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Financial Accruals for Clinical Trials – A Primer

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Just as Stonehenge and the Bermuda Triangle have puzzled the masses over the years, so too have clinical trial financial accruals baffled generations of drug developers. Intelligent minds capable of understanding the mysteries of disease epidemiology — or even the mysteries of the U.S. Food and Drug Administration (FDA) — can go numb when confronted with the task of generating an expense estimate without the benefit of an invoice. Fortunately, the situation is not as dark as it seems. With a bit of understanding and insight, estimating a clinical trial financial accrual can be a relatively benign process.

Important Accrual Terms and Definitions

An accrual, or "accrued expense," is simply an estimate of all billable work performed on your company's behalf over a given time period (usually a month or a quarter). Put another way, you are trying to estimate the total amount of bills/invoices you will ultimately receive for work carried out within a particular period. This task is required because companies generally report expenses on an accrual basis rather than on a cash basis. Cash basis accounting/expensing is not the standard methodology because it does not accurately reflect the true financial picture. For example, suppose I hire a gardener to mow my lawn for $50. He performs the job in January, but I do not pay him until March. Under accrual-basis accounting, I would record the US$50 expense in January because that is when the gardener performed the billable work. Under cash-basis accounting, I would record the $50 expense in March, because that is when I paid the gardener. Recording the expense on an accrual basis would better reflect the financial situation, since the period the expense is recorded matches the period when the expense was incurred. Furthermore, I cannot manipulate or distort my reported expense simply by refraining from paying my gardener for a month or 10.

Another important term to understand is "accrued liability," which is the total accrued expenses to date minus the total invoices paid to date. Put simply, it is the estimated amount owed at a given point in time. While the accrued expense sits within the company's income statement — also called profit and loss statement (P&L) — the accrued liability sits in the company's balance sheet.

Perhaps one of the most significant concepts to take away from this discussion is that, in the world of accruals, invoices have no effect on your specified expenses; invoices affect the specified accrued liability only. In summary, accrued expense is defined as how much expense you have incurred over a given period, and accrued liability is how much you owe on all of your expenses up to a certain point in time.

Why Understanding Accruals Is Important to a Drug Developer

The most fundamental reason why drug developers need to understand accruals is simply that their respective companies need their help to generate accurate financial statements. Clinical trials expense is one of the biggest expense categories for biopharmaceutical companies. Because accrual estimates play a huge part in a company's declared expenses, it is essential that the development staff assist the finance department in generating and maintaining clinical trial accrual models. Faulty accrual models can result in materially inaccurate expense estimates, and the ramifications of this can range from an external

auditor rebuke (which embarrasses the Chief Financial Officer (CFO) in the eyes of the Board of Directors) to a required restatement of a company's public financial statements (which leads to loss of company reputation, a plunging stock price, and, possibly, loss of jobs for the firm's officers and those who serve them). In addition to the potential accounting repercussions, a lack of accrual understanding may have a tangible effect on budgeting/forecasting accuracy. One common cause of budget variance is that, while actual expenses are accounted for on an accrual basis, the budget is projected on a cash basis, i.e., based on expected invoice payments. For example, suppose that over the next four months a clinical trial is expected to incur $1 million in expense, for which a $1 million invoice will be received and paid during the fourth month. If the budget is cash-based, there will be $0 budgeted for months one, two and three, and $1 million budgeted in month four. However, the expenses are accrued at $250K per month for each of the four months (assuming a straight-line accrual). While the year-to-date variance after month four looks fine, each monthly variance — as well as the year-to-date variance prior to month four — could cause confusion and consternation.

The Challenge of Accruing for Clinical Trials

There are two primary reasons why accruing expenses for clinical trials is challenging. The first is that there are typically large numbers of vendors and billing entities for a given trial. The second is that the nature of some entities' expenses are often complex (e.g., expenses associated with contract research organizations (CROs)). For example, a large phase III trial might consist of hundreds of investigator sites, multiple CROs, central laboratories, site management organizations (SMOs), and many others, all of which must be accrued for in every period. Additionally, to appropriately accrue for CRO expense, one must take into account each of its various functions: project management, site monitoring, data management, and so forth.

