TECHNICAL ARTICLE — PEER REVIEWED

Ultra Fast Track Project Execution on an International Biopharmaceutical Production Facility

Britton Wolf

ABSTRACT: In 2006, Lucentis ®, a drug for the treatment of age-related macular degeneration (AMD) was approved by the US Food and Drug Administration (FDA). AMD is a retinal disease which causes irreversible vision loss, and is a major cause of blindness in adults over 55 years of age. Once approved, evidence of rapidly escalating demand precipitated a new business requirement for Genentech, namely an expansion of manufacturing capacity. To that point Genentech's manufacturing capacity had been primarily US based. However, diversification issues prompted Genentech to consider locations globally. After an in depth site review process, Singapore was selected as the location for this potential new facility. However, by this time the business drivers had evolved to necessitate a 24-month execution window, from the start of preliminary engineering to the commencement of product qualification lots. The qualification is the first step in licensing the new ECP1 (E-Coli Product 1) production facility.

KEY WORDS: Cost, fast track, modular construction, planning, project team, and schedule

In 2006, Genentech, a biotech company, needed to expand manufacturing capacity to meet demand for a new drug. Genentech had 24 months to build a new production plant in Singapore. This article will explore this untra fast track project execution.

The biopharmaceutical industry presents many challenges. Drug development and clinical trails can take a decade or more and require large capital outlays. New products are often unique and require both process scale-up and adaptation of new and existing technologies to support large-scale production.

Equipment suppliers may be called on to push the envelope of their existing designs to meet requirements. Extensive process automation and control intersect most systems, and continually evolve as process knowledge increases. Materials of construction can be varied and many are not "off the shelf."

Contractors are required to employ "clean construction" techniques and all parties must be vigilant over contamination concerns, which can permanently disable a facility.

Government oversight agencies have stringent documentation requirements associated with design, installation, and operation of drug related facilities. This "validation and qualification" process is both resource intensive and time consuming.

On boarding and training of operational staff on a new process and an unfamiliar facility requires a minimal gestation period. Finally, most companies are reluctant to make a full financial commitment on a new facility until final drug approval is received from the FDA.

The combination of all these factors can add months, or even years, to an execution schedule for licensure of a new facility. However, the ability to get a new drug to market, in sufficient quantities to meet the needs of a patient population, is crucial. Delays could lead to patients forgoing the latest treatments and medications, resulting in reduced efficacy for the public.

Investing in a full suite of project planning, monitoring, and control mechanisms, is a prudent and necessary step to ensure project delivery. This investment must start in the front end planning stage. This ensures that the most appropriate execution strategies are selected. It also puts into place the necessary software platforms and resources to provide support during the entire project life cycle.

A special focus on end-to-end project planning, schedule development, and team integration, with comprehensive feedback is an absolute necessity. That is, if an ultra fast track schedule is to be met. In addition, an integrated cost control scheme must be developed, in tandem with the execution plan and early phase schedule development. This is to ensure that costs remain within the original authorized amount.

Execution Strategy And Schedule Control

From its inception, the ECP1 project team acknowledged the exacting demands of an execution strategy necessary to meet the project requirements. To complicate matters, this would be the first project executed in Singapore by Genentech, with no existing site infrastructure or local market knowledge.

Preliminary intelligence indicated that the local resource and materials markets were under pressure, affecting both subcontractor availability and construction pricing.

Multiple execution options were studied with the goal to determine the appropriate project approach given the many challenges.

The results were a multi-pronged solution which included the following.

- Project modularization.
- A unified and aligned project team practicing Class "A" behaviors with tight coordination between all stakeholders.
- An integrated project master schedule, including engineering, procurement, module fabrication, site construction, automation, commissioning, qualification, validation and business critical operation. And,
- Emphasis on post construction licensure critical activities with extensive planning and feedback mechanisms to ensure schedule compliance.

Project Modularization

An early stage study indicated that a traditional stick-built construction approach would not meet the schedule requirements. Instead, a new modular approach was selected which was determined to be the only viable method to meet the required end date.

An innovative strategy with 24 double-sized module blocks (25'Wx21'H'x45'L) was developed (see figures 1 and 2).

The entire process and utility side of the facility was prefabricated into these module

blocks, including all equipment and supporting kit. The modules were built in Charleston, SC. and shipped 8000 miles to Singapore via ocean going vessels. Once on-site, these module blocks were set via crane (like building blocks), interconnections executed, building sheathed in skin, and the process was ready for commissioning.

The modular approach provided numerous advantages, including the following.

- Modular construction allowed for 300,000 craft-hours to be executed in a controlled environment with a more experienced, productive workforce.
- Module shop conditions allowed for continuous craft overtime and shifting options, accelerating construction.
- Modular engineering could be highly overlapped with module fabrication.
- Local module fabrication facilitated owner involvement to resolve engineering and design issues, as well as ensure quality control.
- Modular construction allowed for progression of structural, mechanical, electrical and architectural works, while the Singapore site was in early stages of preparation.
- Modular construction allowed for Singapore site resources to be lowered, reducing risks associated with craft and material availability, as well as craft density concerns.

