



VinCro Clinical Trial Cost Estimator® Instructions

Introduction

The *VinCro Clinical Trial Cost Estimator®* is designed to assist you in arriving at a full service price for your clinical trial. The *VinCro Clinical Trial Cost Estimator®* is not meant to be a program whereby a few critical fields are inputted and a cost for the clinical trial is automatically calculated. Clinical trial designs and costs vary widely and by providing too many automatic assumptions, much flexibility is removed. The *VinCro Estimator* is designed to assist you in your clinical trial cost estimation while still providing you with the flexibility to calculate the cost of any clinical trial.

Please complete all the information in section 1 "Study Timeline" and "Specifications" as these numbers may be used in later calculations.

By entering the estimated hours that each task would take to complete and by using our sample quotation as a guide you can arrive at the approximate cost of your own clinical trial. Of course, various trials/tasks may take more or less hours depending upon the specific requirements of your particular trial.

The *VinCro Estimator* is designed to provide an approximate cost for your clinical trial, so a "Cost Adjustments" section can be found at the end of *VinCro Clinical Trial Cost Estimator®* to make additional adjustments if necessary. Additional items may be added into or subtracted from the "Cost Adjustments" section as required. For example, we have assumed that all sites require a close out visit; however, if a site did not enroll any patients and did not perform any activities, some sponsors may elect to perform a close out visit by telephone. Therefore, you may want to subtract calculated costs. Negative hours may be entered in the "Cost Adjustments" section, which will subtract from the overall cost.

We have estimated pass through expenses, which include monitoring expenses i.e. flights, hotels, meals, CRF printing expenses, central laboratory, regulatory, teleconferences, shipping etc. at ~ 25% of the CRO service costs. Depending upon your specific project these pass through costs may vary substantially.

Please be aware that the *VinCro Cost Estimator* utilizes VinCro hourly rates and suggested times for performing specific tasks i.e. project management of your trial. CROs may differ significantly on the amount of time they wish to allocate to your trial and thus at a higher hourly rate may offer a comparable price.

If you require assistance using *VinCro Clinical Trial Cost Estimator®* please call VinCro CMS at 613-526-4267 and we would be most pleased to assist you.

By e-mail info@vincro.com or svarrin@vincro.com (Shawn Varrin, President).

Estimated Study Timelines

VinCro has provided guideline assumptions for study timelines. Timelines may differ depending upon your specific trial requirements.

- **Start Up Period:** ~12- and may be 17 weeks depending upon trial
- **First Patient First Visit to Last Patient Last Visit (FPFV to LPLV) :** trial dependent
- **Last Patient Last Visit to Data Base Lock (LPLV to DB Lock):** 2-4 weeks
- **Statistical Analyses:** 2-4 weeks
- **Clinical Study Report:** 2-4 weeks

We have utilized the number of weeks that are on the critical path of the trial i.e. length of time that the trial may be extended for each variable. Some of these tasks may be done in conjunction with other tasks i.e. the CSR may be partially prepared while the statistical analysis plan is being written and it can take 2-4 weeks for completion subsequent to the SAP.

Estimated Specifications

- Please be as accurate as possible when estimating your clinical trial specifications as these inputs may be utilized in further calculations.
- Number of central IRB sites can be dependent on investigators and the therapeutic area in which the trial is being conducted.
- Interim monitoring visits may typically occur every 6 –8 weeks, but are trial dependent.
- An investigator meeting may take the place of Initiation visits, but this may be sponsor dependent.
- VinCro has assumed that all sites will require a close out visit.
- We have attempted to include the per-patient cost paid to investigators in your clinical trial estimate. Institutional overhead at investigative sites typically can range from 0-30+%, therefore we have suggested that an average of 25% for investigator overhead be included in the per-patient fee.

Study Start Up

- Activities include the preparation and distribution of CDAs and feasibility questionnaires, study team training teleconference or face to face meetings, and preparation of various procedure manuals, templates, trial specific forms, source document worksheets and contractual obligations etc.
- Team training has been allocated as an 8 hour teleconference.
- Ongoing team training, if required, may be placed in the “Cost Adjustment” section. This may be relevant for trials of longer duration than 2 years where resource changes may occur during the course of the trial.