Because of the volume and complexity of the task, companies generally use software-based financial models to estimate clinical trial accruals. The more elaborate the model, the greater the potential accuracy of the accrual, but also the more painful the monthly information-gathering and data-input process. For instance, if your CRO accrual model utilizes enrolled subjects as the only cost driver, that would require only minimal input data, but it would also be less precise than if the model required multiple cost-driving inputs, such as enrolled subjects, site initiations, site visits, and case report forms (CRFs) cleaned. The higher the number of required data inputs, the greater the likelihood your clinical trial managers will run off in horror when they see the finance team approach. Therefore, it is important to design your accrual models with the proper balance of accuracy vs. information-gathering burden for your particular company. The factors to consider when determining this balance include the size of your company, the manpower available, the reporting capabilities of your clinical trial management system, and the number and complexity of your clinical trials.

Clinical Trial Accrual Methodologies

First, it is important to note that there is no standard accrual methodology for clinical trials; different companies accrue in different ways. Nevertheless, analyzing some common accrual methodologies and would be useful, particularly for the two biggest expense categories: CRO fees and investigator grants.

Contract Research Organization Expenses

For CRO expenses, the simplest accrual methodology would be the straight-line method. To accrue on a straight-line basis, one takes the total CRO contract amount and divides this number by the total estimated trial duration in months, i.e., if a $50 million CRO contract is expected to last for 25 months, one would simply accrue $2 million per month over 25 months. Of course, like most things that seem too good to be true, there are potential pitfalls to this methodology. First, straight-line accruals can cause a disconnect between the amount expensed and the actual amount of activities performed. For instance, if actual trial activity is proceeding much more slowly than planned, accrued expenses will give the false impression that trial is moving along swimmingly. Also, you may have difficulty getting your company's external auditors to buy into straight-line accruals, especially if your company is relatively small and/or has a low number of clinical trials.

Another CRO accrual methodology allocates expenses based on units of work activity. A typical CRO contract provides details of the specific work units that make up the contract's total cost, i.e., number of monitoring visits, number of CRFs cleaned, etc. While one could, theoretically, develop a model that incorporates each and every specified work unit, the level of detail would be onerous. A preferable way might be to categorize all of the unit costs into larger, more manageable buckets. These cost buckets would then be allocated by a predetermined cost driver. For example, one could create a "site-related cost bucket" for accruing costs based on the number of sites initiated, a "subject-related cost bucket" for accruing costs based on number of subjects enrolled each month, and so forth. The more cost buckets you utilize in your model, the more precise your monthly accruals becomes, assuming your drivers are correct and your data inputs are accurate and timely.

