
Optimizing Global Clinical Trial Investments: Using @RISK for Patient Enrollment Forecasting in 23 Countries

Presented by VOI Consulting, Inc.
to Palisade Health Risk Analysis Forum

Introduction

Today's Topic

- Using @Risk Monte Carlo software to improve the design, placement and efficiency of global clinical trials.
- Why is this important?
 - High complexity, high risk decisions, with a great deal at stake.
 - Every single day that a drug's launch is delayed in clinical trials or the regulatory review process, approximately \$37,000 of additional development costs are tacked on and the lost revenues in the U.S. alone can equal \$23 million.
 - (2008, April 10). Pharma must adapt to changing market dynamics in 2008. Current Partnering, Retrieved May 10, 2009, from <http://www.currentpartnering.com/articles/>

Today's Topic

- VOI Consulting, Inc., a life-sciences advisory firm, was recently hired by a top 10 multinational pharmaceutical company to determine the relative suitability of over 30 countries as locations for drug / biologic clinical trials in five therapeutic categories.
- To our (admittedly incomplete) knowledge, this is the first time that Monte Carlo Analysis has been used to model patient recruitment purposes for international clinical trials.
- The analysis shown here is adapted from one of these five projects, a 23 country analysis for a Phase III clinical trial for a cancer drug.
- For confidentiality reasons, the names of our client, the trial, the oncology agent and the specific type of cancer are not disclosed.
 - Hereafter, we refer to the agent as “Agent X”, the specific cancer as “Cancer Y” and the clinical trial as “Trial Z”
 - Similarly, where budget figures are cited, we have replaced our client’s proprietary figures with industry averages obtained through secondary research.

VOI Consulting: Introduction

- Value of Insight or VOI Consulting is a life sciences advisory and publishing company serving the biopharmaceutical industry since 1998.
- Clients have included 17 of the top 25 drug companies, start-up to large cap biopharmaceutical firms, clinical research organizations, investment banks, private equity firms, venture capitalists, others.
- Consulting Services:
 - Strategic opportunity analysis
 - Partnership and licensing
 - Clinical trials design and location
 - Market entry decisions
 - Post-generic brand defense strategy
 - Pricing strategy
 - Competitive intelligence
 - Data modeling and forecasting using probability-based techniques
 - Regulatory compliance
- In short, anything after the molecule is designed.

- Leading Publications:



Todd Clark Introduction

- President of VOI Consulting
- Author of many pharmaceutical industry publications, including PharmaHandbook and GenericHandbook.
- Frequent source for industry trade publications.
- Nearly 20 years experience in the life sciences field.
- Member of pharmaceutical advisory boards for two research firms.
- Certified expert witness in pharmaceutical patent litigation.
- MBA, Kellogg School of Management, Northwestern University.
- Adjunct professor of business, Tulane University and Loyola University.

Overview of Global Clinical Trials

Context of Global Clinical Trials

- Pharmaceutical and biotech companies are the greatest contributor to research on a global scale, spending approximately \$130 billion on R&D in 2008. Of this amount, 60 to 70% was spent on clinical stage activities.
 - PhRMA. (2009). Pharmaceutical Industry Profile: 2009. Washington, DC.
- Clinical research has experienced a significant degree of globalization in recent years.
 - Approximately half of all pivotal studies submitted to the FDA contain at least some foreign data.
 - Between 2004 and 2007, the number of FDA-regulated investigators increased by 15.9% in Central and Eastern Europe (CEE), by 12.1% in Latin America and by 10.2% in the Asia-Pacific region. Meanwhile, the number of North American and Western European investigators declined by 5.2% and 6.1%, respectively.
 - Weschsler, Jill (2008, September). Global trials draw regulatory scrutiny: FDA is conducting more inspections to ensure that foreign clinical research meets GCP standards. *Applied Clinical Trials*
 - Gambrill, S (2008, August). Central and Eastern Europe triples global trial participation. *CenterWatch Monthly*
- Although lower cost is the most frequently cited reasons for clinical trial globalization, the primary benefit comes from faster time to market.
 - DiMasi JA. The value of improving the productivity of the drug development process – faster times and better decisions. *PharmacoEconomics* 2002;20 (Suppl 3): 1-10

The need for an effective and efficient clinical development process has never been more pressing:

- With increasing regulatory emphasis on safety, growing competition for patients and saturation levels at established investigative sites, clinical trials have become more expensive, more difficult and more demanding:
- According to the U.S. General Accounting Office:
 - “over the past several years it has become widely recognized throughout the industry that the productivity of its research and development expenditures has been declining; that is, the number of new drugs being produced has generally declined while research and development expenses have been steadily increasing.”
 - <http://www.gao.gov/new.items/d0749.pdf>
- Pfizer reports that expenses associated with clinical trials have grown from 30% of development costs in the 1980s to 60% today.
 - http://www.pfizer.com/research/clinical_trials/clinical_trials.jsp

Why are clinical trials becoming more difficult?