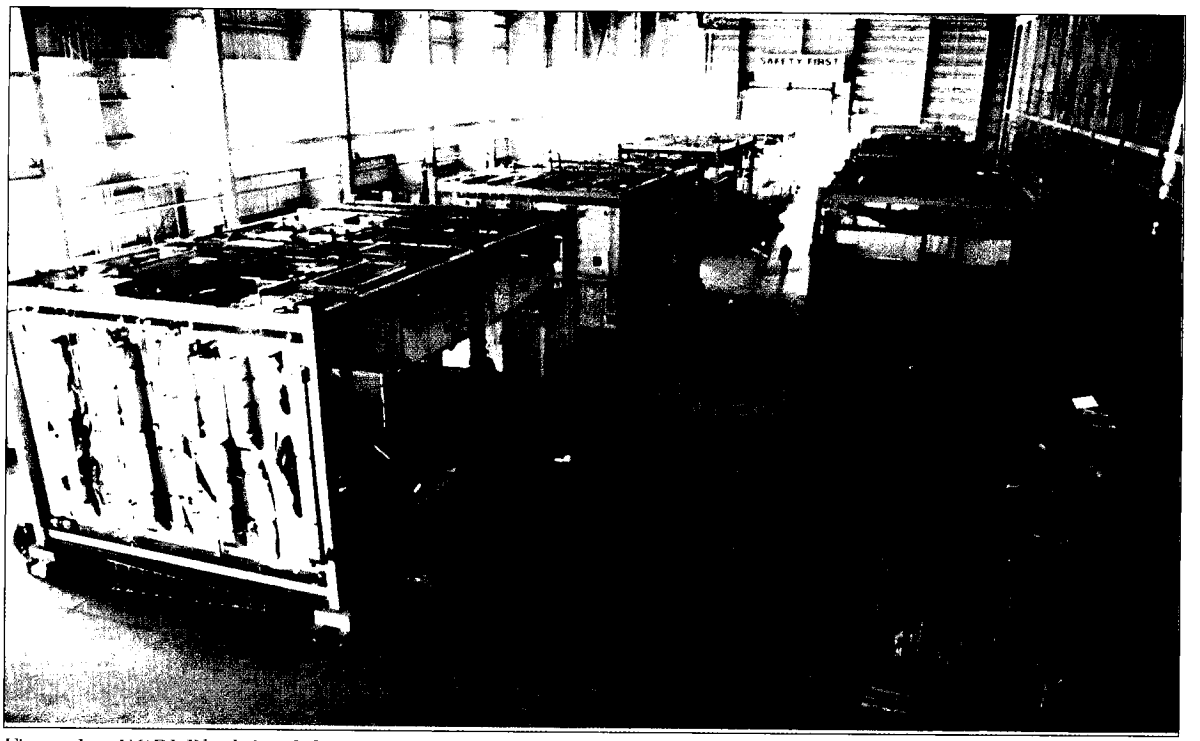

Figure 1— ECP1 Block Module Fabrication

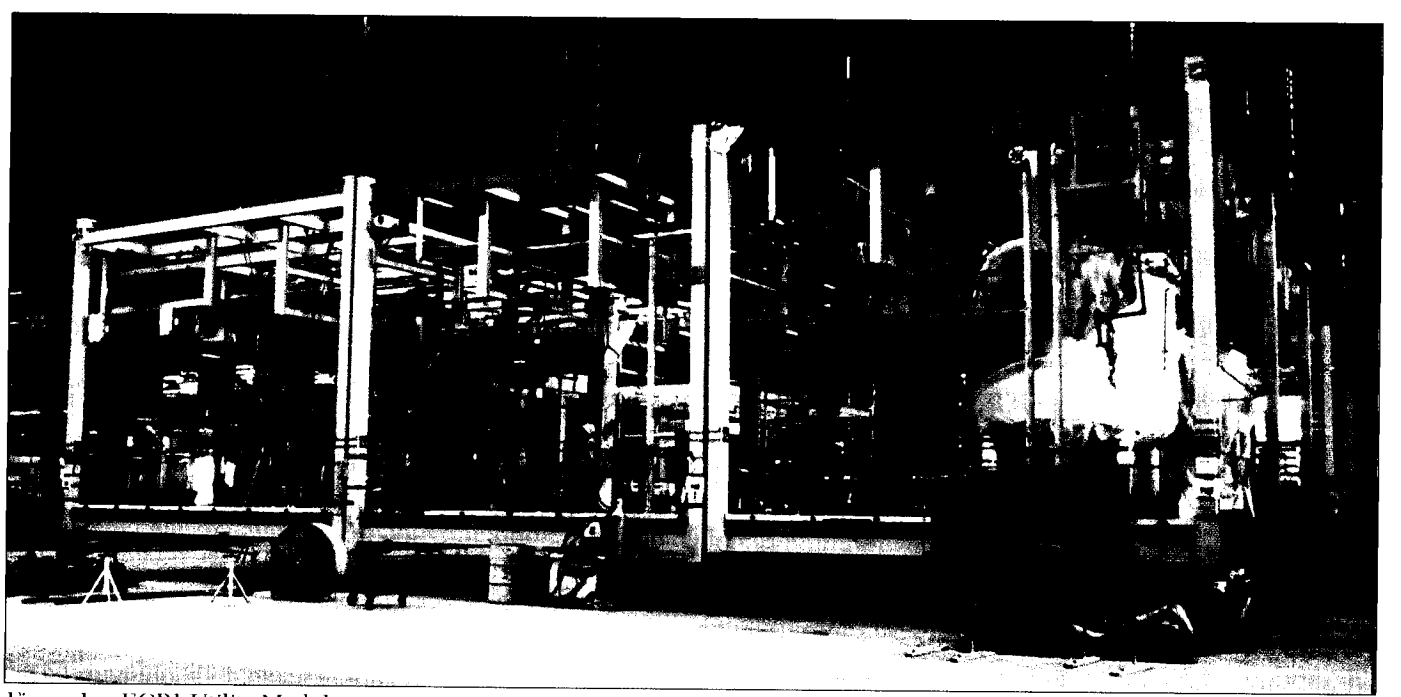

Figure 1— ECP1 Utility Modules

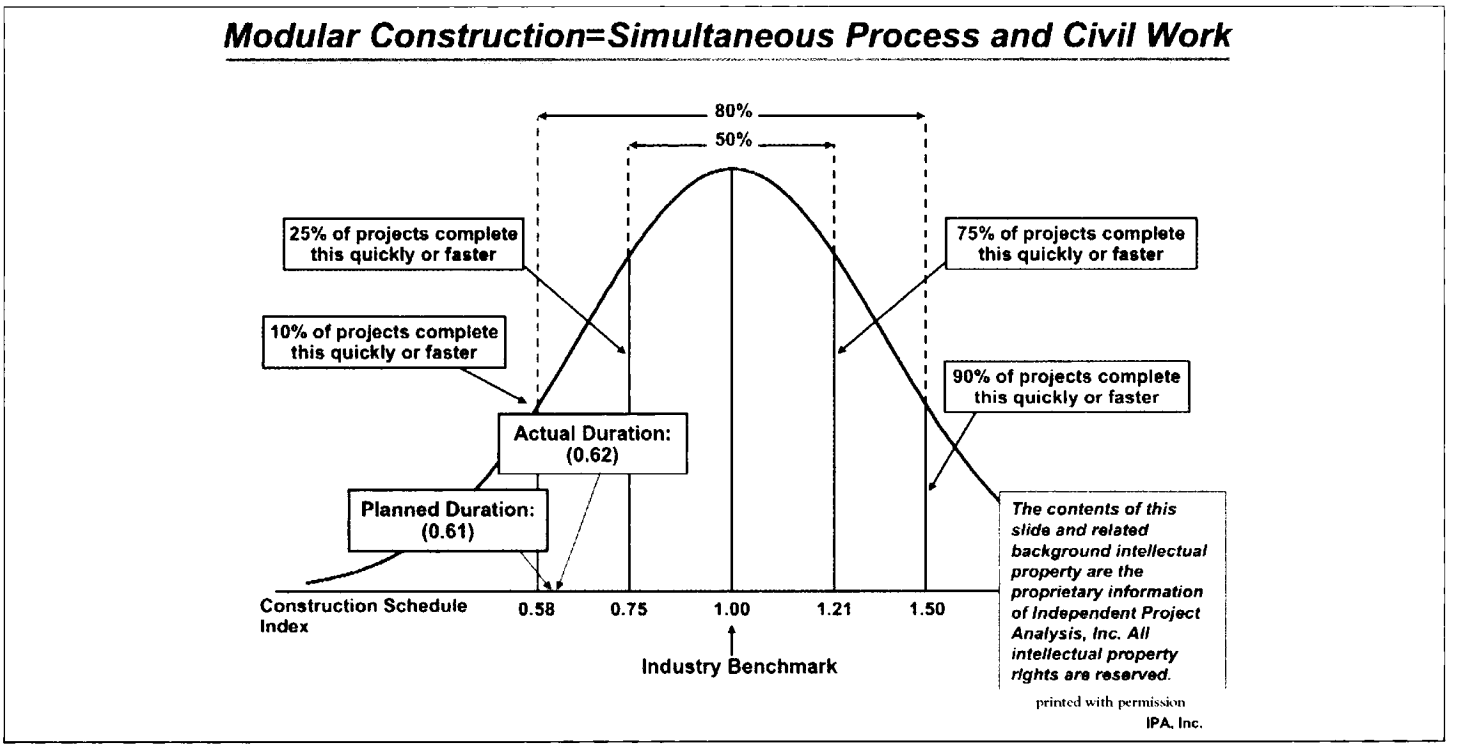

Figure 3— ECP1 Construction Schedule Benchmark

The use of modular construction was instrumental in reducing the construction duration of the project. The resulting construction schedule benchmarked in a 90 percentile range, against industry average duration of execution (see figure 3), and set the stage for overall project schedule success.

Unified Project Team

Given the compressed schedule, an effort was placed on unifying all stake holders in order to promote efficient and effective communication.

It was recognized that a key to success would be a tightly coordinated and aligned team, with the ability to identify pinch points and act swiftly to resolve any issue. This challenge was compounded by the numerous stakeholders and the large distances that separated them.

The major separate teams included: process design, procurement, detailed modular design, automation, detailed site design, modular fabrication, site construction, as well as teams for commissioning, qualification, validation and all the separate operational groups (see figure 4).

To accomplish this goal, first, Class "A" principles and behaviors were emphasized to generate an ethos of honest, results-oriented communication. This was further promoted via team building and visible leadership, with constant positive interaction.

Class "A" behaviors were compiled by Oliver-Wight and are acknowledged by Genentech as a path to greater performance. These principles include the following.

- one set of numbers;
- realistic plans;
- a passion for accuracy and simplification;
- performance measurement;
- embracing accountability;
- never uncertain-always open;
- democracy in planning-autocracy in execution; and,
- a knowledgeable workforce with clear roles and responsibilities.

Contracts were implemented that promoted cost efficiency and schedule adherence, as well as linking together the success of the major stakeholders. These contracts included cost and schedule targets with incentives, none of which could be earned by a single organization unless all organizations (and the overall project) were successful.

A disciplined and regular communication regime was initiated within the sub teams and across the project.

A regimented file structure and sharing scheme was put in place to provide current data and information across the organization.

Finally, an overall integrated project master schedule was implemented that would provide constant feedback to facilitate execution.

Integrated Project Master Schedule

To meet the schedule control goal, a standard integrated schedule platform was required. The tool selected was Primavera Project Planner V5.0. This tool was previously in use by Genentech and many of the stakeholder's organizations.

During the front end planning stage, critical target milestones were developed and passed to the sub teams for confirmation. This provided the duration windows for the sub schedules (see figure 5).

From the outset each sub-team was chartered to develop the appropriate details and robust logic that fit into the overall master schedule and formed the basis of end-to-end project reporting (see figure 6).

