CLINICAL TRIAL PLANNING

PERFORMANCE
BLUEPRINT

APPLICATION BRIEF

A WEB-BASED
PERFORMANCE MANAGEMENT APPLICATION

COGNOS | INNOVATION CENTER
for Performance Management™

INTRODUCTION

This *Clinical Trial Performance Blueprint* application brief demonstrates a Web-based, Cognos 8 Planning application that a pharmaceutical R&D team can use to optimize expense forecasting and tracking. The goal is to increase reporting accuracy, reduce resource costs, and increase drug approval time.

Implementing this process will enable finance and clinical trial management organizations to better anticipate resource requirements and expenses in order to meet FDA filing requirements. Through the use of an approach driven by plan enrollment, organizations can become more efficient in the planning, tracking, and resource allocation of these projects.

OVERVIEW

The importance of managing the clinical trial process can not be understated. Currently, pharmaceutical company budgets exceed $400 million in total expenses, which accounts for 37 percent of total research and development costs (according to *Cutting Edge Information*). While trials costs are increasing, so is the complexity of the process, as it expands beyond finance to include both internal and external clinical development functions. Clearly, a more proactive approach is required—one that better matches the reality of clinical trials expense generation. The *Cognos Clinical Trial Performance Blueprint* is designed to help financial professionals and clinical trial managers better forecast, plan, and manage trial expenditures through an activity-based approach that matches expenses to activities, in contrast to time-based accrual methods. Through a review of fixed and variable cost-driven enrollments, clinical trial expense models can be developed to streamline and simplify the bottom-up forecasting process by increasing plan accuracy and timeliness to help make better resource allocation decisions.

MODEL OBJECTIVES

The *Cognos Clinical Trial Performance Blueprint*:

- Increases visibility into the impact of patient enrollment.
- Enhances decision-making through understanding of performance differences between sites and across studies.
- Enables real-time consolidation of the entire portfolio forecast.
- Creates forecasts linked to and driven by underlying protocol design data.
- Provides version, scenario, and *what-if* analysis.
- Updates and recalculates for actual spend activity.
- Eliminates the need for error-prone Excel spreadsheets.

The models and processes outlined in this document represent a generic best practice and are fully flexible to meet the specific needs and requirements of any global bio-pharma company.

MODEL USERS

Users of the *Cognos Clinical Trial Performance Blueprint* within finance and R & D might include:

Department		
Finance		**Roles and Responsibilities**
	Director of Planning and Forecasting	Responsible for the forecasting process. Includes setting budgets for each protocol.
R&D		
	Clinical Trial Manager	Responsible for managing a specific trial.
	Therapeutic Program Manager	Responsible for managing therapeutic area trials.
Senior Management		
	Head of Development	Responsible for overall development.

KEY COGNOS PLANNING BENEFITS

Cognos 8 Planning software delivers key benefits to the clinical trial process:

- Optimized resource allocation.
- Increased visibility into enrollment and accompanying expense tracking of clinical trials.
- Simplified gathering and validation of clinical trial enrollment data.
- Flexible model development adaptable to unique business processes.
- High-participation work flow and Web-based deployment for data collection and consolidation.
- Real-time workflow to evaluate planning process status.
- Real-time consolidation for an instant global view of sample distribution.
- Real-time, browser-based calculations immediate results.
- Single operational system usable across multiple products and sales forces.
- Scalable architecture with proven deployments to thousands of users.
- Support for SAP, Oracle, and other ERP systems.

Planning Process Inputs

The clinical trial planning process manages a number of inputs by project phase over time. These inputs (or influences) include protocol assumptions, fixed costs (central and site), patient retention and recruitment, and organizational targets. Each of these inputs provides data that drives clinical trial performance. (See figure 1).