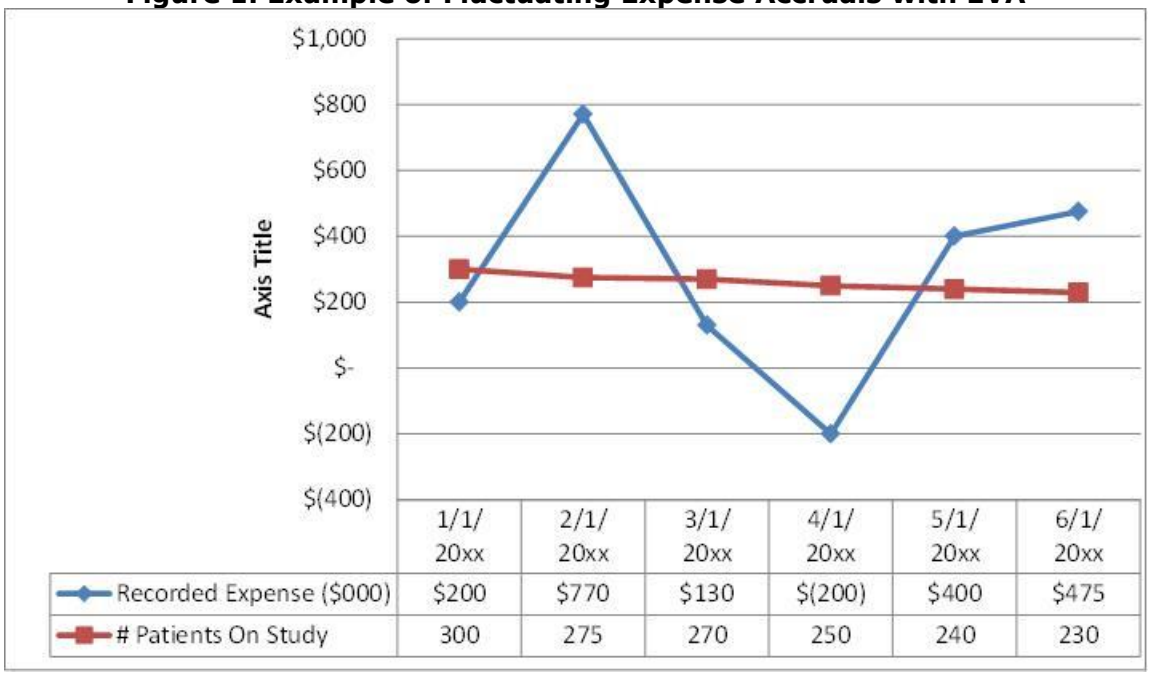
Earned Value Analysis (EVA) is an accrual methodology that has become increasingly popular to accrue CRO and other service provider expenses. EVA attempts to measure the progress of a trial and compare it to the funds expended. For instance, an EVA report might show that 60% of the budgeted costs for site monitoring has been expended, but only 40% has been completed. The CRO typically provides a timely monthly EVA report that takes into account a clinical trial's timeline, scope of planned activity, and associated budgets. The monthly invoice typically arrives later and might include charges for activities in previous months and exclude charges for activities in this month that have not been finalized. In terms of financial accruals, the report's tracking of work units and associated costs generally provides a very good way to track incurred expenses to date.

The big advantages of using EVA as a financial accrual tool include: relative ease and timeliness of data collection (you simply obtain and record what's in the report), theoretical completeness of accounting for activities to be accrued, and the comfort of being able to easily explain your accrued expense and tie it to an outside source document. The disadvantages include: incremental cost for the report; having to wait for the CRO to provide the EVA report before Finance & Accounting can close the books, and — most significantly — uncertain data quality, since EVA reports are based on estimates. Figure 1 shows the CRO expense trend for a large Phase 3 trial, based on actual EVA reports. Although study activity and subjects on study were stable over the period, EVA-generated expenses fluctuated from almost $800K in February to negative $200K in April, and back to $400K in May, which made no sense. The point is that, although EVA may be a good alternative, it may not be the accruals panacea that some would hope and, like all other methodologies, should be vetted for feasibility of design and plausibility of results.

Investigator Grants Expenses

Investigator grant accruals are primarily driven by two primary variables: the number of subjects enrolled for a given period and the cost of subject visits, also known as "cycle

Figure 1. Example of Fluctuating Expense Accruals with EVA



costs" (with one visit per cycle). If your company does not have a high number of trials, it might be feasible to set up investigator grant models in very granular form: by individual site, individual subject, and specific visit (see Table 1). The biggest advantage of this methodology is that you cannot get more precise in a meaningful way. The disadvantage is that gathering site-specific subject enrollment and visit data on a monthly basis might be challenging, and the difficulty increases as the number and size of trials increase.

