planning	9,513	80
9 Investigator meetings	22,210	184
Site set-up		
10 Site identification	6,796	84
11 Pre-study site evaluation visits	59,669	676
12 Site planning/start-up	45,143	520
13 Ethics committee approval	48,547	600
14 Site budget development (investigator payment negotiation)	11,853	160
15 Site initiation visits	13,037	176
Clinical		
16 Monitoring visits – on site	370,722	4,200
17 Monitoring – administration and travel	377,785	4,200
18 Monitoring – site close out visits	50,487	572
19 Management of trial supplies – drugs	11,033	160
20 Management of trial supplies – other	0	0
21 Investigator payment administration	11,853	160
22 Medical review of CRF	0	0
23 Medical review of SAE	5,674	36
24 Pharmacy monitoring	14,446	153
	1,074,336	12,101
Support Services		
25 Project management (40% of cost of activities above)	429,735	4,840
Total cost	1,504,071	16,941

CRF, case report form; SAE, serious adverse events.

activities as: tracking progress, trouble-shooting, coordination and motivation of the team/sub-contractors.

Payments by the Pharma are based on milestones that are specified in a Milestone Payment Schedule. For example, 10% of the total cost of the contract is released when the Contract is Signed, 20% on First Person Recruited, 20% when 50% Patients Recruited, 20% on 100% Patients Recruited, 15% on Database Locked and the last 15% when the Final Integrated Report is provided. Project management is treated as a time-based activity, with the cost of project management being calculated as a monthly fee or a percentage of the contract cost. In this case, for illustrative purposes only (Table 2), project management is factored in as being a 40% overhead cost.

5. Limitations of approach

The limitations of the approach described in Section 4 are manifest during the implementation of the clinical trial and are as follows:

- The monitoring of the project implementation against the Milestone Payment Schedule does not necessarily provide a true indication of progress. For example, a number of milestones in the schedule relate to the number of patients recruited, as a percentage of the overall target. Although the number of patients recruited is of interest, in itself it does not always mean that the project is on track. Even if patient recruitment is on or ahead of schedule, it does not guarantee that the CRFs associated with each patient recruited are of a sufficient quality or that the forms have been collected from the investigational site and entered onto the central database in a timely fashion.
- The current approach does little to integrate the different perspectives of the Pharma and the CRO. The CRO is focusing on ensuring that the specified activities in the schedule are completed to budget, as those are the metric on which funding is based. The Pharma is more interested in the quality and timeliness of what is being delivered, yet the Milestone Payment Schedule does not necessarily provide that information.
- Payment for project management is not linked to the production of any deliverables, rather being paid automatically at certain milestones/trigger points through the project. Hence there is little attempt, or method, to monitor project management performance.

6. Alternative approach

6.1. Managing the outputs from the system

The first step is the generation of a deliverable budget from the CRO activity schedule. Activities can be grouped around the production of an associated deliverable. For example, as shown in Table 3, activities linked to 'Protocol Design', 'Protocol Familiarisation' and 'Review of Protocol Translations' all lead to the deliverable 'Final Protocol approved in writing'.

Care needs to be taken in defining deliverables. Although the term deliverable is used to describe Pharma/CRO contracts (Hughes, 2004) in reality there is often a lack of clarity in terms of what is meant by a deliverable. For example, the number of patients recruited is often quoted as an example of a deliverable, yet, as has been discussed earlier, this is an example of a milestone that, in some cases, can give a misleading impression of project progress. The key is to establish the true deliverable, in the sense that it provides unambiguous evidence of progress. Therefore, 'Final Protocol approved in writing' is a deliverable, as the approval can be verified by the signatures of the relevant parties. Likewise an activity such as 'Investigator meetings' is mapped to a deliverable 'Number of Investigator meetings documented' that can be verified through the number of meetings that have the accompanying formal documentation adequately completed to the necessary quality standards. Once a deliverable budget is generated it allows monitoring of the project, and payment for progress, to be based upon the outputs (deliverables) rather than the inputs (activities or milestones based on activity completion).