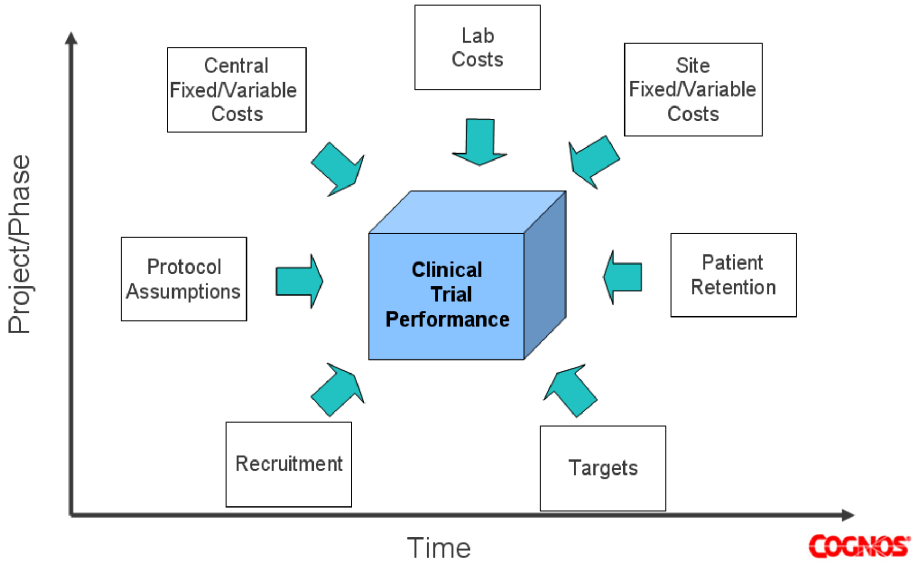


Figure 1: Inputs to the Planning Process

These inputs must be analyzed to answer such questions as:

- What trials are not meeting their enrollment requirements?
- If requirements aren't met, what must we change (enrollment expectations, advertisement, number of administrators, number of clinical sites, etc.)?
- If we were to secure more resources, how would we allocate them?

The more readily companies can answer these questions, the more effectively they can distribute resources. Common knowledge? Yes—nonetheless, most companies struggle to build an effective planning model based on Clinical Trial Management (CTM) systems along with tools like Microsoft Excel. There are many reasons why: Data is difficult to access or understand; spreadsheets strain under the weight of complex calculations; input from various clinical trial managers, laboratories, CROs, and financial analysts comes in different formats, at different times, or at irregular intervals.

To simplify the problem, most companies use an accrual method to track expenses, an approach flawed by inherent latency in the billing process. Driver-based planning and modeling present a solution. Using a driver-based model, pharmaceutical companies ensure that they are allocating the right mix of resources in the right amount to ensure clinical trials meet their filing dates. A driver-based approach:

- Facilitates communication across all stakeholders in the clinical trial process.
- Provides a standardized corporate rationale for clinical trial planning.
- Provides a consolidated view of clinical trials across the organization.
- Enables resources to be transferred to under-performing clinical trials to insure completion.
- Accommodates the input of thousands of field-level reps.
- Offers senior executives visibility into overall clinical trial spend.

DRIVER-BASED PLANNING

Finance experts tend to agree that conventional planning, budgeting, and forecasting methods involve too much detail and too little focus on the key metrics that drive expenses. Driver-based planning is based on common components that typically underlie a given expense.

The *Cognos Clinical Trial Performance Blueprint* model uses data based on a number of drivers. Driver data for clinical trial cost measures can include:

- Investigator fees
- Procedure cost
- Enrollment rate
- Investigator overhead cost
- Investigator fees (PP)
- Clinical lab fees (PP)
- Trial protocol
- Number of visits
- Patient retention percentage

The resource allocation model outlined below lets finance and clinical trial managers allocate resources to insure the success of their respective clinical trial projects. Through an operational system that both tracks changes and controls workflow, clinical trial managers can react quickly as changes are made.

The *Blueprint* model can accommodate multiple trial phases and resources allocations, which offers both internal and outsourced clinical trials a single, standardized system for resource planning and tracking, while maintaining specific assumptions for each project.

CHALLENGES TO CLINICAL TRIAL FORECASTING

Materiality and understanding drivers

As noted, clinical trials represent the biggest direct spend component in most bio-pharma companies' R&D budgets. Executing large, global Phase 3 clinical trials frequently cost more than $20 million.

It is important to be able to understand, model, and consolidate project costs at the portfolio level to run *what-if* scenarios and analyses. It is also important to understand the performance characteristics of particular sites or countries. Modeling performance data makes it easier to analyze the data and make more effective resource allocation decisions. For example:

> *"Per-patient costs for running studies in Russia are low, but patient enrollment always undershoots and we end up spending more by adding additional centers. What would be the impact of running more of the study in France where costs are higher, but patient drops are lower?"*

Complexity and process

Clinical trials managers are acutely aware of the difficulty inherent in producing robust, accurate, phased budgets and forecasts.

Payments to investigators, which typically comprise 60-80 percent of trials costs, are often made without invoice, since investigators do not issue them. Without an invoice or purchase order, deriving an accurate and timely picture from accounting systems is problematic indeed.

The *Clinical Trial Blueprint* uses patient visits as the cost driver. Data is more readily available, and often more timely than accounting systems' commitments data.

Most companies follow some of the practices outlined in the *Clinical Trial Blueprint*, but often the results are not easily shared and consolidated with other financial forecast or budget data. The result is that different departments have different sets of numbers and a lot of time is spent debating, reconciling, then re-keying data between systems.