- As of February 2009, there were approximately 2,900 new drug compounds in clinical trials or undergoing FDA review, a 52.6% increase over 1999 levels.
 - » VOI Consulting analysis of data found in: PhRMA. (2009). Pharmaceutical Industry Profile: 2009. Washington, DC. Developing countries are the U.S., Canada, countries of Western Europe, Japan, Australia and New Zealand.
- The average number of days to complete a trial grew by 70% from 1999 to 2005 while enrollment rates declined by 21% and retention rates fell by 30%.
 - Tufts Center for the Study of Drug Development, “Growing Protocol Design Complexity Stresses Investigators, Volunteers,” Impact Report 10, no. 1 (January/February 2008).
- One study found a 40% jump in the number of enrolled patients in studies conducted by major pharmaceutical companies between 2006 and 2008 alone.
 - Les Entreprises du Medicament (LEEM). (2008). The attractive position of France in International Clinical Research: 2008 survey assessed by Leem. Paris, France
- VOI Consulting estimates that it would require approximately 5.8 years to fully enroll all currently open Phase III cancer trials if only U.S. locations were used. This compares to 1.9 years using both U.S. and global trial sites – a reduction of 3.8 years that translates to improvements in pharmaceutical industry performance and faster access to therapies for patients.

The Promise of Globalized Trials:

- Number of Patients Enrolled per Active Trial Site: Established versus Emerging Markets

	Patients per active site 2008	Change (in patients) since 2006		Patients per active site 2008	Change (in patients) since 2006
Established Markets			Emerging Markets		
France	7.6	+ 1.3	Eastern Europe	13.0	+ 2.6
Germany	8.3	+ 1.5	Latin America	11.4	+ 2.3
United Kingdom	8.1	+ 2.5	Asia	11.1	+ 0.1
Canada	6.5	+ 0.3			
United States	5.7	- 0.4			
Average Above Countries	7.2	+ 1.0	Average Above Regions	11.8	+ 1.7

- Les Entreprises du Medicament (LEEM). (2008). The attractive position of France in International Clinical Research: 2008 survey assessed by Leem. Paris, France

But what makes a country suitable for a clinical trial?

- At a general level, things like:
 - Population demographics
 - Degree of motivation for enrollment (e.g. access to advanced health care, ability to skip wait lists)
 - Cultural attitudes towards clinical trials
 - Economic conditions
 - Medical practices, health systems and patient pathways (what doctor sees what patient where)
 - Quality of clinical trial sites/clinical investigators and staff
 - Patient/clinical investigator availability
 - Efficiency of review and approval process
 - Clinical trial application demands (administrative, translation burden, etc.)
 - Relative cost of conducting clinical trials
 - Logistical issues (patient transportation and location, import/export of supplies, etc.)
 - Adherence to international trial standards
 - Size of / access to of domestic pharma markets
 - Intellectual property considerations
- For every specific trial, the importance of the above factors varies and additional issues come into play.

With this partial list of considerations, we can see the complexity involved and the need for probability-based analysis becomes clear!

The Assignment

Objectives

- Trial Z required a minimum total enrollment of 690 patients.
- The sponsor's enrollment timeline was 26 months.
- The majority of countries with meaningful abilities to conduct clinical research were in the Trial Z evaluation set. These included:
 - Major research centers such as the United States, France, Germany and Japan
 - Countries with emerging clinical trial infrastructures such as China, India, Brazil, Poland, South Africa and Russia.
- Placing Trial Z in countries where recruitment would ultimately fall short of target levels would result in unnecessary loss of patent life and divert scarce resources from productive to unproductive locations.
- The objective of our analysis was to avoid these problems by determining the best countries in which to place the trial so as to meet enrollment goals on schedule.

Enrollment Criteria

- In addition to being diagnosed with Cancer Y, potential patients had to meet certain other criteria before they could be admitted to the trial.
- These inclusion criteria included:
 - The patient's particular subtype of Cancer Y
 - Stage of cancer at diagnosis
 - Prior history with various forms of therapy
 - Functional status 1 or 2 on the Eastern Cooperative Oncology Group Performance Status Scale (ECOG PS)
- In addition, since Cancer Y is a particularly malignant form of cancer with very limited survival rates, the relevant population for Trial Z was the number of people diagnosed annually (incidence) rather than the number of people ever diagnosed (prevalence), thus leading to a smaller pool of available participants.