Key to this strategy was a sub schedule group/owner who proposed the level of detail required for their scope of work. This level of detail was reviewed and agreed to by experienced planners and the other sub teams (see figure 7).

Some of the crucial steps taken to implement this schedule strategy included the following.

- Early agreement of a common WBS structure.
- Early identification of major sub schedules, including owner, engineer(s), module fabricator, site construction, and automation.
- Dedicated and skilled planners on site at the major organizations. Planners brought specific knowledge of their respective industries and teams to build their schedules.
- Agreement on level of detail, approach and tie points for the sub schedules.
- Weekly planning meetings with the owner acting as gatekeeper, arbitrator of issues, and overall schedule integrator.
- Weekly update cycle with analysis and actionable feedback to all sub teams. And,
- Extensive use of earned value, productivity and other metrics to verify and communicate progress.

Once the schedule was developed and in execution mode, status data flowed into the master schedule and consolidated progress information flowed out to all teams. This provided the basis for decision-making and corrective action.

This level of information, provided by a comprehensive integrated schedule, enabled the project team to stay on track and played a major role in meeting the project goals.

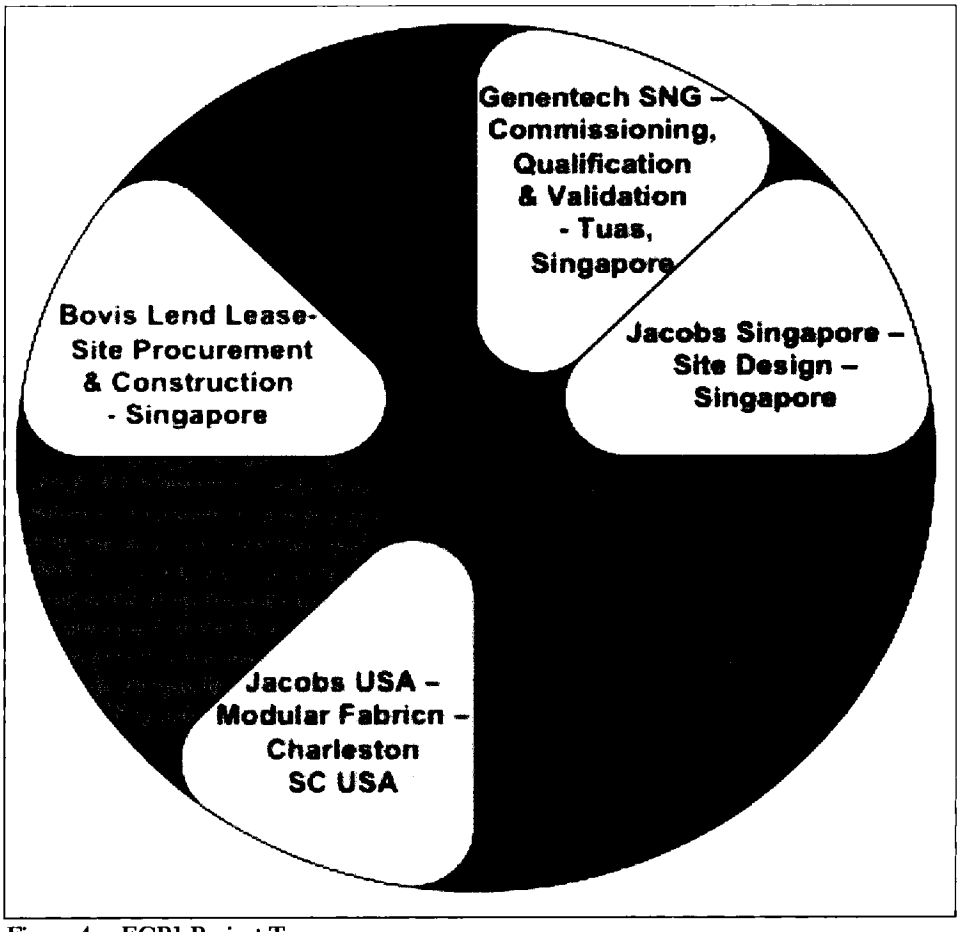

Figure 4— ECP1 Project Team

Licensure Critical Activities Planning And Feedback

Many a project has cleared the hurdles of engineering and construction, only to founder in commissioning, qualification, or validation. With this in mind, a strong emphasis was placed on pre-planning and scheduling of all post construction licensure critical activities. These are the activities necessary to receive plant licensure.

It was deemed imperative to establish the ability to track progress, identify issues, and provide actionable feedback to the "swat teams" at this crucial stage of the project.

To accomplish this task, a process was put in place to knit together the numerous back-end workflows required to meet licensure.

Some steps taken to establish this process included the following.

- Early formation of sub teams with weekly meetings to discuss execution strategies.
- Early generation of multiple execution scenarios, which were analyzed and resulted in system logics being developed and reviewed in order to build an optimal execution plan.
- Loading all critical resources in the schedule to verify staffing levels and availability, including quality, automation, commissioning agents, system leads, instrument techs (I&C), manufacturing specialist (MSAT), validation engineers, operators, and facilities support.
- Loading critical equipment as a resource to ensure use availability to support commissioning and start-up.
- Loading all required documents and approval steps to ensure completeness of GMP documentation and requirements.
- Inclusion of business critical infrastructure in the project master schedule.
- Development of clear and illustrative progress exhibits, including milestones and look ahead schedules, critical path and float analysis, system completion matrices and progress curves.
- Weekly update cycle with analysis and actionable feedback to all execution sub teams. And,
- Sub teams chartered with the responsibility and accountability to perform to plan.

The outfall of this process was numerous important exhibits, including an overall health report (see figure 8). This report consolidated the progress of all sub teams, and detailed float and performance graphs. These provided the next level of reporting detail (see figure 9). With numerous detail exhibits, these included a family of curves on GMP and quality documentation tracking (see figure 10).

This "good manufacturing practices" (GMP) and quality documentation was required to be in place prior to licensure.

Another important area of focus was resources bottlenecks, both staffing and equipment. Critical resources were identified. Detailed logic, along with availability data, was loaded in to the schedule. This allowed the generation of

both staffing and equipment use graphs (see figures 11 and 12). This information allowed the sub teams to verify and optimize their execution plans.

The early focus on licensure critical activities, with significant planning, and instituting of mechanisms for structured schedule "checks and balances" enabled all sub teams to meet their schedule requirement dates. This ensured a smooth and predictable process in bringing this new facility online.

Budget and Change Control

As with most projects, staying within the authorized funding target is a critical measure of project success. This can be extremely challenging on a schedule driven project, given the often acknowledged trade-off between cost and schedule. To accomplish this goal, an integrated cost platform was required to aggregate, review, and forecast all project costs.

The central platform chosen was Unifier version 8.7, which had been recently instituted as a Genentech standard. This platform allowed for consolidation of all project costs and provided the stakeholders with up to date actual and forecast cost information.