Table 1. Example of Granular Accrual Model

(USD$)	Screen/ Baseline	Day 1	Week 4	Week 6	Week 8	Subsequent Treat	Subsequent Treat	30-day FU	Total (to date)
Dr. Lieberburg (Budget)	**2,475**	**825**	**775**	**675**	**2,775**	**1,775**	**1,775**	**259**	
Pt. ABC	x	x	x	x	x				
Pt. DEF	x	x							
Pt. GHI	x	x	x	x					
Total $	**7,425**	**2,475**	**1,550**	**1,350**	**2,775**	-	-	-	**15,575**
Month 1 Expense	11,450								
Month 2 Expense	4,125								
Dr. Morrisey (Budget)	**2,000**	**750**	**700**	**600**	**2,000**	**1,500**	**1,500**	**300**	
Pt. IOU	x	x	x	x	x				
Pt. UPS	x	x							
Pt. FBI	x	x	x						
Total $	**6,000**	**2,250**	**1,400**	**600**	**2,000**	-	-	-	**12,250**
Month 1 $	9,650								
Month 2 $	2,600								
Dr. Carberry (Budget)	**3,000**	**1,000**	**1,100**	**750**	**3,000**	**1,525**	**1,525**	**325**	
Pt. HBO	x	x	x	x	x				
Pt. SHO	x	x							
Pt. TBS	x	x	x						
Total $	**9,000**	**3,000**	**2,200**	**750**	**3,000**	-	-	-	**17,950**
Month 1 $	14,200								
Month 2 $	3,750								

If a granular model is not feasible, you can develop a consolidated model that combines investigator grant costs for all enrolled and/or anticipated sites for a trial into one aggregate model, as if there were only one mega-site. You first come up with theoretical "average" cycle costs for your trial. All subjects who enroll, regardless of site, are incorporated into this one comprehensive model. If the average cycle costs shift over time (for instance, due to higher-cost sites enrolling a greater proportion of subjects than lower-cost sites, or due to adding additional sites that cost more or less than the average), you adjust the model accordingly (see Table 2). In this model, every subject enrolled in the trial, regardless of

Table 2. Example of Consolidated Accrual Model

(USD$)	Dr. John	Dr. Paul	Dr. George	Dr. Ringo	Average (Use to Accrue)
# Patients	25	25	25	25	100
% Weighing	25%	25%	25%	25%	100%
Cycle / month 1	10,000	9,000	12,000	10,000	10,250
Cycle / month 2	5,000	4,000	4,500	3,500	4,250
Cycle / month 3	5,000	4,000	4,500	3,500	4,250
Cycle / month 4	5,000	4,000	4,500	3,500	4,250
Cycle / month 5	5,000	4,000	4,500	3,500	4,250
Cycle / month 6	5,000	4,000	4,500	3,500	4,250
Total Variable Costs	**35,000**	**29,000**	**34,500**	**27,500**	**31,500**
Fixed Costs*	1,000	1,250	1,000	900	1,038
Grand Total	**36,000**	**30,250**	**35,500**	**28,400**	**32,538**

* "Fixed Costs" include set-up costs & other requested site fees

site, will be accrued in the same manner, i.e., $10,250 after month one, $4,250 after month two, and so forth. Because you cannot track individual subjects, you must assume that all subjects go through all specified cycles (subject to a standard drop-out rate). The biggest advantage of a consolidated model is that gathering model inputs is much easier than with a granular model, especially if you have very big trials and/or a high number of trials. The biggest disadvantage is that the assumptions built into the model might not reflect reality. One way to mitigate this risk is to periodically adjust the cost and duration assumptions according to the latest available information. For example, if you notice that Dr. Ringo is enrolling the majority of the subjects in the trial, and Dr. Ringo's grant costs are lower than average, you would adjust average cycle costs down.

Closing the Accrual Loop at the End of the Trial

As you may have realized by now, accrual models are based on many assumptions and, as such, are imperfect. The goal is to generate and continually tune the models to maximize accuracy, within practical limits. The only time you can truly reconcile your accrued costs with your actual costs is at the end of a study, when you have received all of your trial-related invoices. At this point, you will find yourself in one of three situations:

- You have under-accrued for your trial, i.e., your model accrued less than the trial's total invoices (see Figure 2 below).
- You have over-accrued for your trial, i.e., your model accrued more cost than the trial's total invoices (see Figure 3 below).

- You are in accrual nirvana, i.e., your model's accrued costs exactly match your total invoices (see Figure 4 below).

If you are in an under-accrual situation, your finance department will book an additional expense to make up the shortfall. If you are in an over-accrual situation, your finance department will book a "reversal" (or "credit") entry to reverse out the surplus. If you are in an ideal accrual situation, your finance department will buy you lunch.

