Clinical Trials Infrastructure in Centres

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Objectives

- Identify infrastructure attributes of clinical trial site
- Gain understanding of processes and infrastructure involved in bringing a trial from concept to local activation
- Identify centre- and investigator-level strategies for efficient conduct of high-quality trials

Infrastructure

- Noun
  - The basic, underlying framework or features of a system or organization

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ASCO SPECIAL ARTICLE

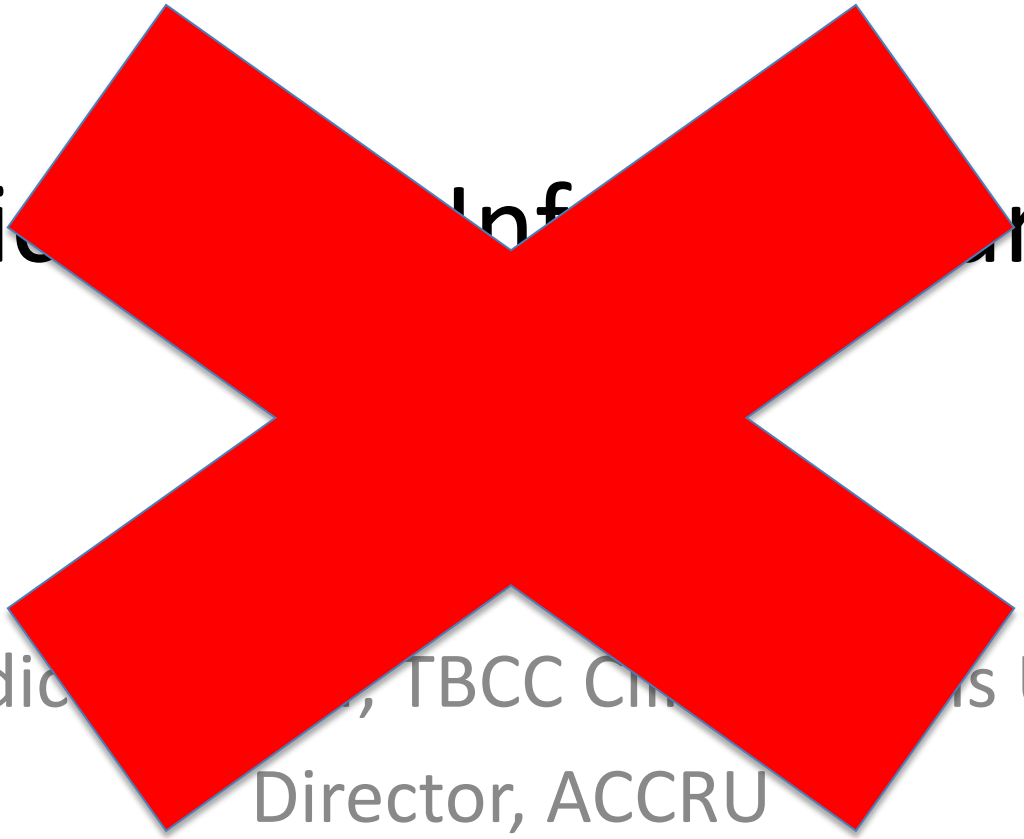
American Society of Clinical Oncology Statement on Minimum Standards and Exemplary Attributes of Clinical Trial Sites

Robin Zon, Neal J. Meropol, Robert B. Catalano, and Richard L. Schilsky

Infrastructure Requirements

- Non-physician staff
  - Dedicated research coordinator
  - Nursing, lab, pharmacy, administration
- Appropriate access to
  - Diagnostic imaging
  - Pathology, laboratory services
  - Pharmacy
- Quality Assurance
- High Educational Standards
  - At all levels, for GCP but also continuing education
- Diversification of trial portfolio, high accrual
- Clinical Trial Awareness Programs
- Legal department (contracts, liability coverage, etc.)
- Financial Oversight
  - Budgets, invoicing, payment tracking, etc.

Clinic Inf re in



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How To Avoid Becoming A Statistic

Bernie Eigl

Someone who's been there and is still trying to figure it all out

Question 1

- What is the average time from concept approval to central activation for a cooperative group study?
  - A. 2 months
  - B. 6 months
  - C. 1 year
  - D. 2 years
  - E. I’m still waiting, let you know when we get there.

Question 2

- What is the average time a study site takes to open a trial?
  - A. 3 weeks
  - B. 6 weeks
  - C. 12 weeks
  - D. 24 weeks
  - E. 36 weeks

Question 3

- What proportion of clinical trials meet their accrual targets at the time of closure?
  - A. 10%
  - B. 20%
  - C. 40%
  - D. 60%
  - E. 80%

Question 4

- What proportion of clinical trials are terminated after accruing ZERO patients?
  - A. 5%
  - B. 10%
  - C. 20%
  - D. 40%
  - E. 60%

Question 5

- What do these stand for?

- GCP
- GMP
- GLP
- GBP

Answers/Scenario

- You have a great concept, and pitch it to a receptive audience at NCIC (or CALGB, RTOG, industry, etc)
- How long before it is a “real” study, ready for sites to activate?