At the outset, all major cost categories were identified and appropriate

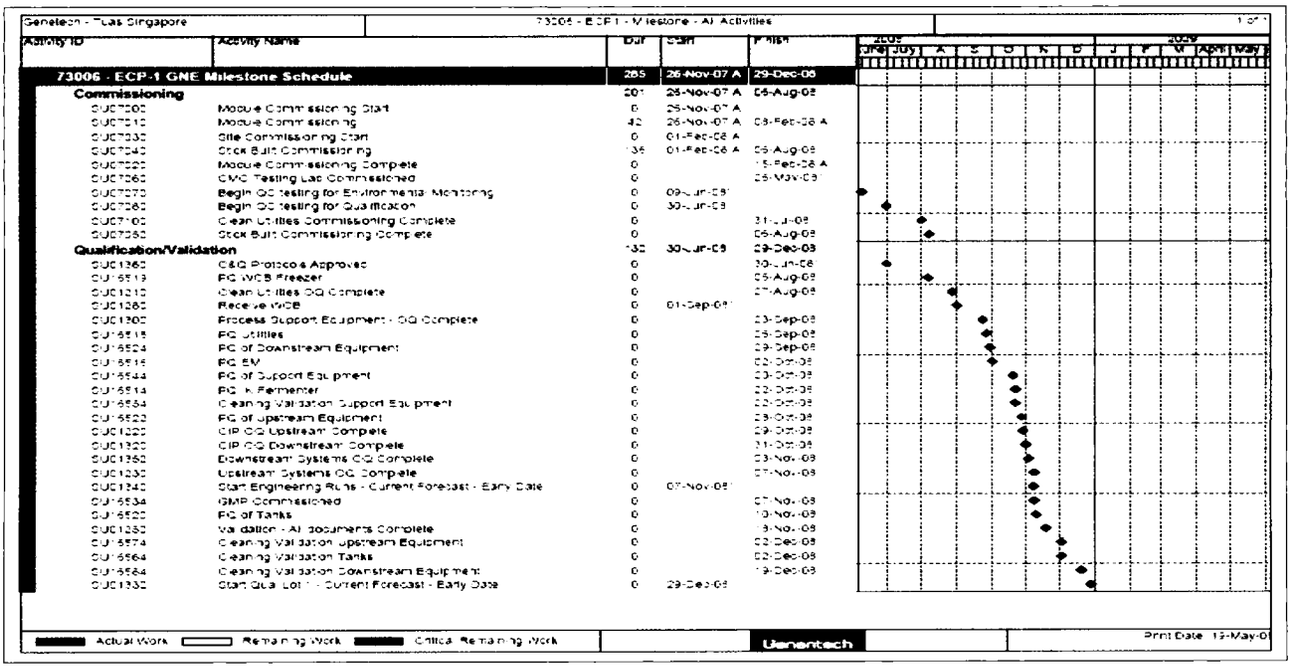

Figure 5— ECP1 Milestone Schedule

Project ID	Project Name	Total Activities	Actual Completed Activities	Actual In-Progress Activities	Actual Not-Started Activities	Start	Finish
ECP-1	ECP-1 Master	16015	15441	174	400	04-Sep-06 A	28-Sep-10
73006	73006 - ECP1- Milestone Schedule	138	96	0	12	04-Sep-06 A	24-Nov-09
73006.03.02	73006.03.02 - ECP1 - Jacobs - Detailed Design - Modules	660	660	0	0	25-Apr-07 A	11-Dec-07 A
73006.04.02	73006.04.02 - ECP1 - Jacobs - Procurement - Modules	1261	1261	0	0	24-Jan-07 A	20-Feb-08 A
73006.05.02	73006.05.02 - ECP1 - Jacobs - Construction - Module Fa	1146	1146	0	0	02-May-07 A	09-Apr-08 A
73006.05.03	73006.05.03 - ECP1 - BLL - Des/Proc/Const	2905	2905	0	0	12-Apr-07 A	16-Oct-08 A
73006.09	73006.09 - ECP1 - CQV	3684	3675	8	1	29-Oct-07 A	16-Mar-09
73006.10	73006.10 - ECP1 - Tech Transfer Schedule	208	140	7	61	24-Sep-07 A	30-Apr-10
73006.11	73006.11 - ECP1 Quality Documents	2875	2875	0	0	30-Jan-08 A	02-Jan-09 A
73006.12	73006.12 - ECP1 - Method Transfer	150	149	0	1	15-Jan-08 A	28-Feb-09
73006.20	73006.20 ECP1 - Finance	77	77	0	0	05-Jun-08 A	21-Feb-09 A
73006.21	73006.21 - ECP1 - HR	50	49	1	0	10-Jan-08 A	17-Apr-09
73006.22	73006.22 - ECP1 - CIT	11	11	0	0	01-Mar-08 A	03-Sep-08 A
73006.23	73006.23 - Design and Build of V & M Testing Laboratory	146	137	7	2	29-Oct-07 A	31-Jul-10
73006.24	73006.24 - ECP1 - FEES	589	559	28	2	31-Oct-07 A	31-Mar-09
73006.25	73006.25 - ECP1 - Automation	48	47	1	0	10-Mar-08 A	02-Sep-08
73006.27	73006.27 - ECP1 - Materials Management and OE	504	504	0	0	12-Feb-08 A	21-Feb-09 A
73006.28	73006.28 - ECP1 - PQ and Validation	632	457	70	105	02-Jun-08 A	06-Apr-09
73006.29	73006.29 - Singapore SAP Business Plan - Version 5.3	472	397	50	25	09-Nov-07 A	20-May-09
73006.30	73006.30 - ECP1 - Operations Work Stream	163	163	0	0	01-Jul-08 A	21-Feb-09 A
73006.32	73006.32 ECP1 - Quality System Plan	61	55	1	5	01-Apr-08 A	19-May-10
73006.45	73006.45 - ECP1 - Product 1 Engineering Runs & Qual Lots	70	30	0	40	14-Dec-08 A	09-Jul-09
73078	73078 - LBXS - Product 2/Singapore Process Transfer	195	48	1	146	14-Feb-08 A	28-Sep-10

Figure 6— ECP1 Master Schedule

independent resources and reporting mechanisms put in place. These were used to construct a dynamic, yet responsive, organization which could both identify and respond to monetary events.

The major cost categories and focus reports included the following.

- **Engineering** - weekly productivity reporting and cost forecasting.
- **Modular Construction Costs** – weekly craft productivity and material buy-out reporting.
- **Singapore Site Construction Costs** - monthly performance reporting and cost forecasting.
- **Equipment Costs** – monthly buy-out reporting.
- **Capital Labor Costs** – monthly staffing review and cost forecasting.
- **Capital Interest Costs** – monthly review and cost forecasting.
- **Other Owner Costs** – monthly review and cost forecasting.

Unifier brought the advantages of a predetermined cost WBS structure (CSI), a defined work flow process, as well as a common vocabulary to discuss costs and change, all of which added to team execution efficiency.

The Unifier platform produced standard reports, from the lower level WBS to the summary level consolidated project reports, all of which included budget, committed, forecast, and invoiced cost data (see figure 13).

Because of strict corporate requirements, an additional area of focus was cash flow management. Given the real-time consolidation of actual costs married with a rigorous approach to project planning and schedule control, the project successfully minimized any cash flow variances (see figure 14). A similar methodology was used to track the Genentech internal staffing labor costs (see figure 15), an area that can often be overlooked when dealing with so many dynamic cost elements.

Essential to a well executed project, is a change control philosophy and process. One that documents the relevant change, and facilitates the decision-making process. Integral to the Unifier cost control program is a change management module (see figure 16). This module captured all cost impacts and reflected in the forecast (and resulting draw to contingency (see figure 17), which is so necessary for management to adjudicate the critical issues required to ensure project success.

Some of the key points included in projects change control philosophy and process, included the following.

- Clear understanding of sub team scopes.
- An overall team doctrine to minimize change.
- A sub-team view to both identify necessary change early and to quickly assess the impact of changes from other sub-teams.
- A standard methodology for all sub teams to prepare and route change requests.
- Management attitude to quickly adjudicate all changes. And,
- A central software platform to capture and report the impact of change.

Because of a strict adherence to the proper "checks and balances" of change control, the project avoided the entanglements that can often slow progress and detract from success.

The business requirements of this project presented Genentech with numerous schedule, execution, and cost challenges. These challenges were overcome by first acknowledging the scale of the obstacles (schedule), and the consequences of failure (patient efficacy), which highlighted the need to invest early in a series of interlocking solutions.

Those solutions included the following.

ECP1 P5 Schedule Status Worksheet - end March 2009

Schedule Title	Owner Org	Plan Owner	Owner Scheduler	Status	License Critical	Resource Loaded	Update Cycle	Activity Count
Milestone Schedule	GNE	George	Rich	Update Mode	Y	N	Weekly	108
Detailed Design - Modules	JEG	JEG	JEG	Completed	Y	Y	Weekly	660
Procurement - Modules	JEG	JEG	JEG	Completed	Y	Y	Weekly	1,261
Fabrication - Modules	JEG	JEG	JEG	Completed	Y	Y	Weekly	1,146
Engineering / Procurement / Construction - Singapore Site	BLL	William	Prabodh	Completed	Y	N	Weekly	2,905
Automation Documents	GNE	Mark	Ramon	Completed	Y	N	Weekly	48
Quality Documents	GNE	John	Rich	Completed	Y	Y	Weekly	2,875
Commissioning / Qualification Validation	GNE	Kim	Rich	Update Mode	Y	Y	Weekly	3,684
Performance Qualification	GNE	Todd	Ramon	Update Mode	Y	Y	Weekly	632
Engineering Runs & Qual Lots	GNE	Harry	Rich	Update Mode	Y	Y	Weekly	70
Product 1 Tech Transfer	GNE	Hoang	Rich	Update Mode	Y	Y	Weekly	208
Method Transfer	GNE	Lesa	Rich	Update Mode	Y	Y	Weekly	150
Finance	GNE	Peter	Ramon	Completed	N	N	Bi-weekly	77
Corporate Information Technology	GNE	Brad	Ramon	Completed	N	N	Bi-weekly	11
Materials Management	GNE	Matt	Rich	Completed	N	N	Bi-weekly	504
Operations	GNE	Jozef	Ramon	Completed	N	N	Bi-weekly	163
Human Resources	GNE	Cecelia	Ramon	Update Mode	N	N	Bi-weekly	50
Singapore SAP Business Plan	GNE	Andrew	Ramon	Update Mode	N	N	Bi-weekly	472
Design & Build of Testing Laboratory	GNE	Kelly	Ramon	Update Mode	N	N	Bi-weekly	146
Quality System Plan	GNE	Lesa	Ramon	Update Mode	N	N	Bi-weekly	61
Environmental Health & Safety / Maintenance	GNE	PKH	Ramon A.	Update Mode	N	N	Bi-weekly	589
Product 2 Process Transfer	GNE	Jay	Ramon	Update Mode	N	N	Bi-weekly	195
								16,015