6.2. Considering multiple perspectives

The mapping of the activity schedule onto a deliverable budget provides a tool for aligning the perspectives of the CRO and the Pharma. The activity schedule reflected the work, which could be structured as a WBS and the deliverable budget the outputs, which could take the form of a PBS. While the activity schedule will still be required for the CRO to monitor the inputs to

Table 3. Extract of deliverable budget for phase II/III clinical trial

Activity schedule (part of)			Deliverable budget (part of)		€	
Activity	€		Deliverable	Activities	PM	Total
Project set-up		2,3,4,25	Final Protocol approved in writing	6,888	2,755	9,643
1 Investigator training	2,723	5,25	Final CRF approved in writing	2,069	828	2,897
2 Protocol design	5,658	7,25	*Initial Project Plan signed off*	3,885	1,554	5,439
3 Protocol familiarisation	474	8,25	Final Analysis Plan signed off	9,513	3,805	13,319
4 Review of protocol translations	756	10,25	Final List of Investigators provided	6,796	2,718	9,515
5 CRF design	2,069	1,9,25	No. of Investigator Meetings documented	24,934	9,973	34,907
6 Patient informed consent		11,25	No. of Sites Evaluated formally	59,669	23,868	83,537
7 Project planning	3,885	6,12,13,14,15,25	No. of formal Site Set-ups completed	118,581	47,432	166,013
8 Analysis planning	9,513	16,17,19,20–24,25	No. of CRF pages monitored and in-house	791,514	316,606	1,108,121
9 Investigator meetings	22,210	18,25	No. of sites formally closed	50,487	20,195	70,683
Site set-up			Total	1,074,336	429,735	1,504,072
10 Site identification	6,796		Additional project management deliverable			
11 Pre-study site evaluation visits	59,669		*Project risk management plan formally approved*			
12 Site planning/start-up	45,143		*Number of minutes of project review meetings approved*			
13 Ethics committee approval	48,547		*Lessons learnt report formally accepted*			
14 Site budget development	11,853					
15 Site initiation visits	13,037					
Clinical						
16 Monitoring visits – on site	370,722					
17 Monitoring – administration and travel	377,785					
18 Monitoring – site close out visits	50,487					
19 Management of trial supplies – drugs	11,033					
20 Management of trial supplies–other	0					
21 Investigator payment administration	11,853					
22 Medical review of CRF	0					
23 Medical review of SAE	5,674					
24 Pharmacy monitoring	14,446					
	1,074,336					
Support services						
25 Project management (40% of activity cost)	429,735					
Total cost	1,504,071					

Italics denote project management-related deliverable PM, Project management; CRF, case report form; SAE, serious adverse events.

the project, monitoring the Deliverable Budget enables both the CRO and the Pharma to focus on the outputs from the process. The use of the deliverable budget also enables monitoring of other sub-contractor budgets to the same or similar deliverables. When they perform routine monitoring visits, Clinical Monitors charge for travel and accommodation expenses. These activities can be linked to monitoring deliverables. Budgets for drugs packaging and interactive voice response randomisation can also be mapped to deliverables, allowing other stakeholder perspectives to be incorporated.

6.3. Treatment of project management

The deliverable budget in Table 3 shows how project management is factored into the signing off of the deliverables. Rather than treating project management as a time-based activity, with payments for project management spread evenly across the project, the cost of project management, in this example €429,735, is allocated across the deliverables proportionally, based on each deliverables cost. For example, the deliverable 'Number of CRF pages monitored and in house' has a cost of €791,514, which is 73.6% of the total budget. Therefore 74% of the total project management cost, €429,735 × 0.736 = €316,606, is allocated to this deliverable. This almost certainly ends up with project management effort being higher at the beginning and the end of trials than in the middle, but it is not a reason to manipulate the planned budget.

In addition to project-related deliverables, project management-related deliverables may also be established. In this example 'Initial Project Plan signed off' is a project management deliverable that the client has contracted to pay for. There may be other project management activities that are not explicitly linked to the contract, but which are carried out in order to achieve value-added to the CRO. In order to develop a longer-term relationship with a particular Pharma a CRO might wish to demonstrate its project management capability. This can be done through the production of project management deliverables, such as lessons learnt reports (see Table 3). If the activities associated with these deliverables are not included in the contract then they will be monitored in a separate but related budget, for internal CRO use. If the client has agreed these activities are part of the contract, they will be included in the main deliverable budget.

