TUPE0439

Modeling Phase III Microbicide Clinical Trial Costs

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Issues

Licensure trial sizes for Phase III microbicide studies have been estimated between 4,000 and 10,000 participants and are expected to take between 2-5 years to complete. Samples sizes are based on statistics for valid clinical study (p value, power), local incidence of HIV transmission and drop-out rates. Currently, six first generation microbicide studies are being conducted around the world. The sample size can vary widely based on these factors, making financial planning difficult.

Description

Given the complex nature of microbicide efficacy studies and the large financial commitment required to conduct these studies, a costing model was developed to identify major cost drivers and to project cost expenditures over time. Initially, a static model was developed that comprehensively estimated costs and timeline based on one sample size. A dynamic simulation model was then built that allows user input to vary by study size, statistical parameters,enrolment forecasts, number of sites, costs associated with salaries, laboratory procedures and facilities. The outputs are study size, overall study timeline, timeline of visits, and cash flow.

Objectives

- Create a comprehensive multi-site clinical trial forecasting tool
- Calculate trial size and associated costs based on a range of statistical and operational parameters
- Allow model operation by clinical and project management
- Permit instant, high level feedback to a wide range of variables
- Communicate ramifications of scenario assumptions to stakeholders

Study Parameters (Inputs) & Summary Results

Known & estimated line-item costs may be input and effects shown

IPM Forecasting Tool: Study Parameters and Overview — Run a Stored Scenario | Save Current Inputs as a Scenario | Active Scenario: Staggered | Run Model | Show Staff on fully-staffed basis | Show Staff on As Needed basis

Project Start Month: January 2006 — Screening Start Month: June 2006 — Study Finish Month: Nov 2009 — Staffing Mode: Fully Staffed

Study finishes 42 months from Screening Start Month, 39 months from today and 30 months under the model's horizon.

Calculate Trial Size	Input values
p-value	0.005
Power	90%
Incidence in placebo arm	2.5%
Product Efficacy	50%
Years patient on drug	1
Solve for: Trial size	8,191

Calculate Subjects and Visits		
To be screened	29,539	
To be enrolled	9,846	
To complete study	8,191	
Total Visits	157,612	
Subjects per Site	1,024	Average
Visits per Site	19,701	Average

Study Overview		
Number of Sites	8	
Professional Staff at Sites	172	Fully Staffed
Support Staff at Sites	257	Fully Staffed
Study Months	42	
Screening Visits	29,538	
Enrollment Visits	8,246	
Net Regular Visits	97,309	

Summary of Study Costs by Category:	
Site Staff Costs	$16,897,811
Site Lab Costs	$10,895,429
Data Management	$5,658,254
Drug Product	$6,919,500
Annual or Per Site Support	$11,688,001
Patient Associated Costs	$10,303,171
Study Costs	$18,965,800
Sponsor Costs	$4,912,115
Total Cost of Study	$86,240,081

Summary of Study Costs Per:	
Site	$10,780,010
Completed Patient	$10,529
1st 12 Months	$24,976,441
2nd 12 Months	$21,842,434
3rd 12 Months	$29,122,611
4th 12 Months	$9,833,565
5th 12 Months	$0

Study Assumptions:	
Screened:Enrolled Ratio	3.0:1
Loss-to-Follow Rate	10.0%
Loss to PG Rate	10.0%

Based on inputs in Calculate Trial Size and Study Assumptions, 29,538 patients will have to be screened and 8,246 enrolled to have 8,191 patients complete the study and thereby comply with the power and p-value requirements.