Executing the Assignment

Phases of the Assignment

- The original assignment called for three separate phases:
 - Phase I: Research and analysis.
 - Phase II: Construction of a standard spreadsheet model containing “most likely case” recruitment forecasts for each country.
 - Phase III: Applying probability-based forecasting to understand the suitability of each country and the likelihood of meeting national and overall enrollment goals.
- Using the results from Phase III, we were able to extend our analysis into a fourth phase, in which we realigned the client’s trial locations with considerable savings and essentially no decline in the probability of meeting enrollment objectives on-time.

Phase I: Research and Analysis

- Extensive secondary and primary research was conducted to determine the characteristics of each market affecting clinical trial enrollment.
- The secondary research component consisted of an exhaustive review of several thousand pages of published articles on the epidemiology, histology (type) and treatment of Cancer Y in the 23 countries under evaluation.
- Primary research was obtained via interviews with 2-4 medical key opinion leaders per country.
 - Approximately 75 interviews were conducted for Trial Z.

Factors Considered

- Among the factors considered in the research and analysis phase were:
 - General / environmental factors as discussed on earlier slide.
 - Trial Z specific factors such as:
 - Incidence of Cancer Y
 - Percentage of patients fitting the enrollment criteria
 - Number of oncologists treating Cancer Y
 - Likelihood and timing of ethical committee approval for Trial Z
 - Number and type of patient contacts with investigators
 - Attitudes of investigators towards Agent X
 - Likelihood that patients would enroll in Trial Z
- The end result of the research and analysis phase was a written analysis with pertinent findings for Trial Z in each country.

Sample Phase I Deliverable

- This document, an analysis of the environment for Type 2 Diabetes trials in China, is representative of the results of the research and analysis phase.
 - *As with the discussion of Trial Z, confidential information has been obscured. We include the diabetes analysis rather than the Trial Z analysis due to coverage of certain topics in the latter document that would likely reveal the client and product under consideration.*
- The document is included to demonstrate that the majority of work takes place in the research and analysis phase.
- Creating the forecasting models that will be discussed today required less than 20% of the total effort – yet without this final 20%, the savings would not have been realized.

Phase II: Constructing the Model

- Information from Phase I was used to construct a standard spreadsheet model of the patient enrollment process for each of the 23 countries.
- Each country-level model relied on data from 54 inputs; the model's ultimate output was an estimate of cumulative patient enrollment across the 26 months of the trial
- As shown on the following slide, constructing the spreadsheet model was a four step process.

The Four Steps of Enrollment Modeling

Step: Model Output	Sample Data Inputs:
<p>Step 1: Patient Traffic</p> <p><i>Objective: Establish the number of Cancer Y patients diagnosed per investigator per month</i></p>	<ul style="list-style-type: none"> • National incidence of Cancer Y • Number of investigators involved in the trial • Monthly patient volume
<p>Step 2: Potential Enrollment Pool</p> <p><i>Objective: Determine how many patients would be eligible for enrollment</i></p>	<ul style="list-style-type: none"> • Epidemiological data on the incidence of specific subtypes of Cancer Y • Number of patients diagnosed by cancer stage. • Comparison of the national Cancer Y patient profile against Trial Z's inclusion/exclusion criteria <p><i>Due to environmental factors and the quality of healthcare systems there was considerable variation in these figures from one country to another.</i></p>
<p>Step 3: Average Monthly Recruitment Rate</p> <p><i>Objective: determine the likelihood that eligible patients would be invited to participate and, if invited, would elect to enroll in Trial Z</i></p>	<ul style="list-style-type: none"> • Access to and satisfaction levels with existing therapies • Investigator opinions about both Drug X and the design of Trial Z • Cultural attitudes towards clinical research
<p>Step 4: Enrollment Schedule</p> <p><i>Objective: establish the timeline for patient enrollment and bringing investigative sites online.</i></p>	<ul style="list-style-type: none"> • Research into procedures and timelines required for: <ul style="list-style-type: none"> • Regulatory and IRB approval • Contract negotiations • Investigator training

Results of Phase II

- The final product of Phase II was a model containing recruitment projections for each of the 23 countries and summary projection for the trial as a whole.
- When compared against our client’s original enrollment targets, these projections provided a starting point for determining the countries which were best suited to host the trial.
- While valuable, the Phase II model is based on standard spreadsheet techniques:
 - It provides only single, bottom-line projections that reflect what our research indicated to be the most likely number of patients recruited in each country each month.
 - Deviations from the base-case estimates, whether caused by “real-world” variability within the model parameters or inaccuracies in the research, cannot be accounted for using this approach.
 - Mistakes in trial location would lead to unnecessary expenditures, delays in completion and could ultimately jeopardize the approval of Agent X
 - It was crucial to gain a more comprehensive understanding of the likelihood of achieving enrollment objectives in each country.