7. Interviews – data analysis

7.1. Method

To support the conceptual thinking reported in this paper empirical research was undertaken in the form of semi-structured interviews. The focus of the research was to answer questions of a 'why?' and 'how?' nature, i.e. why are things done a certain way? Or how can the alternative approach be implemented? The use of interviews lends itself to such a focus (Soltani et al., 2005). The interviews were structured into two parts: the first part aimed to discover existing approaches. If the existing approach was the traditional fixed-price method, further questions explored the reasons for, and limitations of, managing clinical trials in this way and opinions linked to adopting the alternative variable fee/deliverable-based method described in the paper. If the current approach was consistent with the alternative method, questions explored reasons for, benefits of, and implementation issues. This adaptable format allowed issues to be explored depending upon the existing method used.

Ten interviews were conducted by telephone during April 2007. Interviews were selected through the authors' network of contacts in the industry, in particular using the Pharmaceutical Contracts Management Group. Three criteria were used to choose interviewees: (1) had extensive experience in the industry from either a Pharma or CRO perspective, (2) had in-depth knowledge of the contractual arrangements used on the clinical trials, and (3) had in-depth knowledge of how the clinical trials were project managed. The average number of years experience in the industry of the 10 people was between 18 and 19 years, with the longest experience being 27 years and the shortest being 8 years. All 10 were involved in contract and project management in their current roles. In order to obtain opinions from both the Client and contractor perspectives, potential interviewees were approached from both Pharma and CRO organisations. The sample contained eight people employed by Pharma and two by CROs. Table 4, columns 1 and 2 provide details of the interviewees; in giving each person a unique identifier (ID) the prefix P (Pharma) and C (CRO) was used to identify the type of organisation the person worked for.

The interviews were conducted by telephone. Advantages of using a telephone survey include monitoring for quality and allowing for spontaneity (Calvert and Pope, 2005), which were

regarded as important to this study. Contemporaneous notes were taken of the discussions and these notes were typed up immediately after the interview to assist in accurately interpreting responses. The first part of each interview was structured to gain an understanding of the existing type of contract used and basis for monitoring. If the interviewee described an approach that largely involved fixed-price contracts and monitoring of inputs (against milestones) the remainder of the interview focus on exploring the following issues:

- Reasons for doing it that way.
- Limitations of approach.
- Whether the alternative approach (which was described in detail to the interviewee) would address any limitations.
- The barriers to implementation of the alternative approach.
- Ways of implementing the alternative approach.

If the interviewee described an approach that involved the use of deliverables, subsequent discussion focused on:

- Reasons for doing it that way.
- Benefits of the approach.
- Difficulties in implementing the approach.
- How difficulties were overcome.
- Ways of improving the approach.

Of the 10 interviewees only two (IDS – P7 and P8), both from Pharma, described existing methods equating to the deliverable-based approach. The other eight people used a fixed-price method with payments linked to milestones and not deliverables. Three of these also described payment methods on a time basis, i.e. monthly maintenance schedules. See Table 4 for details. Content analysis was subsequently used to identify patterns in the data. This analysis was facilitated by summarising responses in a table, enabling patterns in the data both within areas and between interviewees to be identified. Again see Table 4 for details. Of course, a telephone interview survey method has its limitations (Soltani et al., 2005) and it is dangerous to generalise from small telephone surveys (Matthing et al., 2006); therefore the findings discussed below need to be treated with caution, requiring further research to validate the data.

7.2. Results

7.2.1. Existing approach – fixed price, NOT deliverable-based

7.2.1.1. Reasons for taking approach. Historical reasons were cited by four of the eight interviewees (P1, P2, P4 and C1). In essence, this was the way it had always been done and hence it was 'familiar' (P4). A second reason was convenience, cited by three people (P1, P3 and P4), which was explained by P1 'there is not enough time to consider alternatives' and P3 'there is a lack of resource to monitor CRO'. Two Pharma, P5 and P6, described how the approach was an attempt to put some of the risk responsibility (for not overrunning the budget) on the CRO, though the reality of the situation was perhaps reflected in the comments of one of the CRO, C2: 'we encourage the sponsor to go for a fixed unit price contract as it is more flexible and facilitates the inevitable changes you experience'. These comments are at odds with the desire of a sponsor (P6) to use such contracts to make 'budgets more predictable' and highlights how such differences lay the seed for future conflict.

7.2.1.2. Limitations. All interviewees identified some limitations, with a confirmation from P1 that it led to misalignment of goals: 'CROs are there to increase their margin. It creates a lot of suspicion and conflict.' P4's comments confirmed the likelihood of such conflict as 'contract modifications are expected and accepted'. Other limitations include: no real link to what is delivered (P2), ineffective monitoring (P3, C1 and C2), no relation to the real risk issues (P5) and the approach does not fit all studies (P6).