More often than not, Microsoft Excel is used for modeling clinical trials. Traditional corporate budgeting and forecasting tools and approaches are typically too inflexible to attempt this type of driver-based algorithm. The *Cognos Clinical Trial Blueprint* represents a scalable and flexible solution that enables an entire portfolio of development projects to be modeled using the same robust approach.

Use of project management data

Bio-pharma R&D businesses are driven by projects. Traditional or clinical project management systems, whether home-grown or commercial, already contain the source data needed to build financial models. But traditional budgeting and finance applications are cost-center focused and do not take into account the multi-year project and portfolio management processes that are used to run the R&D business. They cannot or do not use this valuable data at the project level.

The *Clinical Trial Blueprint* model connects to and uses that underlying data to create robust financial forecasts and budgets that are meaningful to both project management and finance.

The key driver is patient enrollment or recruitment. The underlying algorithm uses planned and actual enrollment data, and also takes into account:

- Per-patient per-visit costs for investigator fees and labs.
- Planned drop percentages by visit by country.
- Visit occurrence relative to enrollment.

The *Blueprint* model is able to create a phased forecast based on these drivers.

Financial functionality of project management systems

Typically, commercial project management software solutions contain budgeting and forecasting as an afterthought and lack sufficient functionality to create and maintain a robust forecast.

Some common issues are:

- Inability to link-in and update the plan based on actual spend.
- Phasing based on a representative patient across all visits and not using the relative occurrence of the visits.
- Difficult integration with other financial forecasts to present a consolidated view of the overall department.
- Finance requirements such as accounting periods and foreign exchange rates are not typically supported.

THE CLINICAL TRIALS BLUEPRINT

- With the *Blueprint*'s best-in-class algorithm:
  - ✓ Patient enrollment plans used.
  - ✓ Forecast calculated by country.
  - ✓ Forecast adjusted for anticipated patient drops.
  - ✓ Variable costs driven by patient visits.
  - ✓ Per-patient per-visit costs used.
  - ✓ Relative visit occurrence used to accurately determine phasing profile for budget/forecast.
  - ✓ Fixed costs phased either by date and percentage or direct input.
  - ✓ Planned enrollment updated for actual activity linked from clinical management application or data repository.
  - ✓ Facile linking of forecast data to other R&D forecasts for consolidation into an overall R&D/divisional forecast or budget submission.
  - ✓ Costs can be modeled in either local or corporate currencies, as central (for the whole study) or country-specific (for global studies), with fixed or variable components, or any combination.
  - ✓ Full support for finance requirements such as accounting periods and multiple currencies.
- Real-time consolidation
- *What-if* and scenario planning
- Flexibility to meet changing business requirements without costly IT development.
- Models usually owned, maintained, and operated by business users.

Early-stage and concept studies

The *Clinical Trial Blueprint* works well for larger and material studies, typically Phase 2b onwards with a spend in excess of $1-2 million.

What about smaller studies and concept studies where underlying patient enrollment data is not available? The early-stage portfolio is different in nature and comprises many smaller and shorter duration projects. For this section of the portfolio the *Clinical Trial Blueprint* offers a streamlined approach that uses project start- and end-dates along with the anticipated task-level budget or forecast. All this data would be sourced from whatever project or portfolio management system is in use. The data are linked into the *Blueprint* and used as the basis for a phasing calculation.

An analyst typically has the ability to modify either dollar amounts or milestone dates to reflect additional intelligence considered at the portfolio level or as part of a goal-seeking *what-if* process. This baseline forecast is then combined with actual spend data from the accounting system to produce an updated forecast that can then be integrated with other, non-project, related data to produce an overall department-level forecast. Data from both approaches are linked together so a consolidated portfolio forecast is available in one place.