Phase III: A Probability-Based Model

- Given the limitations of standard spreadsheet models, it was necessary to employ more sophisticated methods to gain a comprehensive understanding of the likelihood of achieving enrollment objectives in each country.
- @Risk was used to conduct Monte Carlo Analysis in order to account for uncertainty and show outcomes in terms of probabilities rather than single values.

Phase III: Applying MCA to the Clinical Trial Enrollment Model

Phase III

- With the original model for each of our 23 countries providing the framework, in Phase III of our project we applied MCA to the Trial Z enrollment model.
- To do this, it was first necessary to break out model inputs into those with known and unknown or variable values.

Known versus Unknown Values

- Of the 54 inputs in each country-level model, seven had known values and 47 had uncertain or variable values.

Examples of Known Values: 7 of 54 inputs	Examples of Unknown or Variable Values: 47 of 54 inputs
Target enrollment	Monthly incidence of Cancer Y
Timeline	Number of patients seen per investigator per month
Scheduled investigative sites per country	Percent of patients meeting Trial Z enrollment criteria
Scheduled number of investigators	Percent of patients informed about trial
	Percent of patients willing to enroll
	Time required for regulatory and IRB approval
In short, anything directly controlled by the sponsor.	In short, everything else!

Assigning Values

- Inputs with known values were unchanged from the standard model.
- For inputs with unknown / variable values we replaced single value estimates with probability distributions, using the original values as mean (expected) values.
- For some variables, our research yielded actual probability distributions.
- For other variables, the size of the standard deviation around the mean ranged from 5% to 20% for each variable based on two factors:
 - 1. The inherent variability of the underlying data.
 - For example, the number of patients diagnosed within a month by each particular investigator is subject to greater variability than the histologic profile of the Cancer Y population within each country
 - 2. The estimated reliability of the particular research finding in question.
 - For example, findings based on large-scale studies were deemed to have a higher degree of accuracy than findings based on a small number of interviews
 - The upper range of standard deviation was assigned to model inputs with greater variability or lower reliability.

Running the MCA Simulations

- After changing our variables from point estimates to probability distributions, we used the Monte Carlo software package to run 10,000 separate simulations on each of the country-level models.

Note on interpreting the probability figures

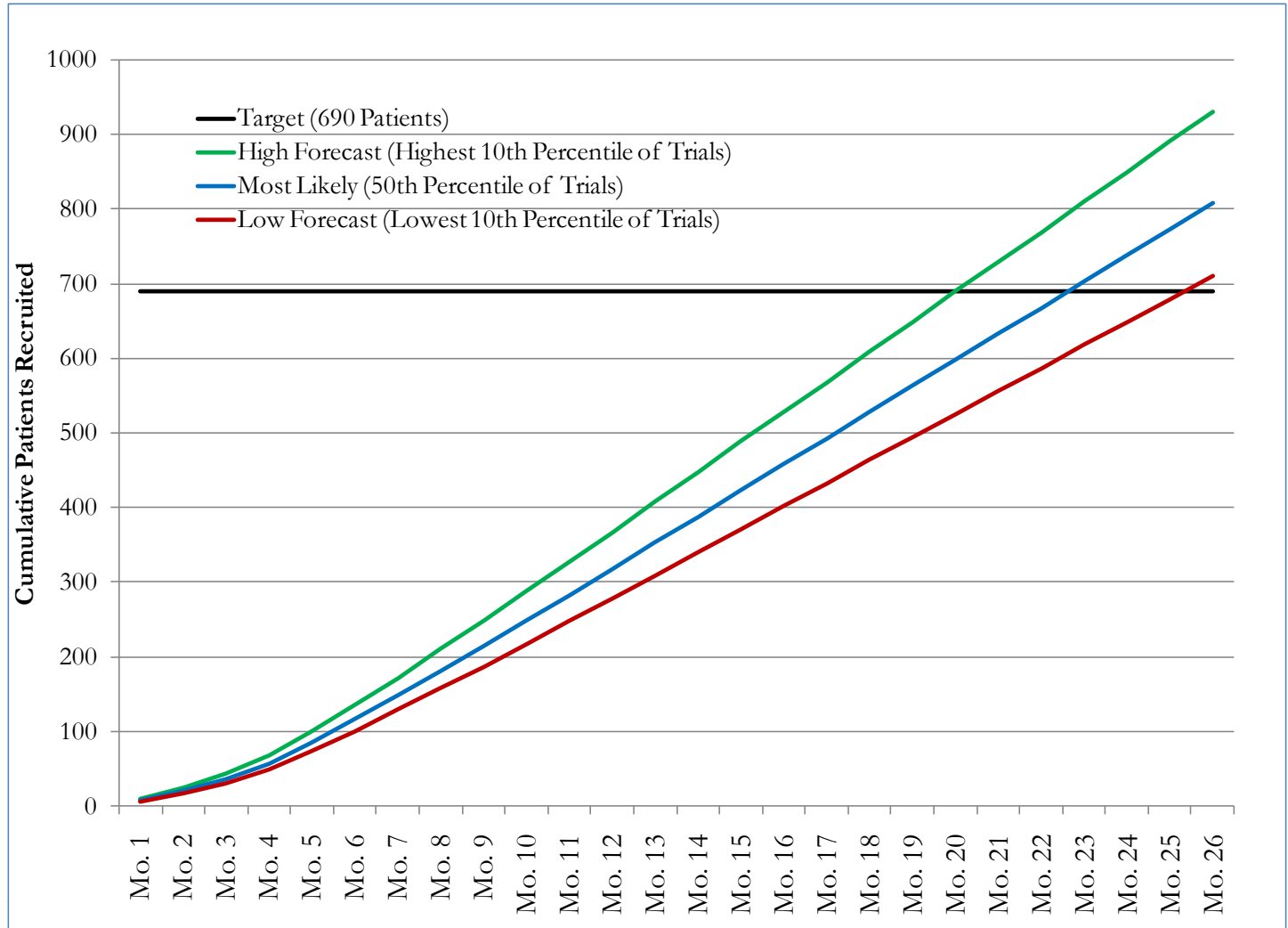
- Results on the following slides show probabilities for reaching the current enrollment goal, both for Trial Z as a whole and in each country.
- The figures are based on the 10,000 simulations conducted and reflect the percentage of these simulations that resulted in a higher or lower value than the target value.
- For example:
 - If a country is forecast to have a 100% probability of meeting the target enrollment rate, each of the 10,000 simulations resulted in a value equal to or greater than the target enrollment rate.
 - If a country is forecast to have a zero percent chance of meeting enrollment goals, none of the 10,000 simulations resulted in a value equal to or greater than the target enrollment rate.
 - If a country is forecast to have a 50% of meeting enrollment, half of the simulations were equal to or above the goal and half were below, etc.