Meetings

- Investigator meetings may be on any scale as determined by the sponsor. We have provided an option for attendance and/or preparation and presentation by various VinCro personnel.
- Investigator Meeting travel time for the CRO is dependent on the location of the investigator meeting.
- Kick off meeting with sponsor. The kick off meeting would include at least 3-5 CRO personnel involved in the clinical trial. If additional personnel are desired, these personnel should be included in the "Cost Adjustments" section in VinCro Estimator.
- Face to Face Meetings may occur periodically throughout the course of the trial. We have estimated that for each face to face meeting, travel and attendance would total ~12 hours. If more than one face to face meeting is requested this may be added in to the "Cost Adjustments" section or you may allocate, for example, 24 hours for face to face meetings i.e. *2 meetings@12 hours each* for travel and attendance.

Clinical Monitoring

Travel time for all visits is typically estimated at 8 hours (4 hours each way). Preparation for visits may be 1 hour or 2 hours and report writing and follow up letter (FUL) may be ~ 3 or 4 hours depending upon the complexity of the report. VinCro typically assumes a one day (8 hour) visit unless instructed otherwise. The advantage of using the *VinCro Cost Estimator* is that you can alter the duration of the visit, for example, to 12 hours on site, while other costs do not typically change. Furthermore, you can see what the effect of changing the on-site time from 8 hours to 12 or 16 hours will have on the cost of your trial.

Validation Visits

It is typical to prestudy/validate ~10 % more sites than may be necessary for the study; however, it is customary to only validate those sites that have not been used in the past year by either the sponsor or VinCro for a trial in the same therapeutic indication. If it is desired that more sites be validated, this can be added into the "Cost Adjustments" items at the bottom of *VinCro Estimator*.

Initiation Visits

Sites may or may not require initiation visits, as it may be decided that the investigator meeting will suffice as the initiation visit. If you do not require initiation visits you can leave hours blank or put "0's" for the # of hours for each task. If you do not require initiation visits for all sites, simply look at Estimator for the unit cost of the initiation meeting and subtract the costs of the initiation visits not to be done by placing the total initiation costs in the "Cost Adjustments" section of *VinCro Estimator*.

We have not made a provision for combined validation/initiation visits but these typically take ~ 3 hours longer (1 hour on site and 2 additional hours for report and approval) than the initiation visit. Validation/Initiation Combination visits may be added in to the "Cost Adjustments" Section.

Interim Visits

Sites are typically monitored every 6-8 weeks but this can be study and/or enrolment dependent. If you project a large number of subjects at each site or have a relatively complicated trial, you may want to project interim visits on a more frequent basis or increase the duration of visits. VinCro has made the assumption that 100% source data verification is to occur.

Close Out Visits

Generally all sites will require a close out visit.

Medical Monitoring

Medical monitoring is the time the medical monitor may spend on your project. This may involve answering protocol specific questions from sites, the PM etc. that need medical expertise, granting waivers for study admission, deviations, reviewing data listings, manual coding of adverse events/concomitant medications etc.

Weekly Study Management Activities

Each of the tasks in this section are typically accomplished on a weekly basis throughout the project and are assumed to begin and end at different times throughout the trial. Thus, it will be found that the number of weeks used to calculate a task are derived from the assumptions made in study timelines. For example, CRA site management activities will begin mid-way through the study start up period to establish relationship etc., continue through to LPLV.

General project management is the amount of time your project manager may spend on your study in the direct management of the project. This time does not include the time for teleconferences and project team meetings, nor managing 3rd party vendors. VinCro makes every attempt to make sure that sufficient time has been allocated to your project by the various resources to provide the highest quality of service possible.

Frequency of client teleconferences is dependent upon the clinical trial. We have simplified the estimate by maintaining a constant frequency of teleconferences throughout the clinical trial, but often sponsors may prefer to have weekly teleconferences during study start up and enrollment periods and then begin possibly on a biweekly teleconference schedule. Thus, it is your choice whether you choose weekly or biweekly.

It is customary to have project team meetings on a weekly basis but this can be trial/sponsor dependent. As above, meetings may begin on a weekly basis and may be reduced to biweekly meetings after, for example, enrollment is complete.

If you choose, for example, to have weekly meetings through to the enrollment period and then choose biweekly from the end of enrollment to the end of trial, you would utilize the "Cost Adjustments" section. For example, if the trial is 60 weeks in duration and you opt to have weekly meetings for the first 30 weeks and then biweekly for the remaining 30 weeks, you would simply calculate the conference cost on a weekly basis and then subtract $\frac{1}{4}$ of the conference cost to derive the cost of weekly meetings for the first half and

then biweekly for the remainder. To illustrate, let's assume the conference cost on a weekly basis is \$10,000 for 60 weeks. If you desire biweekly teleconferences for ½ the study (30 weeks), the conference cost would be the cost for 30 weekly teleconferences (\$5,000) + the cost for 30 biweekly teleconferences (\$2500) for a total of \$7500.00.