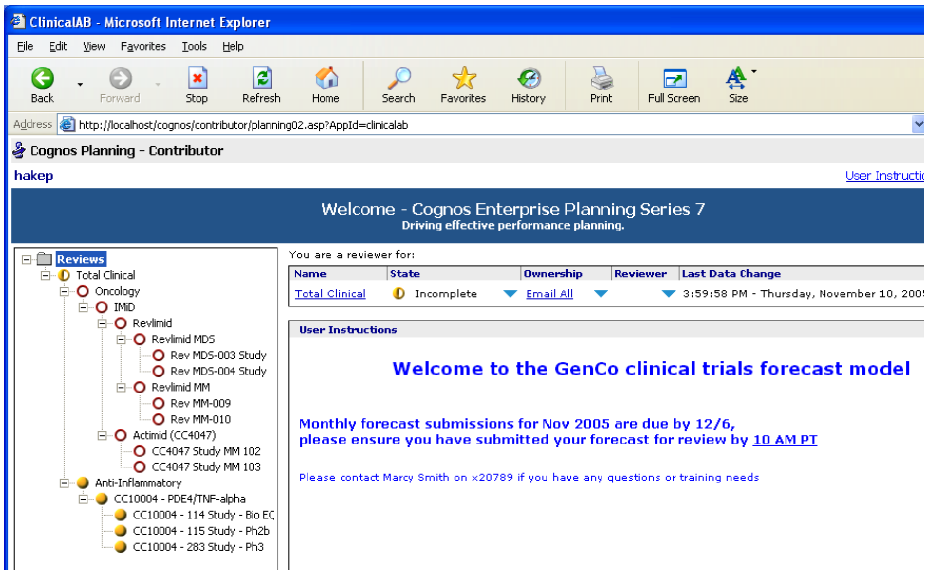
CLINICAL TRIAL BLUEPRINT DETAILS

Workflow

This example shows a typical hierarchy used to model a clinical portfolio. The example consolidates all clinical trials by *candidate* then *therapeutic area*.

- Total clinical
- Therapeutic area
- Drug candidate or compound
- Clinical trial

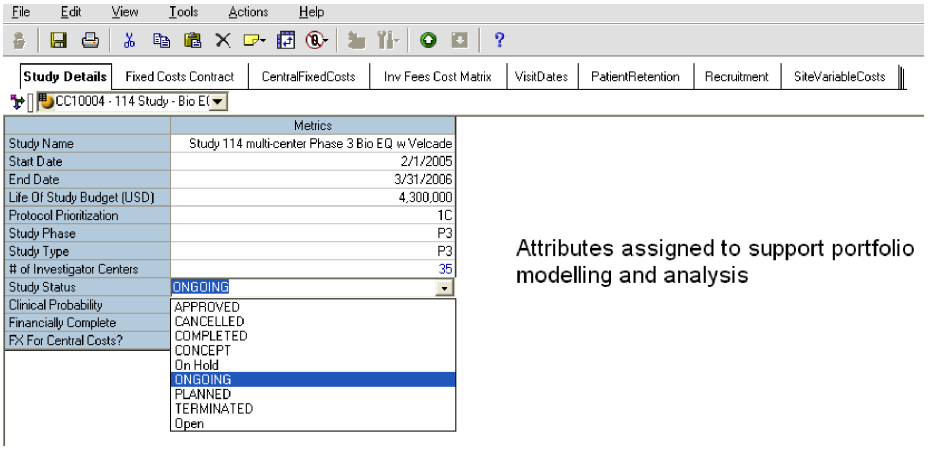
[As the business requires, there may be either more or fewer levels in the model structure. The following merely provides an example.]



Hierarchies and workflows are typically grouped by responsibility to facilitate real-time review at consolidation points. In the example above, a reviewer for the Anti-Inflammatory therapeutic area can view all studies aggregated in real time. The last saved data from the individual clinical trials below any given review level in the model structure.

The color-coded icons in the hierarchy represent different workflow statuses: *yellow* means work in progress, *red* means work not started. Using these visual indicators, a portfolio manager can get a good sense of the status of team progress.

Study Details

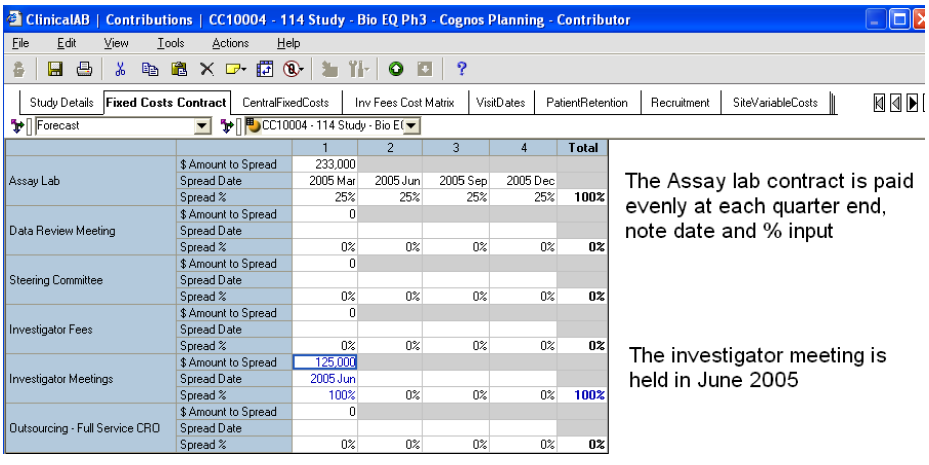


This screen is used to collect high-level attributes about the study. They can be modified or changed in the model or linked in from other systems and made *read-only* to prevent modification.