Summary of Monte Carlo Analysis based on Original Trial Z Plan

- Barring major unforeseen circumstances, we found that Trial Z had a very high (94.7%) probability of meeting its enrollment goal of 690 patients by the end of Month 26.
- In other words, when the results of the 10,000 simulations conducted in each of the 23 countries were summed, the overall trial enrollment goal was missed in only 5.3% of cases.
- The most likely case (mean outcome of simulations) was that 816 patients would be enrolled by the end of the recruitment period.
- Even in the lowest 10th percentile of trials (a reasonable boundary for a “worst case scenario”) Trial Z enrolled approximately 712 patients, or 22 more than required, on schedule.

	<u>Trial Total</u>
Target Patient Enrollment	690
Enrollment period (months)	26
Number of investigative sites	208
Probability of Achieving Target by End of Enrollment Period	94.73%
Trial Z Enrollment at Month 26 (Results of 10,000 Simulations)	
Minimum Enrolled Patients	550.9
Lowest 10th Percentile (fewer than X patients recruited)	711.7
Mean Enrolled Patients	816.3
Median Enrolled Patients	809.4
Highest 10th Percentile (more than X patients recruited)	928.9
Maximum Enrolled Patients	1,306.3
Standard Deviation	86.8
Standard Deviation (%)	15.8%