Trial Costs ($ amounts in USD) — Go To Study Parameters | Go To Cash Flow | Run Model

Study Costs Inputs		Study Costs		
Data Mgt Cost per Visit	$35.90	Data Management Cost	$5.66 million	
		Data Mgt Cost per Subject	$568.75	
Applicators used per day	2			
Cost per Applicator	$2.00	Applicator Costs	$14.38 million	
Clinical Trial Management per Enrollee	$1,000	Clinical Trial Management	$8.25 million	
Clinical Monitoring Cost per Enrollee	$1,200	Clinical monitoring Costs	$11.82 million	
Training Cost per Site Personnel	$1,500	Number of Site Staff	704	
		Site Training Cost	$1.06 million	
Safety Monitoring: % of Enrollees	10%			
Cost per Event	$1,000	Safety Monitoring Cost	$0.98 million	
		Total Study Costs	$42.15 million	Spread pro rata

Support Costs on a per patient or per site basis:				
Office Supplies	$50	per enrolled patient	$0.41 million	Office Supplies
Communication	$25,000	per site	$0.35 million	Communication
Rent & Utilities	$100,000	per site	$1.40 million	Rent & Utilities
Clinic Supplies	$1,000	per enrolled patient	$8.25 million	Clinic Supplies
Vehicles (for all sites)	$10,000	per 150 subjects per year	$0.05 million	Vehicles
Insurance	$80,000	per site	$1.12 million	Insurance
Travel	$7,500	per site	$0.11 million	Travel
		Total Support Costs	$11.69 million	Spread pro rata

Patient Associated Study Costs:

Top-Down Cost Estimate	
Screen Visit Labor Costs	$ 1,717,281
Screen Visit Lab Costs	$ 2,185,812
Enrollment Visit Labor Costs	$ 986,728
Enrollment Visit Lab Costs	$ 2,679,950
Regular Visit Labor Costs	$ 9,445,546
Regular Visit Lab Costs	$ 3,113,882
Last Visit Labor Costs	$ 738,599
Last Visit Lab Costs	$ 2,915,785
Unscheduled Visit Labor Costs	$ 1,288,815
Unscheduled Visit Lab Costs	$ 7,164,160
Study Costs	$ 42,150,000
Annual Support Costs	$ 11,690,000
Total Staff Support Costs	$ 11,751,740
Patient Associated Costs	$ 10,300,000
IPM Costs	$ 4,900,000
Total	$ 113,028,299

Operational Parameters (Inputs) & Summary Results

Site staffing requirements and associated costs are calculated for two designated wage areas

Site staffing — Num of Open Sites = 8 — Active Scenario is Staggered 2

Study management	Site Base Staff	Staffing - All Sites: Idealized for Open Sites	Staffing - All Sites: Number Calculated	Staffing - All Sites: Number At Sites	High staff Costs: Annual per Employee	High staff Costs: Benefits Included	High staff Costs: Hourly Rate	High staff Costs: Total Calc'd Cost	Low staff Costs: Annual per Employee	Low staff Costs: Benefits Included	Low staff Costs: Hourly Rate	Low staff Costs: Total Calc'd Cost
Principal Investigator	1	8	8	14	$145,000	$188,500	$90.63	$4,459,000	$80,000	$104,000	$50.00	$0
Investigator MD	1	8	16	16	$75,000	$97,500	$46.88	$2,880,000	$15,000	$19,500	$9.38	$0
Clinician/Sr Research RN	1	8	36	36	$75,000	$97,500	$46.88	$6,480,000	$15,000	$19,500	$9.38	$0
Research RN	1	8	16	16	$75,000	$97,500	$46.88	$2,880,000	$15,000	$19,500	$9.38	$0
Pharmacist of Record	1	8	14	14	$75,000	$97,500	$46.88	$2,520,000	$15,000	$19,500	$9.38	$0
Pharmacy technicians	1	8	4	8	$30,000	$39,000	$18.75	$1,008,000	$7,000	$9,100	$4.38	$0
Counselors	2	16	43	43	$30,000	$39,000	$18.75	$2,709,000	$7,000	$9,100	$4.38	$0
Laboratory Management												
Sr. Lab Manager	1	8	4	8	$75,000	$97,500	$46.88	$1,440,000	$15,000	$19,500	$9.38	$0
Assistant Lab Manager	1	8	14	14	$45,000	$58,500	$28.13	$2,268,000	$9,000	$11,700	$5.63	$0
Laboratory technicians	1	8	36	36	$30,000	$39,000	$18.75	$2,592,000	$7,000	$9,100	$4.38	$0
Support Staff	17	132	261	299	$45,000	$58,500	$28.13	$19,656,000	$9,000	$11,700	$5.63	$0
Totals	28	220	452	504				$23,549,960				$0