These data are used principally to support portfolio analysis. For example one may be interested in knowing the total planned spend for all CONCEPT studies, or looking at the impact of canceling a program. Picking values from drop-down menus as shown above make this form of analysis simple.

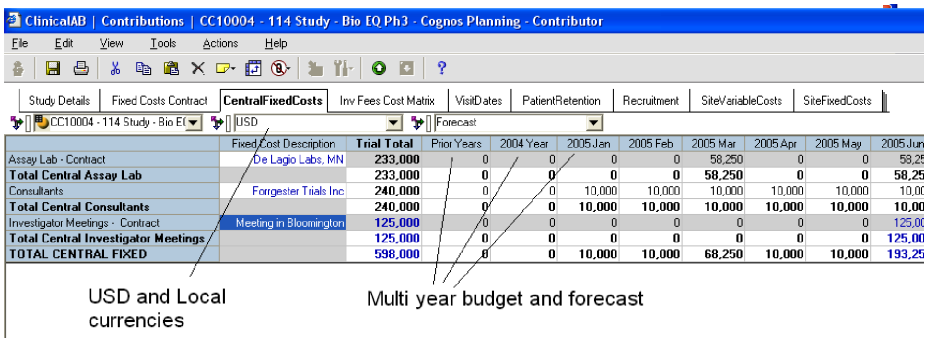
Contract Costs

For the cost components that are fixed—typically based on a contract or other estimate—and do not vary with the number of patients, date and percentage data entry makes input and subsequent changes easier.



Fixed-cost items can also be entered by direct input; it is often easier to input as above, although both methods are supported. Fixed-cost categories would be tailored to meet specific business requirements and not limited to items shown in the screens displayed here.

The *Blueprint* takes this input and performs the phasing calculation to produce the following representation of fixed costs:



Note that the model includes budget and forecast, supports both US dollars and local currencies, and is multi-year. Historic and long-term forecast data are better represented in aggregate as full-year numbers, though the *Blueprint* has flexibility to support non-standard time series. Typically, having the current and next year as months, the prior and subsequent year as a full-year figure, and all other periods as either "Prior Years" or "Future Years" makes the most sense.

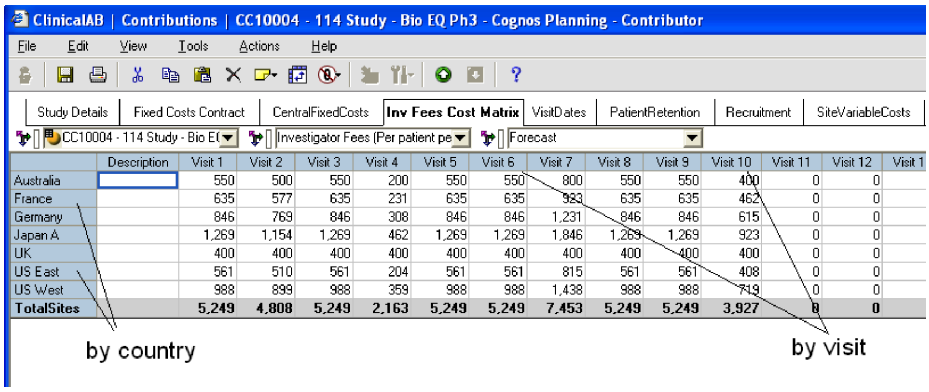
Note in the screen above: "Prior Years" is used for all data prior to 2004, "2004" as a full-year column, and "2005" broken out by month.

Variable Costs

Investigator fees are modeled based on patient enrollment and the underlying protocol design. There are three components, and each is represented in a different screen in the *Blueprint*: Investigator Fees – Cost Matrix, Visit Dates, and Patient Retention.