Trial Z Patient Accrual Forecasts based on Original Plan



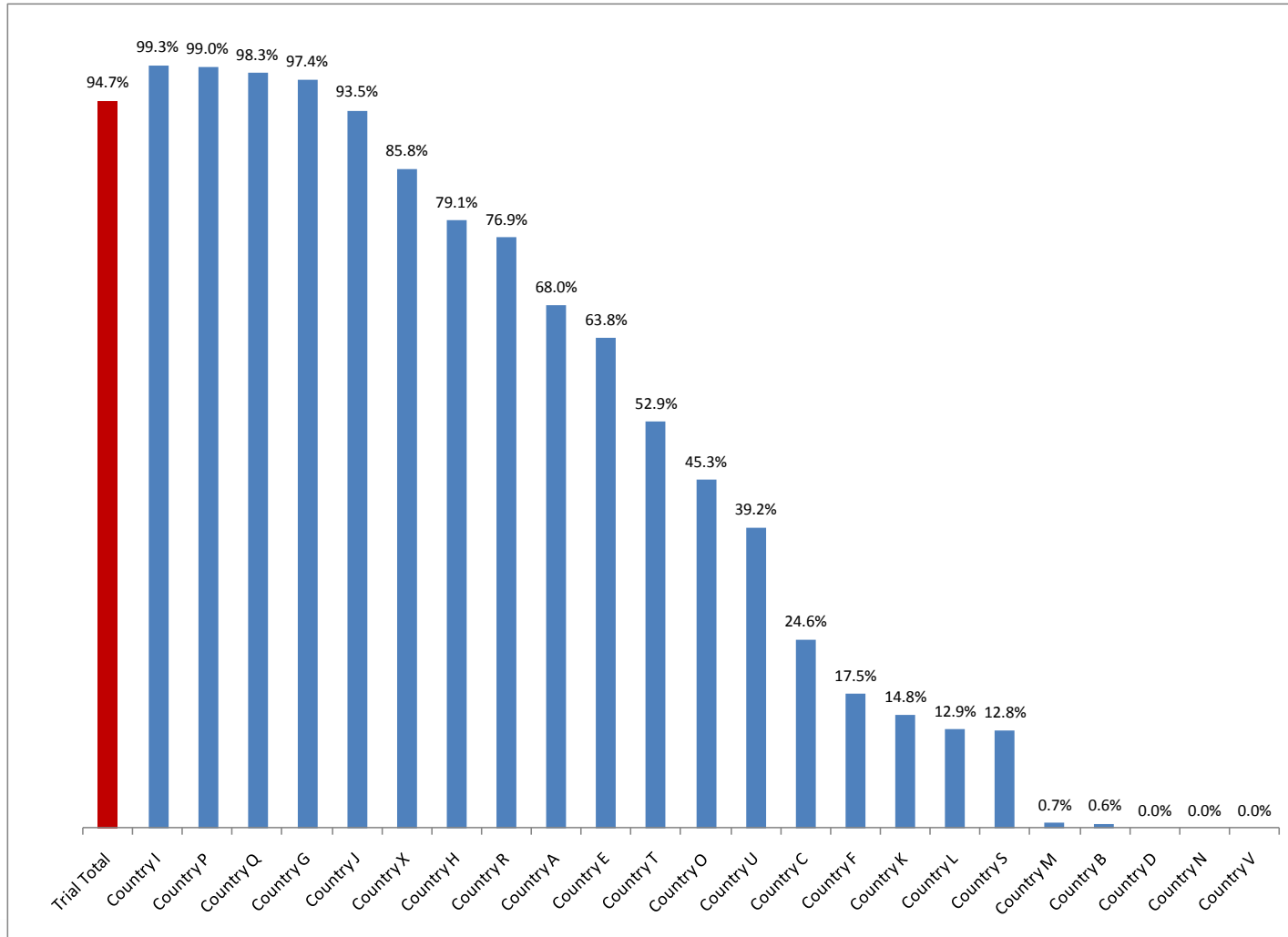
Interpreting the Results

- Clearly, Trial Z as originally planned was on target to meet its enrollment goals within the allotted timeframe.
- Was it, in fact, overpowered resulting in an inefficient use of resources?
 - After all, this is a major pharmaceutical company with dozens of trials going on at any given time.
 - By ensuring such a high probability of success, was Trial Z undermining the company's other research efforts?
- Ultimately, the answers will vary based on a company's goals.
- To this point, however, the trial had been designed using subjective judgment and internal ability to sway resources in the desired direction.
- Comparing the likelihood of success in individual countries held the promise of a more rational, more efficient approach.

Comparison of Sample Over and Under Delivering Countries

	Country I	Country O
Target Patients	20	18
Enrollment period (months)	26	26
Number of investigative sites	11	7
Probability of Achieving Target by End of Enrollment Period	99.30%	0.00%
Trial Z Enrollment at Month 26 (Results of 10,000 Simulations)		
Minimum Enrolled Patients	19.3	2.6
Lowest 10th Percentile (fewer than X patients recruited)	33.5	3.6
Mean Enrolled Patients	44.6	4.3
Median Enrolled Patients	43.7	4.3
Highest 10th Percentile (more than X patients recruited)	56.8	5.1
Maximum Enrolled Patients	99.1	12.0
Standard Deviation	9.3	0.8

Probability of Reaching Target Enrollment on Schedule based on Original Plan - Trial Z Total and Individual Countries



Phase IV: Optimizing Trial Locations Based on MCA

Applying the Results of the MCA Forecast

- The @Risk forecast clearly indicated that the country list and national enrollment targets could be adjusted to the benefit of Trial Z and the sponsor's bottom line.
- Original plan contained a built-in safety margin with more countries and more sites than necessary.
 - Indeed, some countries were essentially guaranteed to be a waste of resources while others had high capacity to host additional trial sites.
- Determining countries where the trial would over or under deliver, allowed us to reduce this safety margin without affecting the probabilities of success.
- Like “just-in-time” inventory:
 - If you don't understand the range of probable outcomes you have to maintain excess inventory and incur the associated carrying cost.
 - If you do understand probable outcomes, inventory (and carrying cost) can be reduced.