Conclusion

There is no single approach for accruing clinical trial costs, although every approach is some variation of those discussed above. The number, size and complexity of your company's trials, the personnel and information resources available, and your company's finance culture should determine the scope and complexity of the approach you ultimately decide to use.

Understanding and having the ability to develop effective models for clinical trials accruals are essential elements of every biopharmaceutical firm's drug development program. Not only does the finance staff need to be savvy on effective methods of expense accruals, but the development staff should also be savvy. Although not immediately intuitive to many people, financial accruals need not be overly complicated or a difficult.

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Figure 2. Example of Under-Accrual

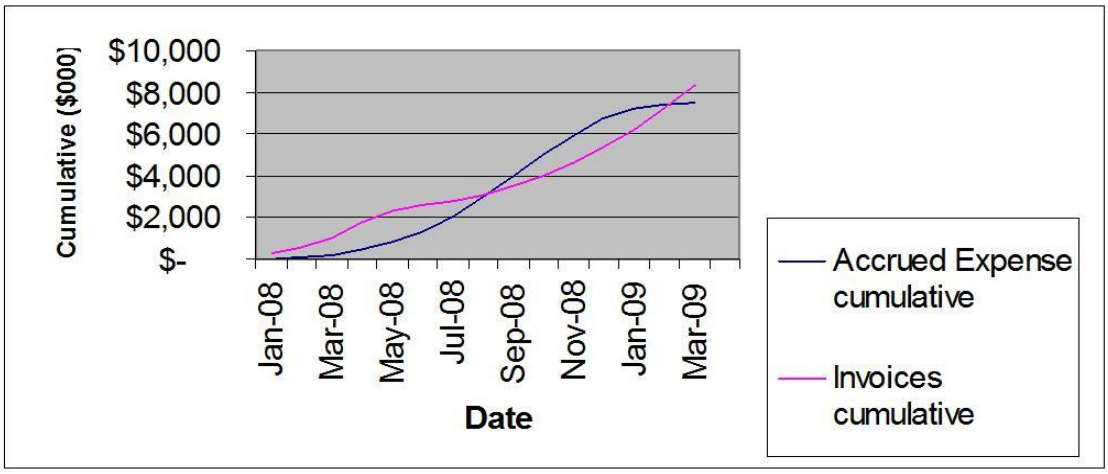

Figure 3. Example of Over-Accrual

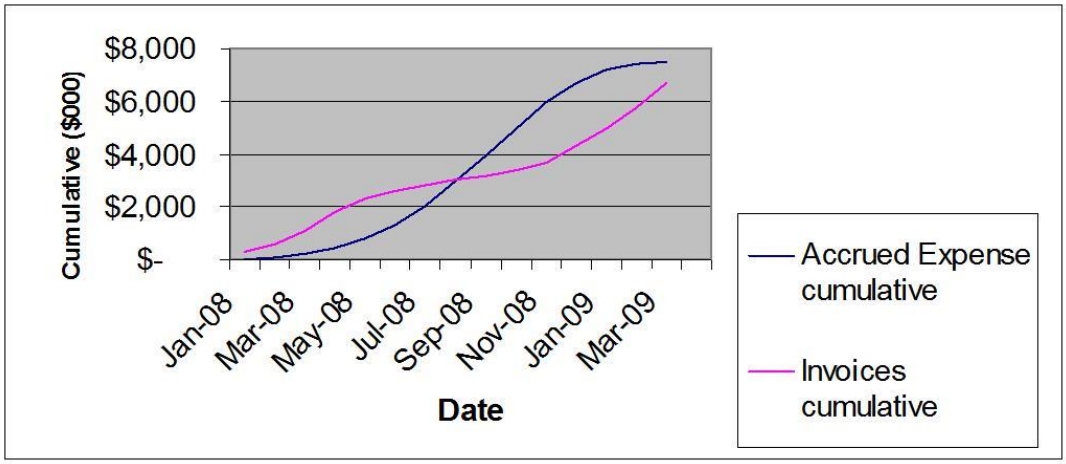

Figure 4. Example of Accrual Nirvana