Figure 7— ECP1 Schedule Responsibility Matrix

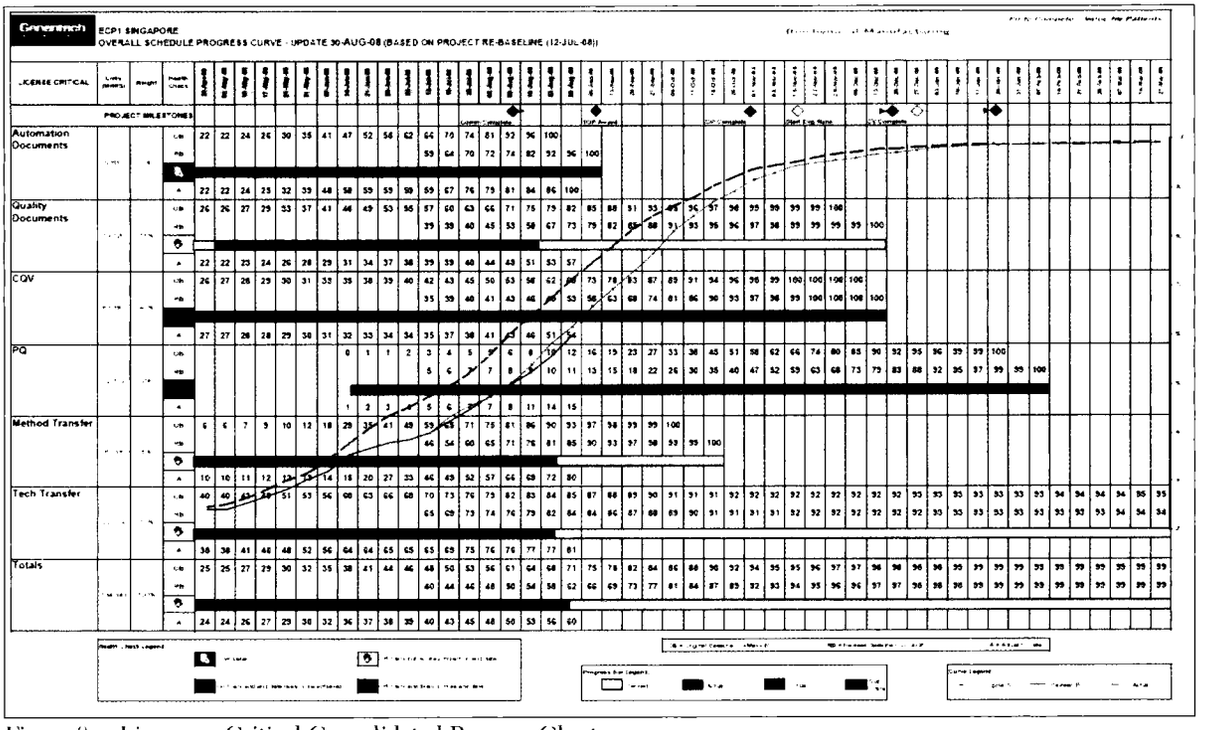

Figure 8— Licensure Critical Consolidated Progress Chart

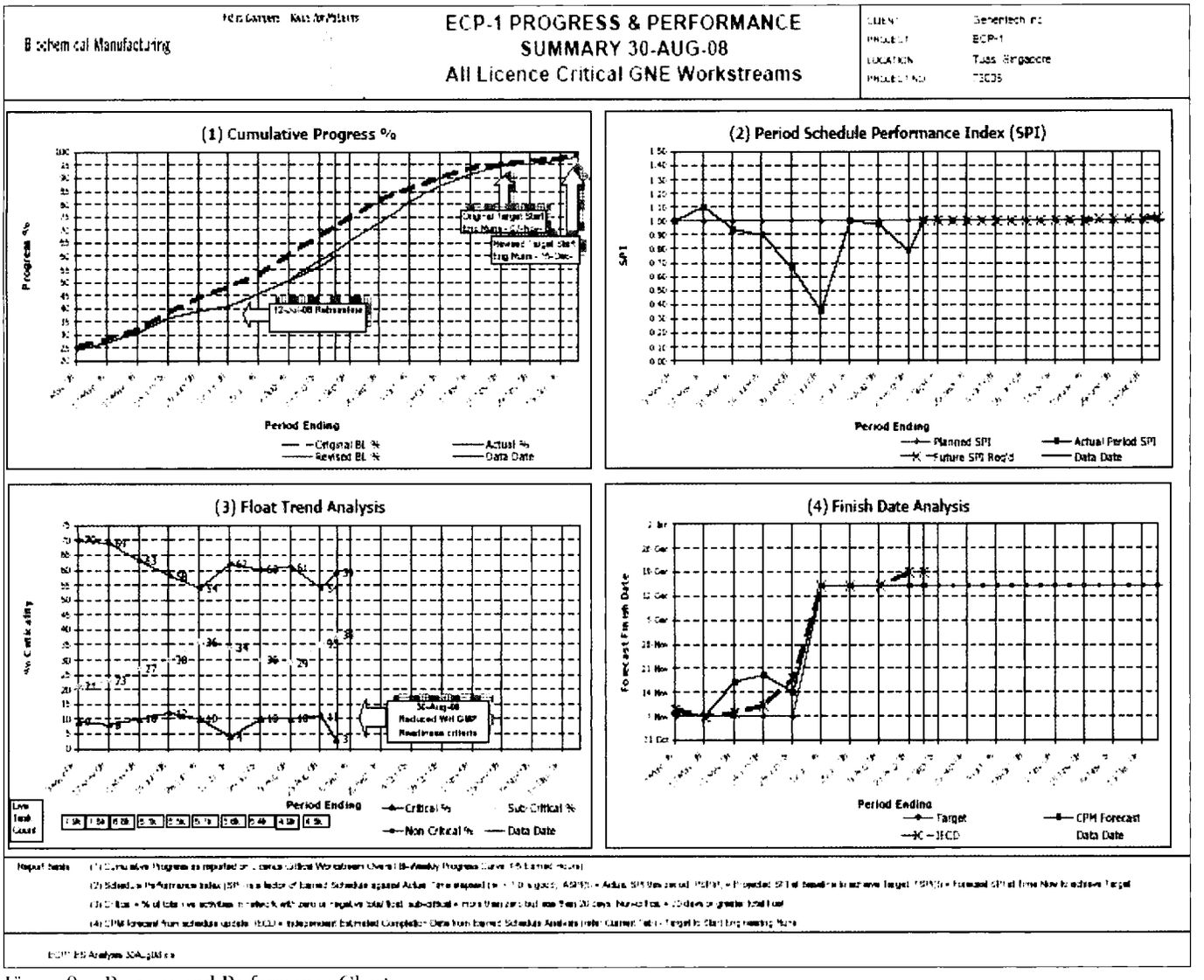

Figure 9— Progress and Performance Charts

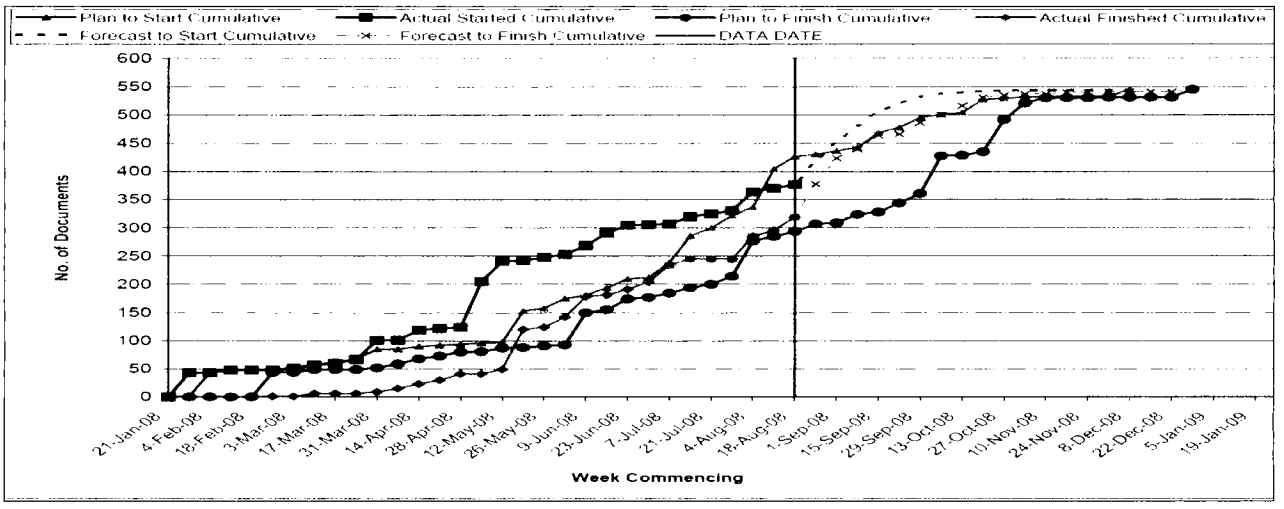

Figure 10— Quality Document Progress

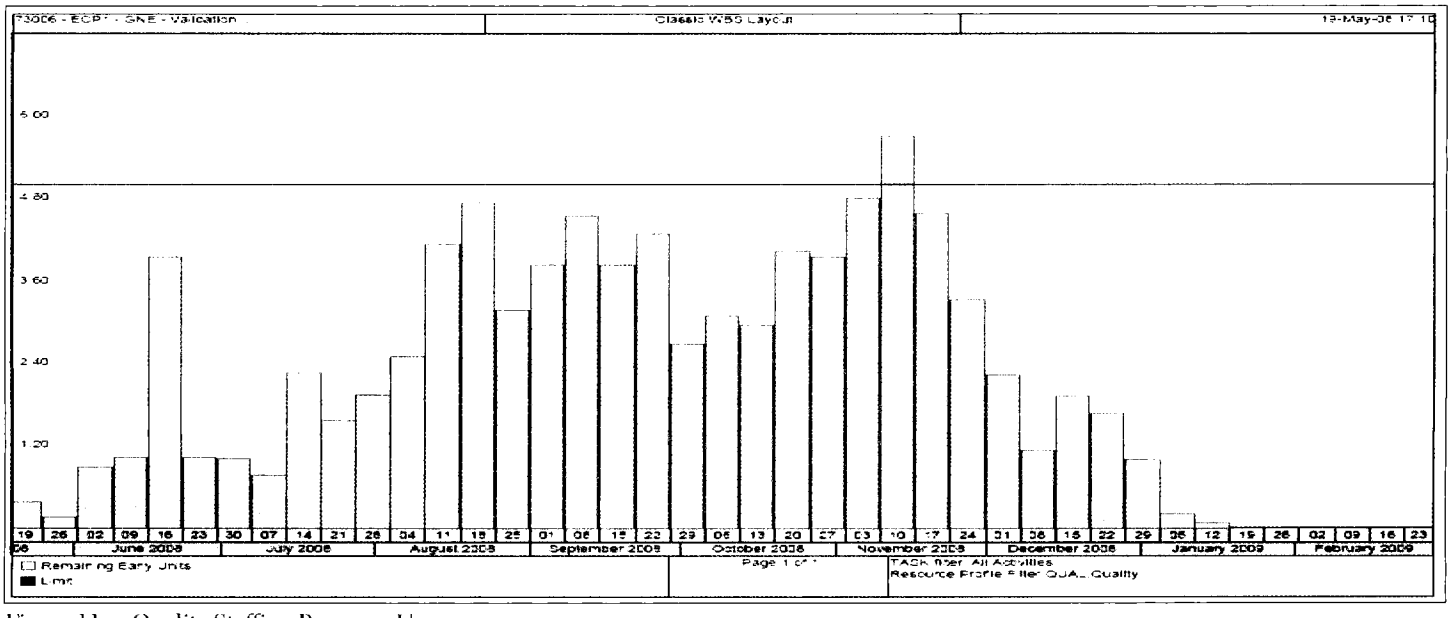

Figure 11— Quality Staffing Resource Use

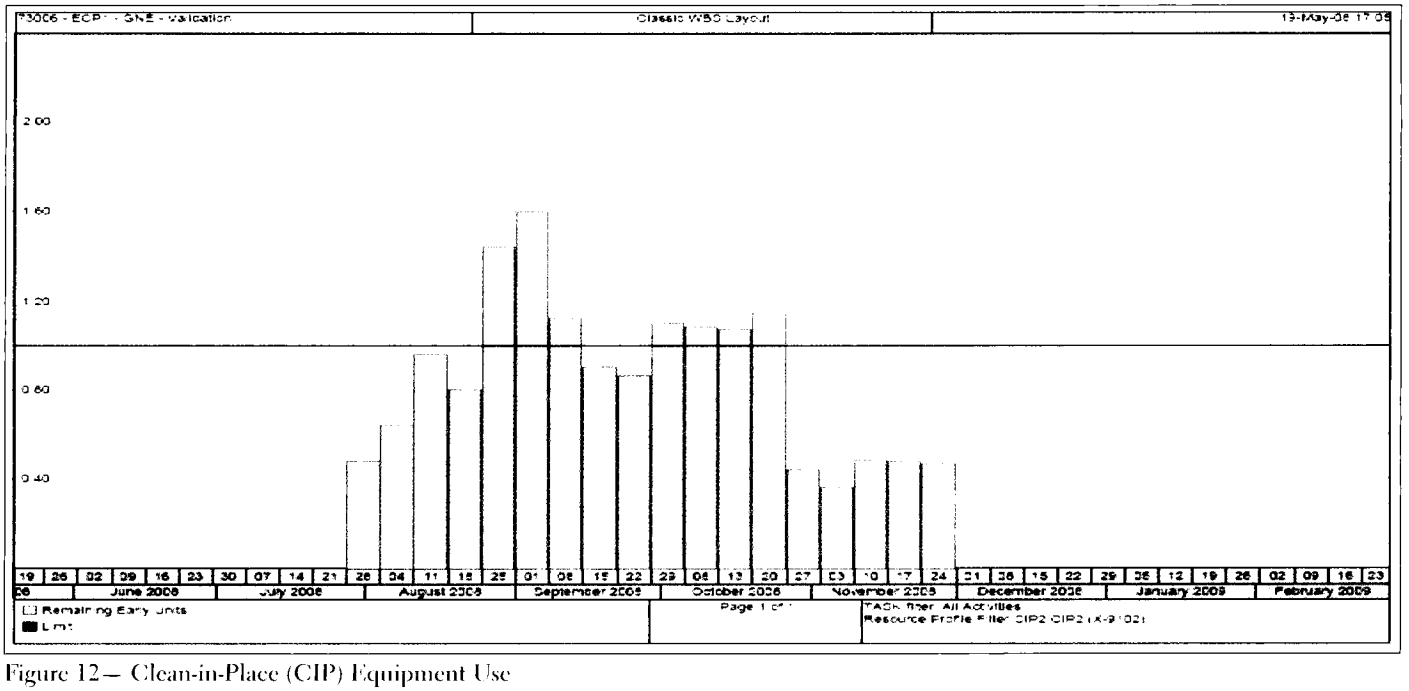

Figure 12— Clean-in-Place (CIP) Equipment Use

Expanded Summary Cost Report - Project Capital (FAC & Cap Labor) and Expense

Project Number: 73006

Project Name: MFG-ECP1

WBS Code	Cost Code Description	Current Estimate	Original Budget	Current Budget	Current Commits	Balance To Commit	Est. to Complete	Forecast	Forecast Variance	Invoiced to Date
Capital										
01-01-000000	CONSTRUCTION	0000000	0000000	0000000	0000000	0000000	0000000	0000000	0000000	0000000
01-02-000000	DESIGN	0000000	0000000	0000000	0000000	0000000	0000000	0000000	0000000	0000000
01-03-000000	OWNER COSTS	0000000	0000000	0000000	0000000	0000000	0000000	0000000	0000000	0000000
01-04-000000	CONTINGENCY	0000000	0000000	0000000	0000000	0000000	0000000	0000000	0000000	0000000
99-99-000000	INTERNAL LABOR	0000000	0000000	0000000	0000000	0000000	0000000	0000000	0000000	0000000
		0000000	0000000	0000000	0000000	0000000	0000000	0000000	0000000	0000000
Expense										
50-01-000000	CONSTRUCTION	0000000	0000000	0000000	0000000	0000000	0000000	0000000	0000000	0000000
50-02-000000	DESIGN	0000000	0000000	0000000	0000000	0000000	0000000	0000000	0000000	0000000
50-03-000000	OWNER COSTS	0000000	0000000	0000000	0000000	0000000	0000000	0000000	0000000	0000000
50-04-000000	CONTINGENCY	0000000	0000000	0000000	0000000	0000000	0000000	0000000	0000000	0000000
		0000000	0000000	0000000	0000000	0000000	0000000	0000000	0000000	0000000
Total:		0000000	0000000	0000000	0000000	0000000	0000000	0000000	0000000	0000000