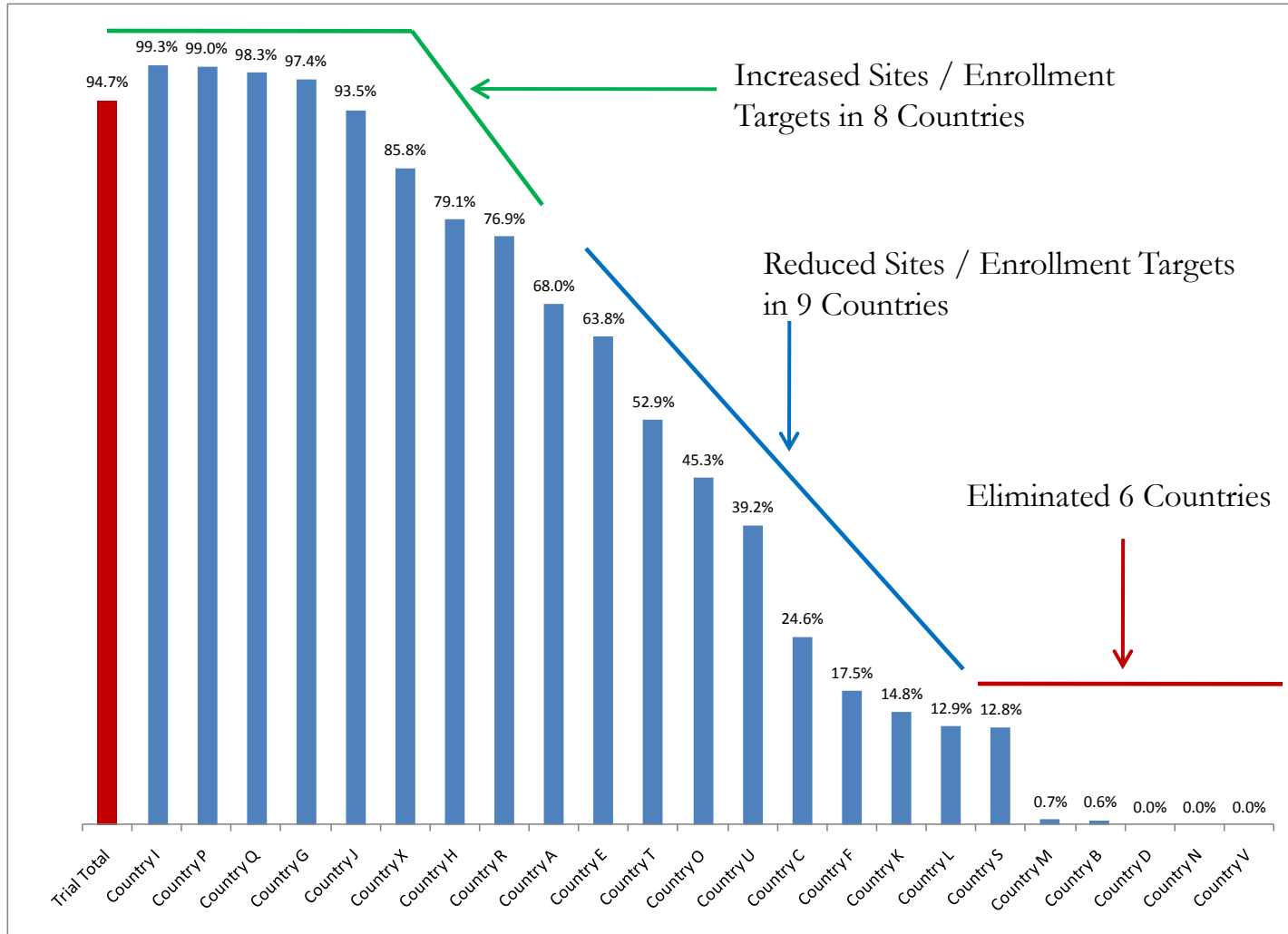
Phase IV: Optimizing Trial Location

- We continued our analysis to determine a mix of countries, enrollment targets and site rosters that would maximize the probability of success while minimizing the trial cost.
 - This was accomplished by applying optimization software to our Monte Carlo-based model and
- We then reran the @Risk simulation based on the revised list of trial locations.