CRA Site Management is an essential component of any clinical trial. At VinCro we ensure adequate time is allocated for the CRA to be attentive to the needs of each of the study sites. Superior site relationships are an essential component of VinCro and just one of the many ways we seek to provide a higher quality service to our sponsors.

Weekly Study Management Assumptions

In weekly study management assumptions, tasks begin and end at various time points throughout the trial. We have made assumptions as to the duration of activities to allow sufficient time allocation for each function. For example, your trial will require project management throughout the entire trial; however, CRA site management will commence after study initiation and will conclude at data base lock. Now it should be acknowledged that arguments may be made that some tasks will commence and conclude at different times; however, we have tried to capture the bulk of the various activities for the purpose of the estimate. If your clinical trial requires more or less hours for various weekly functions, you may calculate the number of additional hours (or subtract, as necessary) and utilize the "Cost Adjustments" Section to provide a more accurate costing. Below are the listed assumptions:

- **General Project Management** – entire trial duration
- **PM Support** - entire trial duration
- **Medical Monitoring** – First Patient First Visit to Data Base Lock
- **Lead CRA** – Half Study Start Up Period to Data Base Lock
- **Budget Tracking** - First Patient First Visit to Data Base Lock
- **CRA Site Management** - First Patient First Visit to Data Base Lock
- **Study Tracking/ Regulatory Recruitment**- Half Study Start Up Period to Last Patient Last Visit
- **Maintain Clinical Files** - Study Start Up Period to Data Base Lock
- **Weekly Status Reports** - Study Start Up Period to Data Base Lock
- **Vendor Management** - Half Study Start Up Period to Data Base Lock
- **Request/Authorize Product Shipments** - First Patient First Visit to Last Patient Last Visit
- **Routine Teleconferences** - Study Start Up Period to Clinical Study Report
- **Routine Project Meetings** - Study Start Up Period to Clinical Study Report
- **General Data Management** - Half Study Start Up Period to Data Base Lock
- **Weekly Database Maintenance** - Half Study Start Up Period to Data Base Lock

Data Management

The assumption is that data management is being performed by paper-based case report form (3 part NCR). Data is stored in an SQL database and is double data entered and exported in SAS dataset format. Central laboratory data and other 3rd party vendor data may be imported into the database as appropriate. Query resolution time includes the time that CRAs spend on query resolution as well as the data management time tracking queries.

Data is double data entered. VinCro experience dictates it is best to typically allocate approximately 3 minutes of entry time per CRF page per data entry technician.

Medical Writing

Our assumption is an ~ 80 page report with 2 drafts and a final report reviewed by the appropriate personnel. Phase III trials may take considerably longer than phase I and II clinical trials.

Pass –Through Costs

We have estimated the pass through costs on a percentage of the CRO fee for ease of use in the *VinCro Clinical Trial Cost Estimator*®. Although some CROs charge a percentage on pass through costs, VinCro does not do this. Pass through costs are based upon actual pass through invoices, as we do not charge a percentage mark up on any pass through costs.

Total Site Fees

“Total site fees” refers to the number of patients multiplied by the cost per patient including the investigator overhead fee. We have estimated an overhead fee on average of ~ 25%.

List of Key Abbreviations

BST = Biostatistician
CDR = Clinical Data Reviewer
COA = Clinical Operations Assistant
CRA = Clinical Research Associate
DEC = Data Entry Clerk
DM = DM Associate
LCRA = Lead Clinical Research Associate
LGL = Legal Associate
MM = Medical Monitor
MWR = Medical Writing Associate
PGM = Database Programmer
PLGL = Paralegal
PM = Project Manager
QA = Quality Assurance Auditor
RA = Regulatory Associate
SA = Safety Associate

This is not a complete VinCro function list as other functions may be necessary to become involved during specific trials.

IRB = Institutional Review Board
FUL – Follow Up Letter
CDA = Confidential Disclosure Agreement
SAE = Serious Adverse Event
CRF = Case Report Form
NCR = No Carbon Required
OH = Overhead
SAP = Statistical Analysis Plan

** Please note that if you have high security settings for macros in Excel you may experience an error message stating that “macros are disabled”; in fact the **VinCro Clinical Trial Cost Estimator**® does not utilize or require macros, therefore you may safely ignore the message and leave macros disabled.