Count: 0

Figure 13— Overall Unifier Project Cost Report

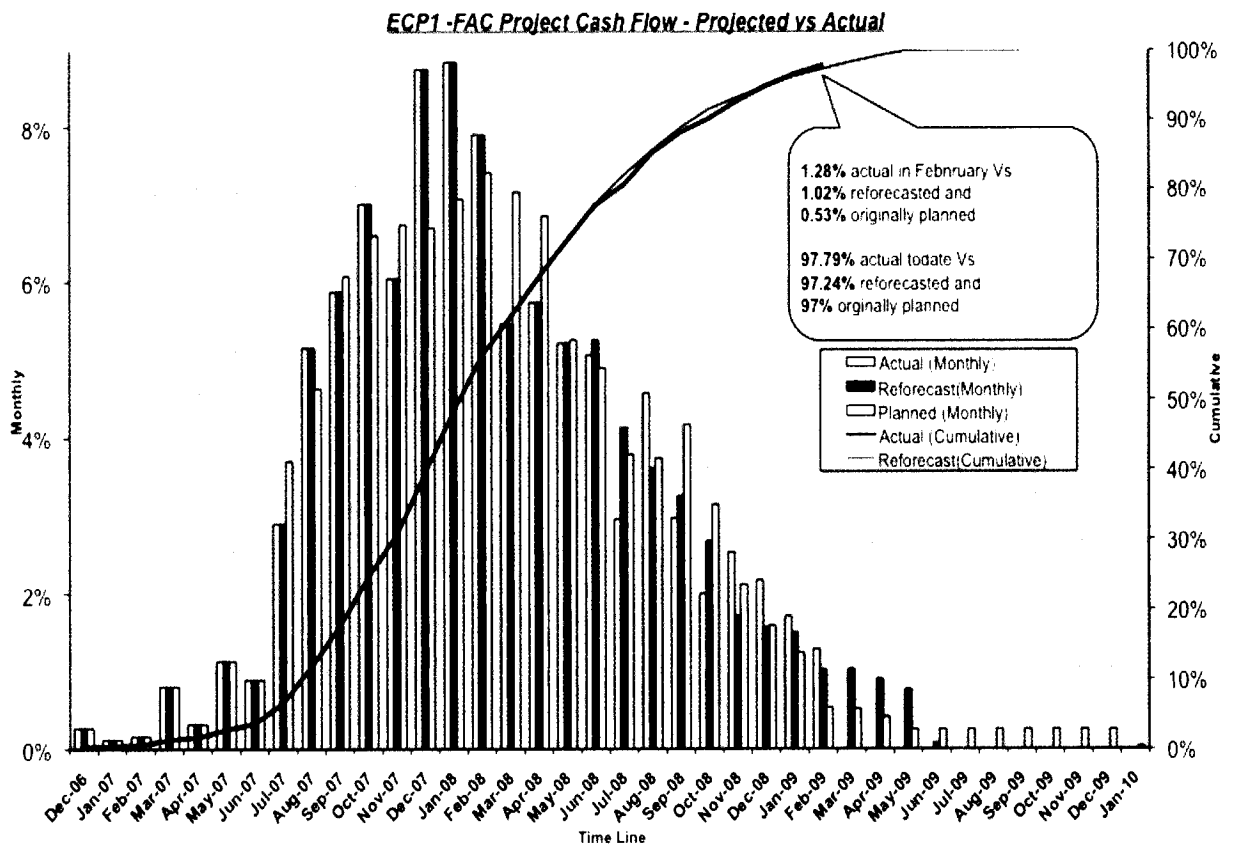

Figure 14— Construction Cash Flow - Percentage Expended vs. Time

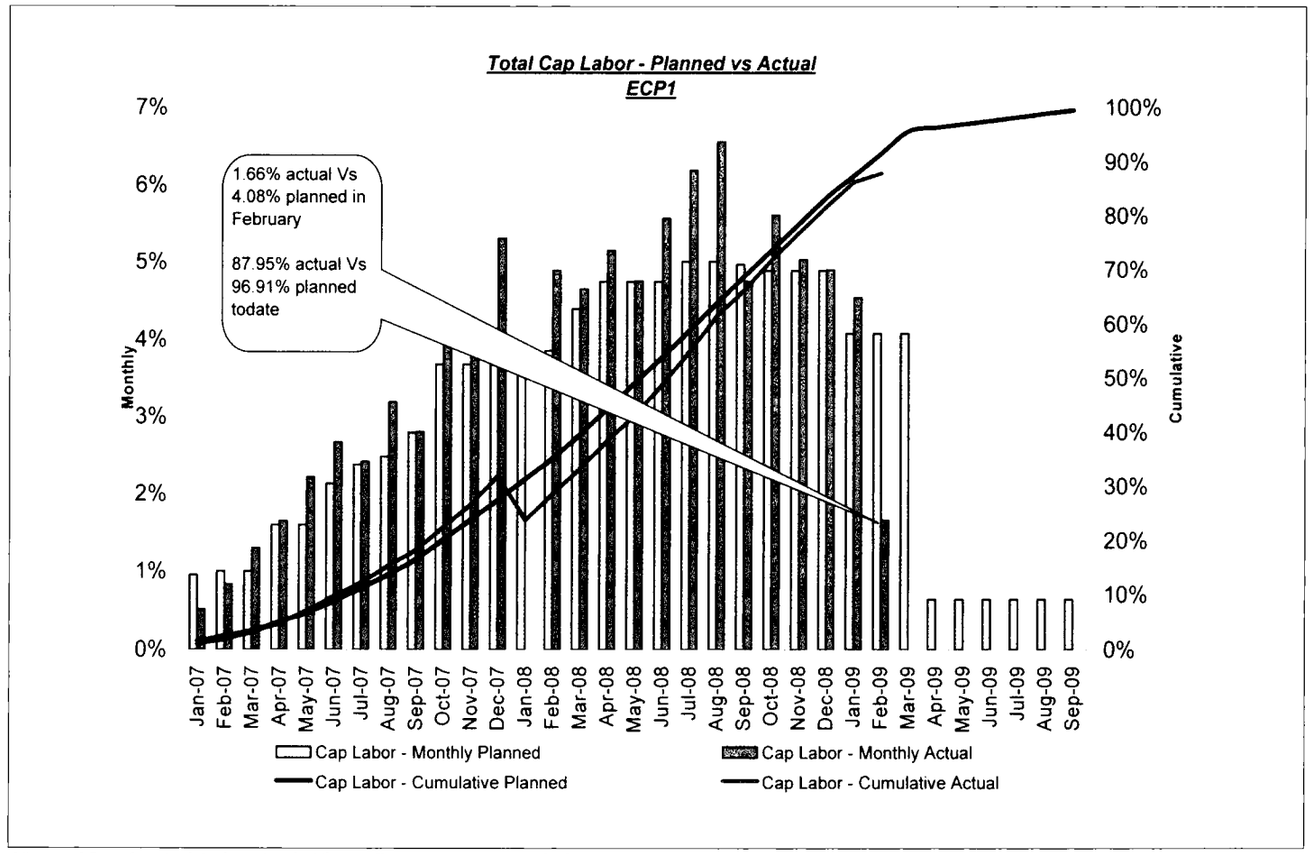

Figure 15— Capital Labor Cash Flow - Percentage Expanded vs. Time

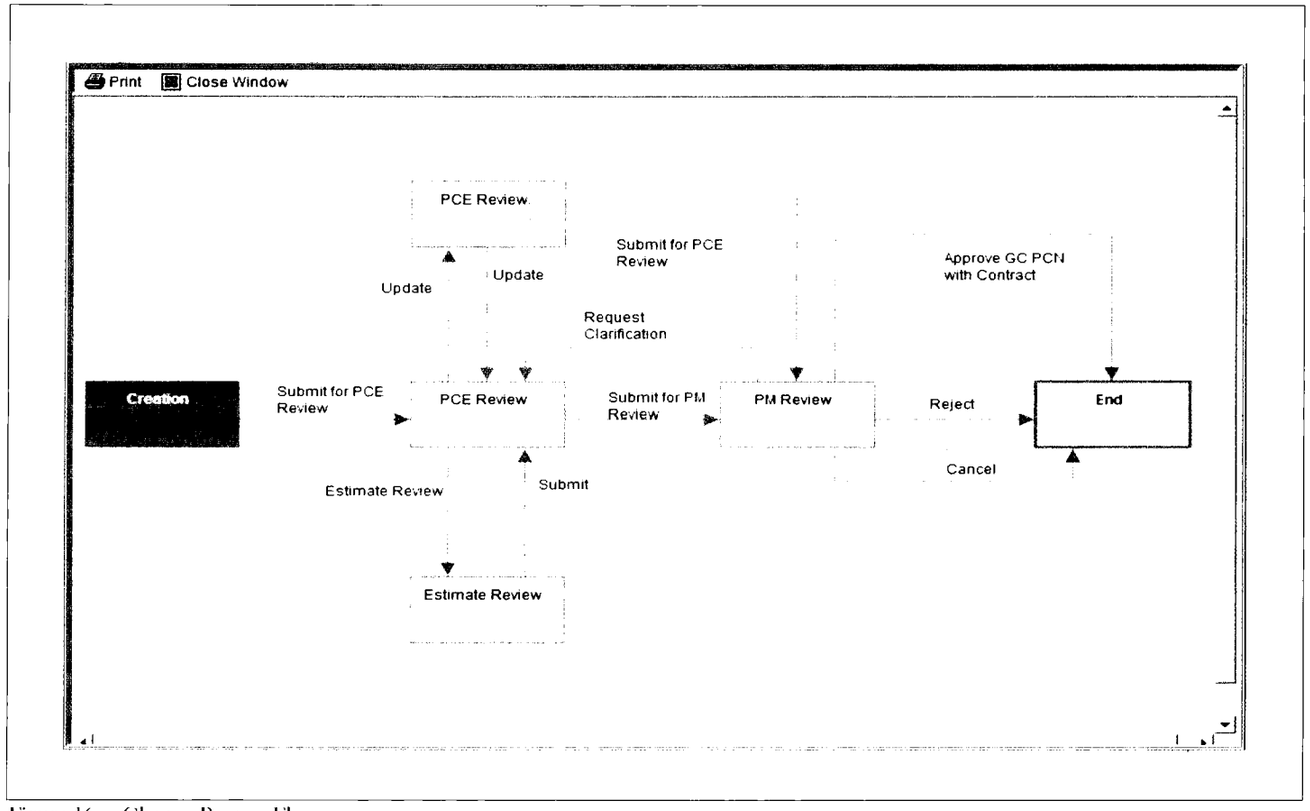

Figure 16— Change Process Flow

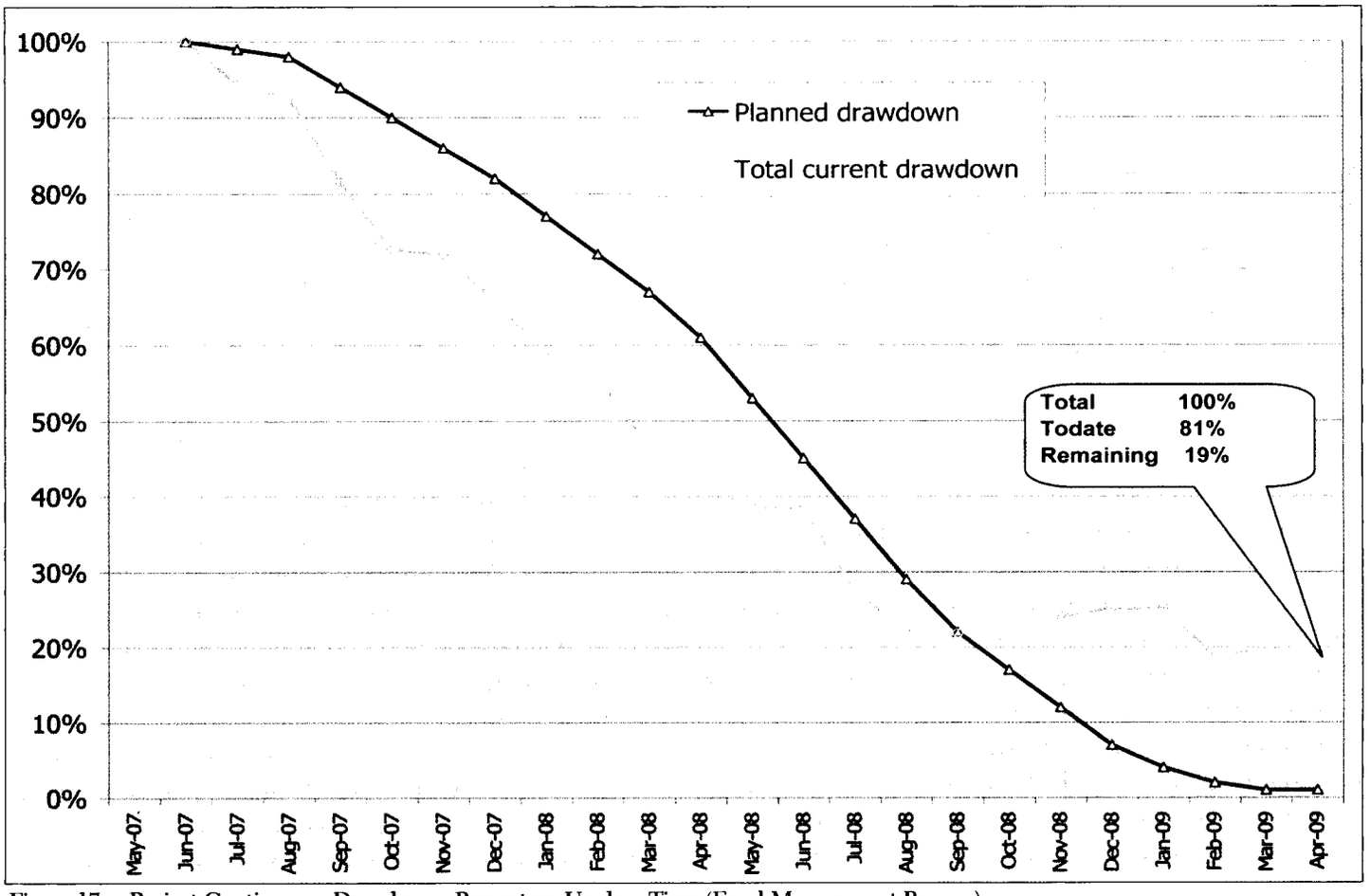

Figure 17— Project Contingency Drawdown - Percentage Used vs. Time (Excel Management Reserve)

- Starting with upfront analysis and timely selection of the execution approach.
- focusing on class "A" behaviors, married to sound practices of project management and controls.
- using mature systems to produce actionable feedback.
- instilling an ethos of action and cooperation.

These resulted in a project that met the extremely demanding schedule requirements. the project beat the industry average cycle time by approximately 50 percent.

Although this was an acknowledged "schedule driven" project, adherence to the end-to-end project plan resulted in a project that included the following.

- experienced relatively minimal change.
- had a one percent under run of the original authorized construction costs.
- used no management reserve; and,
- benefited from under runs in owner's costs.

These are compelling accomplishments, but they are dwarfed by the real achievements. Those included, a high quality facility, constructed with an unblemished safety record, and allowing Genentech to bring a critically required drug to market as planned for the benefit of the patients. ◆

ABOUT THE AUTHOR

Britton Wolf received a BS in Mechanical Engineering from the University of Florida and an MBA in finance from DePaul University in Chicago. He has spent the last 20 years working in the engineering and construction industry with emphasis in the Pharmaceutical and Biopharmaceutical industry. At present he is with Genentech as a Principal Project Manager in Corporate Engineering located South San Francisco CA. He may be contacted at wolf.britton@gene.com.