Lab Test Costs

Up to 50 Sites may be selected with a range of enrolment terms & patterns

Site Selector — Active Scenario is Staggered

					Sites	Staff Number	Staff Cost
Work Days per Month	20.0 Average	Enrollment Target	9,846	Number of Open Sites	8	329	$16,567,811
Work hours per day	8	Enrollment from Site Selector	9,846	High Wage Sites	8	808	$16,567,811
Work Hours per Year	2,080	Difference	0	Low Wage Sites	0	808	$0

Site	Start Month	Wage Area	Enrollees	Enrollment Term: 6 months	12 months	18 months	24 months	Enrollment Pattern Forecast: Aggressive	Normal	Conservative	Flat
Site 1	1	High	1,200	◉	○	○	○	○	○	○	◉
Site 2	1	High	1,200	◉	○	○	○	○	○	○	◉
Site 3	1	High	1,200	◉	○	○	○	○	○	○	◉
Site 4	1	High	1,200	◉	○	○	○	○	○	○	◉
Site 5	19	High	1,200	○	◉	○	○	○	○	○	◉
Site 6	19	High	1,200	○	◉	○	○	○	○	○	◉
Site 7	19	High	1,200	○	◉	○	○	○	○	○	◉
Site 8	19	High	1,446	○	◉	○	○	○	○	○	◉

Clinical & Lab procedures selected by visit type (partial list for illustration)

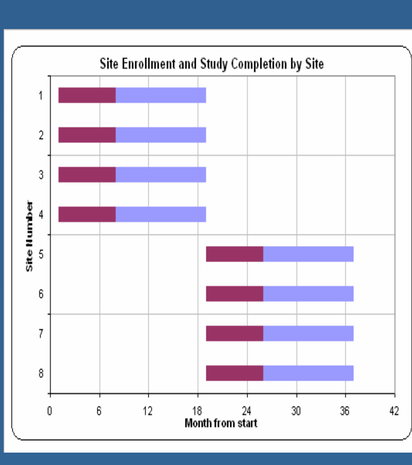
Regular Visit Procedures

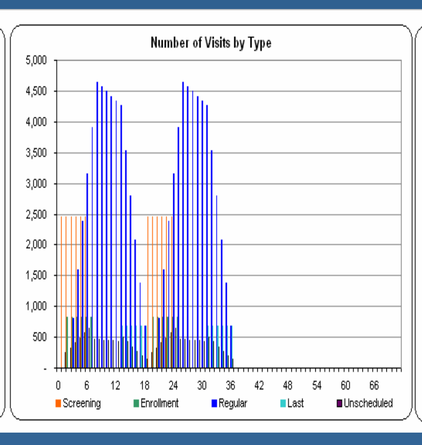
IPM 009 SCHEDULE OF CLINICAL PROCEDURES

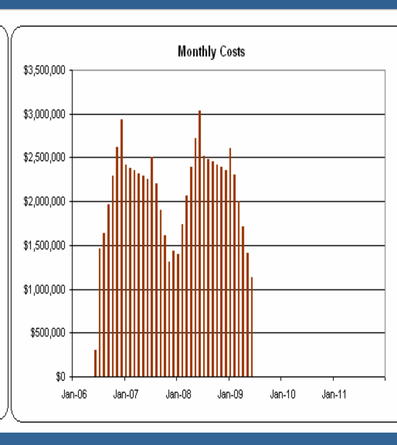
Procedure	Who Performs?	Time Required per Patient	Enable	Per Week	Per Month	Per Quarter	Semi Annually	Annually
Informational Video[c]	Community educators	0.0 minutes	☐	○	◉	○	○	○
Informed Consent[d]	Clinician/Sr Research RN	60 minutes	☐	○	◉	○	○	○
Demographic & Medical History	Research RN	10 minutes	☐	○	◉	○	○	○
Inclusion/Exclusion Criteria	Clinician/Sr Research RN	10 minutes	☐	○	◉	○	○	○
Test of Understanding	Clinician/Sr Research RN	2.5 minutes	☐	○	◉	○	○	○
Locator & Menses Information	Clinician/Sr Research RN	60 minutes	☑	○	◉	○	○	○
General Physical Exam	Investigator MD	60 minutes	☐	○	◉	○	○	○
Symptom-Directed Physical Exam	Research RN	30 minutes	☑	○	◉	○	○	○
Pelvic/Speculum Exam	Investigator MD	5.0 minutes	☐	○	◉	○	○	○
Dispense Study Product	Pharmacist of Record	15 minutes	☑	○	◉	○	○	○