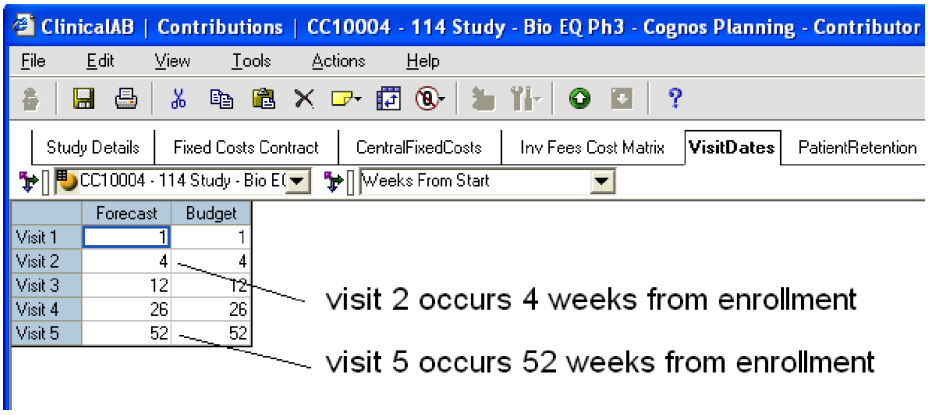
Investigator Fees Cost Matrix

Per-patient per-visit costs are derived from the protocol design and loaded by country and by visit.



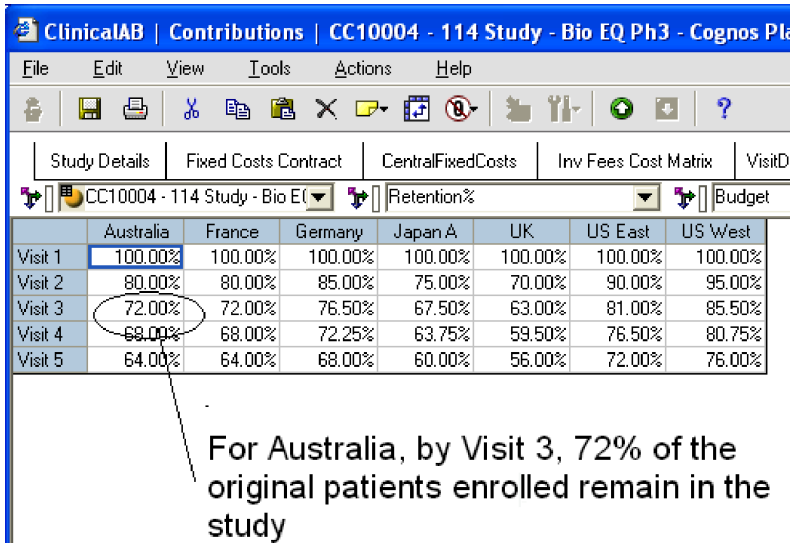
Visit Dates

Visit dates represent the relative occurrence of a visit from enrollment. These data enable a more accurate phasing calculation, by accounting for different costs for each visit and the timing of when those costs are incurred.



Patient Retention

Because of its large impact, patient drop-outs from the study must be included in any forecasting model. The *Blueprint* uses cumulative percentages to model the patients remaining in a study at each visit and by country.

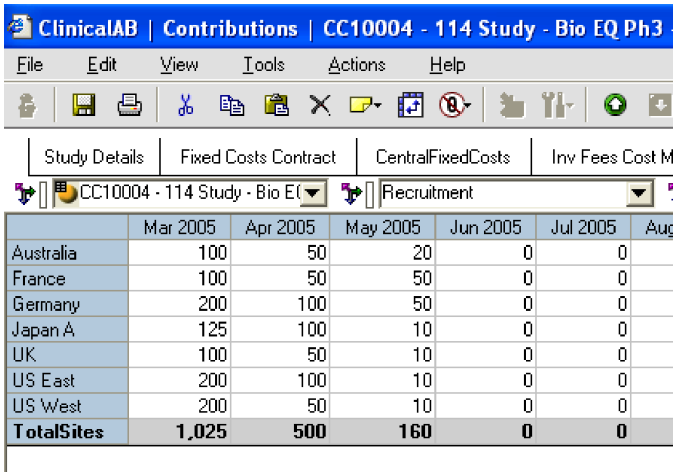


	Australia	France	Germany	Japan A	UK	US East	US West
Visit 1	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%
Visit 2	80.00%	80.00%	85.00%	75.00%	70.00%	90.00%	95.00%
Visit 3	72.00%	72.00%	76.50%	67.50%	63.00%	81.00%	85.50%
Visit 4	68.00%	68.00%	72.25%	63.75%	59.50%	76.50%	80.75%
Visit 5	64.00%	64.00%	68.00%	60.00%	56.00%	72.00%	76.00%

Recruitment

Patient recruitment is loaded by country and by month. The *Blueprint* has the flexibility to model very long studies and recognizes that enrollment for longer duration studies may have begun several years in the past.