7.2.1.3. Would alternative approach address limitations? Five people believed the alternative approach outlined in this paper would address the limitations, one person concurred with the proviso of guide budgets being developed, one was unsure and one did not know. Three people highlighted possible issues if the alternative approach was adopted: assuring the accuracy of CRO timesheets (P1 and P4), adhering to budgetary needs of other departments (P6) and of investors (P5).

7.2.1.4. Barriers to implementation of alternative approach. The key barrier identified was resistance from a key stakeholder. The most frequently mentioned – by three Pharma and both CRO – was finance departments (P2, P4, P6, C1

Table 4. Summary of interviews with pharma and CRO

ID	Job title and years of experience in projects/contracts	Current approach – fixed price NOT deliverable-based	Why done that way	Limitations of current approach	Would alternative approach address limitations	Barriers to implementation of alternative approach	How alternative approach best implemented
P1	Manager of European contracts and outsourcing 8 years experience	Fixed price with milestone payment schedule – progress monitored on completion of milestones	Historical and convenient for CROs – not enough time to consider alternatives	Non-alignment of goals – CROs are there to increase their margin. Creates a lot of suspicion and conflict	Yes – but it would create a problem – assurance over the accuracy of CRO time sheets	CRO would not like it. Not enough time to implement it as own management imposes tight deadlines to get studies started	Internal finance group is already on board. Need the time to persuade our vendors. Need tracking by EVA
P2	Clinical operations section head 17 years	Fixed Unit Price	Evolution and it works – although there is room for improvement	Defining units, no real link to deliverables e.g. monitoring visit is used as a unit	With guide budgets – yes	Finance group need a number for the project cost – would be unhappy about variable price. Getting CRO to cut margins	Business case emphasising the benefits
P3	Head of contracts management 16 years	Fixed unit priced and fixed with milestones	Lack of resource to monitor CRO – fixed unit priced/ milestones gives a rough actual v planned	Still manage to micro-manage despite the lack of resource	Probably yes	Family owned firm resistant to change	Start with small pilot study
P4	Specialist contract management 15 years	Mainly fixed – monthly maintenance payments with other payments on deliverables like pages in house plus some payments on milestones	Fixed Unit Price is driven by the U.S. arm of the company. In Europe fixed priced is looked on as convenient and familiar	The number of units is still fixed. Contract modifications are expected and accepted. Defining units can be difficult	Yes – but it may create other problems like accuracy of time sheets completed	Senior Management, Finance (would perceive a variable contract as an open cheque) and CRO resistance	Need well-researched case, with successful examples followed by a small pilot study

Table 4. (Contd.)

ID	Job title and years of experience in projects/contracts	Current approach – fixed price NOT deliverable-based	Why done that way	Limitations of current approach	Would alternative approach address limitations	Barriers to implementation of alternative approach	How alternative approach best implemented
P5	Project development director 23 years	Fixed price – each contract outsourced individually – tactical Milestone payments 20 % up front 10 – 20% retained as a final payment. Milestones are deliverable where possible	Financial constraints from investors – keen on limiting financial risk. Work with other Pharma companies on joint development programmes so fixed price is easier – no need to ask co-development partner for extra budget. Easier for multiple service providers	The level of the financial contingency added by the CRO is unknown and not necessarily related to project risk	Yes but investor would look on a budget with no financial cap as weak	Investor resistance	No real restriction on implementing this. Need monitoring method – EVA
P6	Head of global strategic pharma development services 13 years	Fixed priced – milestone payment schedule	To pass on some of the responsibility of doing the trial to the CRO. To increase the commitment of the CRO – to make the budgets more predictable and to make sure that the CRO uses a realistic budget	Not entirely successful. Approach does not fit all studies – i.e. oncology. Projects are changeable so the budget changes i.e. not really fixed. Difficult to get the balance between flexibility and control	Possibly. There could be issues around budgeting whether it met the budgeting needs of other business groups within the company	Not too many – if recommended it would be implemented. Could be issue with financial reporting needs – but should be surmountable	Pilot study – already thinking of moving away from 'one size fits all'
C1	Regional director 27 years	Fixed price – milestone payment schedule and usually a monthly maintenance payment	Historical – tried to move to milestones that are closer together with the aim of payment schedules being cash neutral	Nothing to drive the project – not very inventive – little or no feedback	Yes	Senior management, finance and sales – whose bonus payments are linked to bid price	Better pricing and resourcing model. Sell to senior management and finance