- *Note: In the monetary figures on the following slide we have replaced our client's proprietary budget information with industry-standard averages derived from secondary research.*

Revisions to Trial Z Locations

(Chart shows probabilities of success based on original plan)



Results of Recommended Optimization Plan

- Without changing patient recruitment goals or schedules, the analysis allowed reduction in the number of scheduled countries from 23 to 17, the number of total sites declined by 24 and the budget was cut by nearly \$4.1 million, or 8.1%, of the total required under the original plan.
 - We estimate that the actual savings may be two or three times this level, as the costs associated with trial approval, site initiation and ongoing oversight are not fully captured in these figures.
- The savings were achieved with a miniscule (0.5%) reduction in the probability of successful on-time enrollment.
- Put another way, the cost of purchasing an additional 0.5% probability of success is at least \$4.1 million, a very inefficient use of funds.

	Original Plan	Recommended Revised Plan	Difference
Target Patient Enrollment	690	690	Unchanged
Number of Months	26	26	Unchanged
Number of Countries	23	17	-6
Number of Investigative Sites	208	184	-24
Total Budget in US\$ (000)	\$ 50,307	\$ 46,232	- \$ 4,075
Probability of Achieving Enrollment Target on Time	94.7%	94.2%	-0.5%

Conclusion

- There may be legitimate reasons for forging ahead with clinical studies in some countries where the trials will not reach enrollment goals
 - For example, the need to cultivate investigators for future research or the potential for improving local approval chances.
- However, this analysis clearly shows that there are significant benefits to be gained from adjusting the number of countries involved in Trial Z.

It is likely that most global clinical trial initiatives would see similar advantages using MCA – indeed, the advantages would probably be greater:

- First, 690 patients is not a particularly large Phase III effort and Trial Z required a limited number of courses of therapy and patient visits.
- Of importance, Cancer Y, tends to be substantially more prevalent in developed than in emerging countries.
 - As a result, the changes in our revised plan resulted in an increased level of activity in major markets and savings came primarily from a reduction in administrative costs associated with initiating the trial in multiple locations.
 - Savings would have been higher if the focus had been on another disease state that would have allowed a greater shift from high-cost developed markets to low-cost emerging markets.
- Further, Trial Z had a very high probability of reaching its recruitment goals both in the original and revised plans.
 - As a result, the opportunity costs associated with missing the enrollment deadline (e.g. delayed approval) was not a major factor.
- Most trials, however, are far less certain to meet their schedules, and this type of analysis would therefore offer the additional benefit of either reducing trial length or identifying unrealistic schedules.

Summary

- Monte Carlo Analysis offers decision-makers a substantially more meaningful form of forecasting than does standard spreadsheet modeling.
- Considering this, it is somewhat surprising that it has not become a more widely-used tool.
- In our projects, 80% of the work took place during the research phase:
 - For Trial Z, it was necessary to gather accurate research and conduct interviews needed to establish the 1,242 bits of data for 23 country-models with 54 variables each.
- Creating both the basic and Monte Carlo models consumed the remaining 20%.
- Since the research would have been conducted in any case, gaining a comprehensive understanding of the probabilities of success for Trial Z and the ability to reduce trial costs by approximately 10% was thoroughly worth the incremental effort.

Questions

Thank you for your attention!

Todd Clark

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- For those interested, the whitepaper from which this presentation is drawn is available via our website.

About VOI Consulting, Inc.

VOI Consulting is a life sciences advisory and publishing company dedicated to providing pharmaceutical and biopharmaceutical clients with fact-based analysis and business intelligence to meet market challenges in today's highly competitive global environment. By skillfully employing innovative research techniques and advanced analytical tools our services help clients minimize risks, cut costs and maximize commercial opportunities.

The VOI in our name translates to "Value of Insight" and plays on the statistical term "Value of Information," which describes the difference between expected outcomes in the absence of information and expected outcomes in the presence of information derived through applied research techniques, sound analysis and experienced judgment. For our clients – including 17 of the top 25 pharmaceutical companies – this insight translates into measurable success.

Our services are global in reach, are relevant for any therapeutic category and span the entire range of the pharmaceutical lifecycle. Whether our clients are planning a clinical trial or need to assess the market for a generic drug, whether they operate in developed countries or are looking at emerging opportunities in countries like China, India, Russia, Turkey or Latin America, VOI helps them execute better, faster and cheaper.

In addition to our strategic advisory services, Value of Insight Consulting (VOI) has published several dozen books, articles, reports and reference guides for the life sciences field. In particular, our annual publications, *PharmaHandbook: A Guide to the International Pharmaceutical Industry* and *GenericHandbook: A Guide to the US Multisource Drug Industry*, have become the standard resources on their respective topics with customers in more than 45 countries and highly favorable reviews in the business and academic press. VOI's reputation as a leading publisher of healthcare pharmaceutical industry reference books and in-depth pharmaceutical market research reports has distinguished the company well beyond its competition as a trusted source of research and analysis.