Graphic Display of Recruitment, Trial Progress and Associated Costs of Various Scenarios

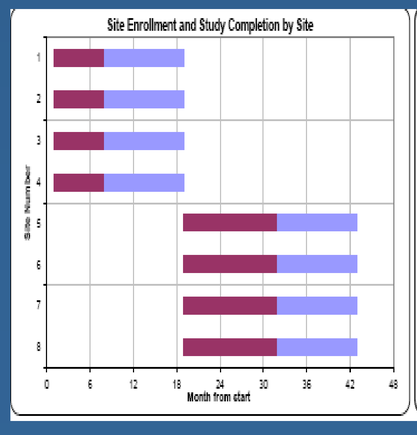
Scenario 1 – 8 sites: 4 open in month one, 4 open in month 18. Same enrolment and completion rates. (see summary results above) Total cost $89.2 million.

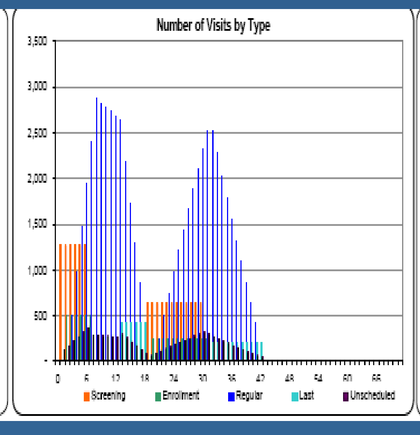


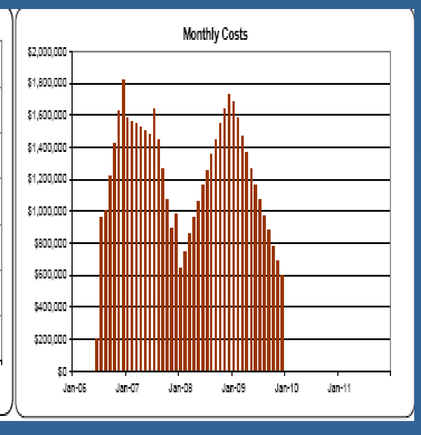




Scenario 2 – same as Scenario 1 except incidence rate set to 4% instead of 2.5% (6,084 to be enrolled). Total cost $60.2 million.







Lessons Learned

Static models are cumbersome modeling tools. Analyses of various scenarios from the dynamic model indicates that there is no one major variable that drives the cost of the microbicide study other than overall study size itself. Additionally, conducting licensure quality clinical research in developing countries is of the same financial magnitude as conducting clinical research in the developed world. Furthermore, the type of microbicide tested, i.e. second generation microbicides containing potent anti-retrovirals, do not add significant costs to Phase III studies.

Recommendation

Planning for large scale studies should involve constructing a model that permits easy sensitivity analysis. Such a tool would result in improved cost predictions and cash management. In addition, planning for the logistical realities of the various enrolment patterns will allow for efficient implementation of studies in that, for instance, staffing needs can adjust accordingly. Finally, the tool should accommodate actual data as it becomes available so that performance can be compared to goals and expectations. As with all modeling exercises, the tool will improve as real-life experience is gained.