C2	Director business development 24 years	Fixed price (milestones) or fixed unit priced	Encourage sponsor to go for fixed unit price because more flexible and facilitates the inevitable changes you experience	Tracking systems are poor – so often do not know whether an individual project is profitable	Don't know	Difficulties in finance group – they like clearly defined budgets	If it was driven by the sponsor would do it
P7	Director clinical research 21 years	Phase 1 – Fixed Unit Priced but for other phases – Variable Time and Materials	Flexibility – ability to quickly respond to project changes	Flexibility – but don't objectively do anything to measure success of this approach – difficult to measure	None – small company, so have autonomy	N/A	Application of project monitoring techniques i.e. EVA
P8	Director – outsourcing and contract management 23 years	Only just started – 6 weeks in new job – but will use deliverable based contracts	The best way – fair	Flexibility. Reduced transaction costs	CRO resistance	Too soon to say	Better definitions of quality and quality/time payment gates

Pharma, Pharmaceutical company; CRO, clinical research organisation.

and C2). The common theme was finance departments like the certainty of fixed-price contracts (even if the reality is that the budget will not be adhered to)! Other groups mentioned were: CROs (mentioned by a Pharma – P2), the whole organisation (a family owned firm resistant to change – P3), Senior Management (P4 and C1), Investors (P5) and Sales (whose bonuses are linked to bid price – C1).

7.2.1.5. How would alternative approach be best implemented? Four people (P1, P2, P4 and C1) stated the importance of selling the approach to resistant stakeholders, through stating a clear business case (P2) and examples of successful implementations (P4). Running a small pilot study of the new approach was suggested by three people (P3, P4 and P6). One of the CRO stated they would adopt it if driven by the Pharma.

7.2.2. Existing approach – deliverable-based
7.2.2.1. Reasons for taking that approach. The two reasons highlighted were flexibility (P7) and fairness (P8).

7.2.2.2. Benefits. Both people identified flexibility as the main benefit and P8 described how the approach reduced transaction costs. One issue that arose is how to objectively measure the benefits, mentioned by P7, and this issue would need to be considered carefully in any further research to assess the effectiveness of the approach.

7.2.2.3. Difficulties. Resistance from CROs was confirmed by P8.

7.2.2.4. How difficulties were overcome. As P8 had only recently adopted the approach it was too soon to say how CRO was overcome.

7.2.2.5. How alternative approach can be improved. Two improvements were identified: better project management monitoring techniques, such as Earned Value Analysis (P7) and better definitions of quality, which would be linked to payment schedules (P8).

To summarise, key findings from the interviews are:

- Confirms prevalence and limitations of fixed-price, time-based approaches.
- Shows willingness of Pharma and CRO to try alternative approach – initially through small pilots.

- Indicates that already some movement towards deliverable-based approach, which is being driven by Pharma.
- Highlights that resistance to new approach from key groups, in particular finance departments, would need to be overcome through selling of the benefits.

8. Summary and areas for further work

In this paper we have presented an approach to the management of clinical trial projects that is based on the concept of Product-Based Planning. The approach aims to address deficiencies in current practice by emphasising the outputs from the project, aligning the different perspectives of Pharma/CRO, and monitoring project management in terms of outputs. This is done through the creation of a deliverable budget that is subsequently mapped onto the CRO activity schedule. Monitoring of progress and payment for performance can then be based on the outputs (deliverables) rather than the inputs or work (activities/milestones). The method also provides a new way of treating project management in clinical trials. Rather than viewing project management as a time-driven support function, project management is factored into the deliverables budget, allowing project management performance to be monitored against outputs (del0iverables) rather than inputs (time spent).

The work carried out to date is primarily conceptual in nature and, although a survey of practitioners has been undertaken, more extensive empirical study is required to investigate the impact of utilising the approach on clinical trials. A fruitful avenue of investigation may well be a comprehensive comparative research, within one organisation, that proofs the advantage of the approach in the pharmaceutical environment. Furthermore, a comparative research could be undertaken within several organisations. As highlighted by the interview data, this could focus on the results of a pilot study of the alternative approach.

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