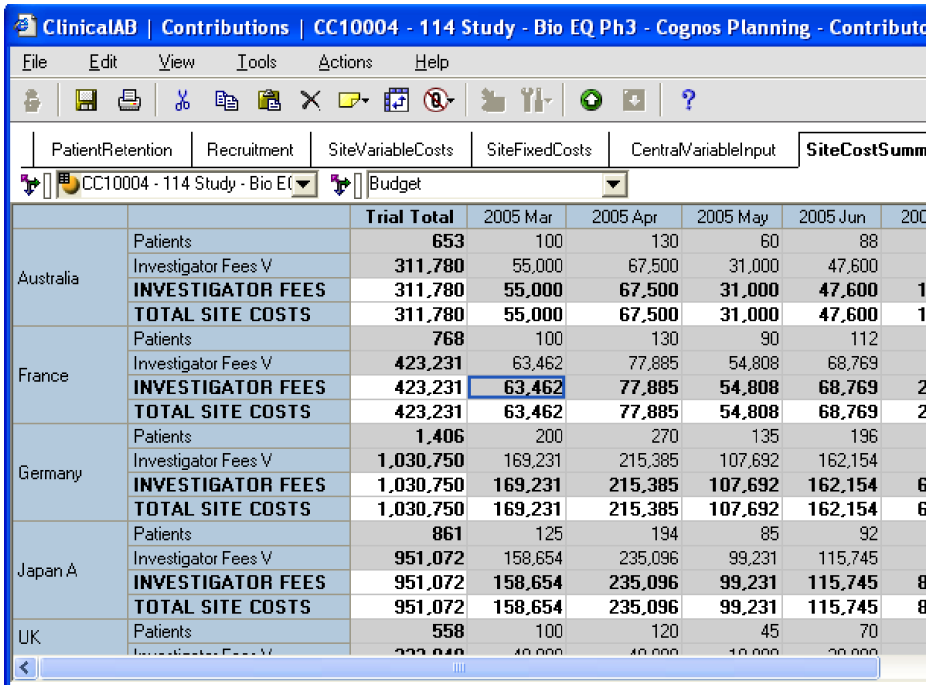
The comparison and analysis of recruitment forecasts against budgets is key to understanding clinical performance. It is simplified by having the data in this format and structure.



	Mar 2005	Apr 2005	May 2005	Jun 2005	Jul 2005	Aug
Australia	100	50	20	0	0	
France	100	50	50	0	0	
Germany	200	100	50	0	0	
Japan A	125	100	10	0	0	
UK	100	50	10	0	0	
US East	200	100	10	0	0	
US West	200	50	10	0	0	
TotalSites	**1,025**	**500**	**160**	**0**	**0**	

Site Cost Summary

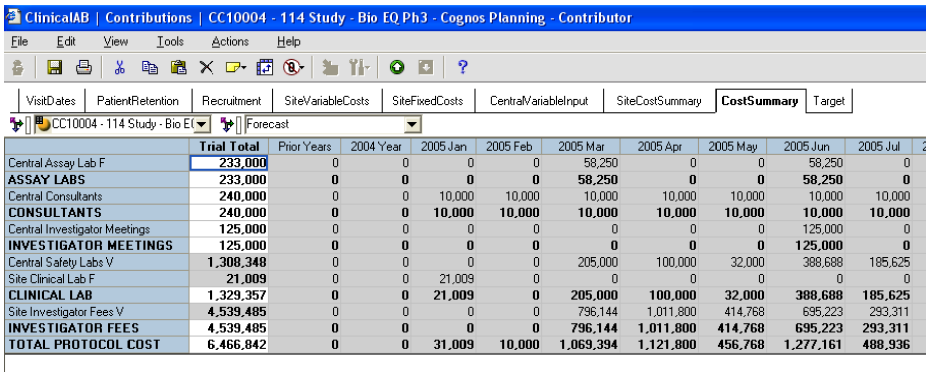
The *Blueprint* algorithm takes the driver data above and calculates a rolling forecast by country for the costs impacted by enrollment. The result is a forecast view by country as follows:



		Trial Total	2005 Mar	2005 Apr	2005 May	2005 Jun	200
Australia	Patients	653	100	130	60	88	
	Investigator Fees V	311,780	55,000	67,500	31,000	47,600	
	INVESTIGATOR FEES	311,780	55,000	67,500	31,000	47,600	1
	TOTAL SITE COSTS	311,780	55,000	67,500	31,000	47,600	1
France	Patients	768	100	130	90	112	
	Investigator Fees V	423,231	63,462	77,885	54,808	68,769	
	INVESTIGATOR FEES	423,231	63,462	77,885	54,808	68,769	2
	TOTAL SITE COSTS	423,231	63,462	77,885	54,808	68,769	2
Germany	Patients	1,406	200	270	135	196	
	Investigator Fees V	1,030,750	169,231	215,385	107,692	162,154	
	INVESTIGATOR FEES	1,030,750	169,231	215,385	107,692	162,154	6
	TOTAL SITE COSTS	1,030,750	169,231	215,385	107,692	162,154	6
Japan A	Patients	861	125	194	85	92	
	Investigator Fees V	951,072	158,654	235,096	99,231	115,745	
	INVESTIGATOR FEES	951,072	158,654	235,096	99,231	115,745	8
	TOTAL SITE COSTS	951,072	158,654	235,096	99,231	115,745	8
UK	Patients	558	100	120	45	70	

Cost Summary

The *Clinical Trial Blueprint* also offers variations of forecast composition not detailed in this application brief. For example, costs that do not vary by country, but are variable (such as a lab contract), or costs that do vary by country, but are fixed (such as country-specific advertising). All these and any other combination are supported by the *Blueprint*.

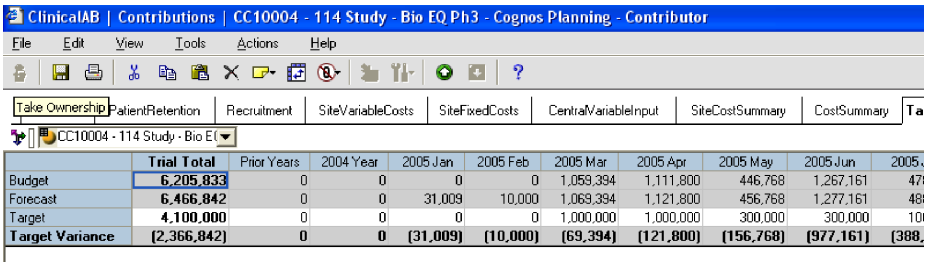


	Trial Total	Prior Years	2004 Year	2005 Jan	2005 Feb	2005 Mar	2005 Apr	2005 May	2005 Jun	2005 Jul
Central Assay Lab F	233,000	0	0	0	0	58,250	0	0	58,250	0
ASSAY LABS	233,000	0	0	0	0	58,250	0	0	58,250	0
Central Consultants	240,000	0	0	10,000	10,000	10,000	10,000	10,000	10,000	10,000
CONSULTANTS	240,000	0	0	10,000	10,000	10,000	10,000	10,000	10,000	10,000
Central Investigator Meetings	125,000	0	0	0	0	0	0	0	125,000	0
INVESTIGATOR MEETINGS	125,000	0	0	0	0	0	0	0	125,000	0
Central Safety Labs V	1,308,348	0	0	0	0	205,000	100,000	32,000	388,688	185,625
Site Clinical Lab F	21,009	0	0	21,009	0	0	0	0	0	0
CLINICAL LAB	1,329,357	0	0	21,009	0	205,000	100,000	32,000	388,688	185,625
Site Investigator Fees V	4,539,485	0	0	0	0	796,144	1,011,800	414,768	695,223	293,311
INVESTIGATOR FEES	4,539,485	0	0	0	0	796,144	1,011,800	414,768	695,223	293,311
TOTAL PROTOCOL COST	6,466,842	0	0	31,009	10,000	1,069,394	1,121,800	456,768	1,277,161	488,936

Target

Both budget and forecast versions are available for the forecast components shown above.

It can also be important to compare and analyze current forecasts against other versions such as flexed budgets or targets. The screen below shows the summary of calculated forecast and budget versions being compared against a target version.



	Trial Total	Prior Years	2004 Year	2005 Jan	2005 Feb	2005 Mar	2005 Apr	2005 May	2005 Jun	2005
Budget	6,205,833	0	0	0	0	1,059,394	1,111,800	446,768	1,267,161	47
Forecast	6,466,842	0	0	31,009	10,000	1,069,394	1,121,800	456,768	1,277,161	48
Target	4,100,000	0	0	0	0	1,000,000	1,000,000	300,000	300,000	10
Target Variance	**(2,366,842)**	**0**	**0**	**(31,009)**	**(10,000)**	**(69,394)**	**(121,800)**	**(156,768)**	**(977,161)**	**(388,**

ABOUT THE COGNOS INNOVATION CENTER FOR PERFORMANCE MANAGEMENT

The Cognos Innovation Center was established in North America and Europe to advance the understanding of proven planning and performance management techniques, technologies, and practices. The Innovation Center is dedicated to transforming routine performance management practices into "next practices" that help cut costs, streamline processes, boost productivity, enable rapid response to opportunity, and increase management visibility.

Staffed globally by experts in planning, technology, and performance and strategy management, the Innovation Center partners with more than 600 Cognos customers, academics, industry leaders, and others seeking to accelerate adoption, reduce risk, and maximize the impact of technology-enabled performance management practices.

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