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JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Processes to Activate Phase III Clinical Trials in a Cooperative Oncology Group: The Case of Cancer and Leukemia Group B

David M. Dilts, Alan B. Sandler, Matthew Baker, Steven K. Cheng, Stephen L. George, Kathleen S. Karas, Stephen McGuire, Gourija S. Menon, Jason Reusch, Debbie Sawyer, Maren Scoggins, Amy Wu, Kai Zhou, and Richard L. Schilsky

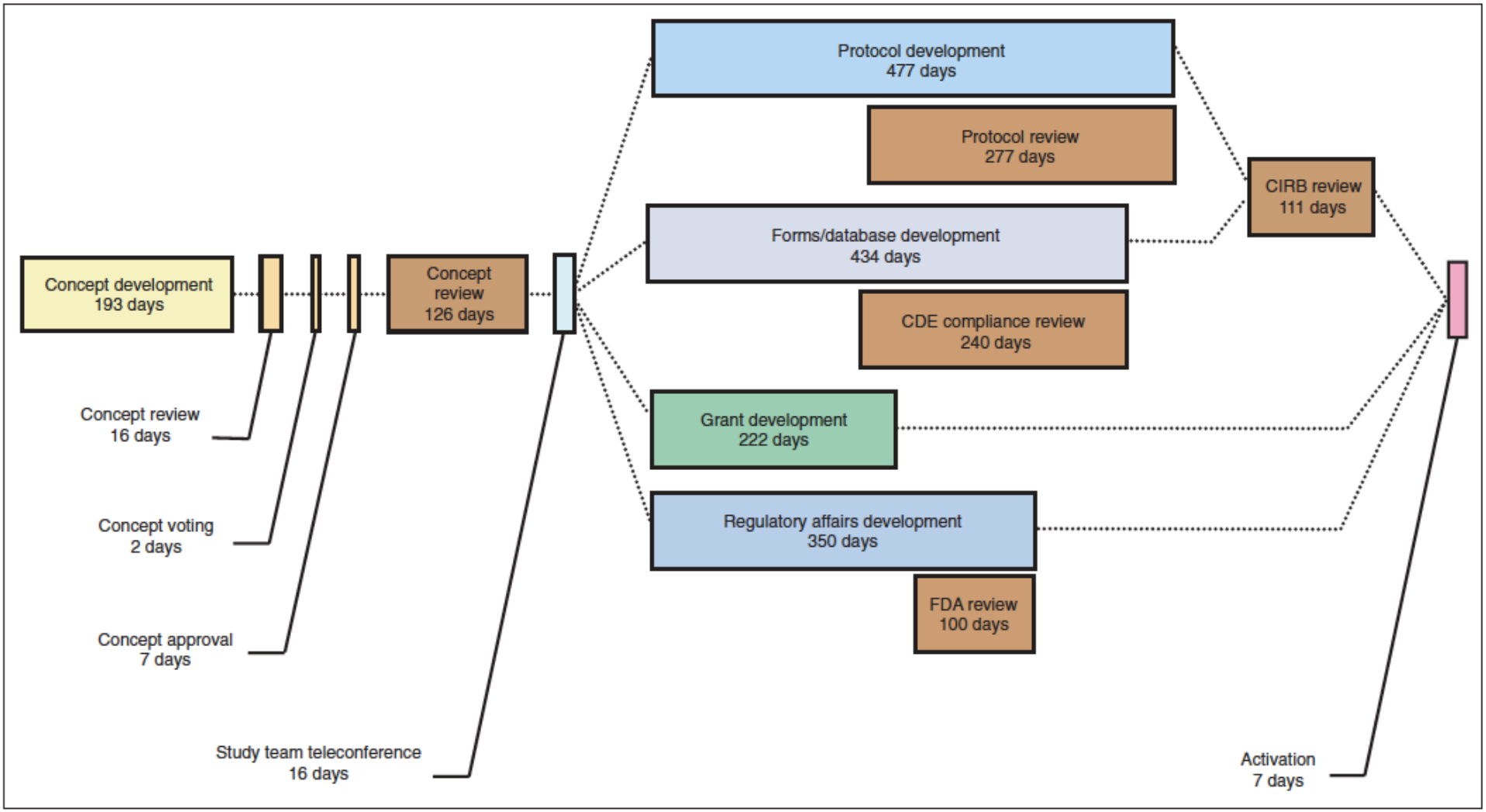
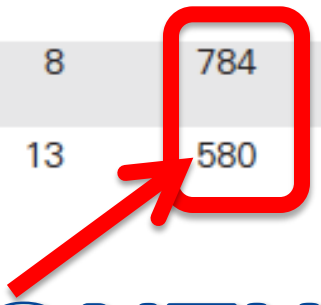

Protocol development
477 days
Protocol review
277 days
CIRB review
111 days
Forms/database development
434 days
Concept development
193 days
Concept
review
126 days
CDE compliance review
240 days
Concept review
16 days
Grant development
222 days
Concept voting
2 days
Regulatory affairs development
350 days
FDA review
100 days
Concept approval
7 days
Study team teleconference
16 days
Activation
7 days

Table 2. Calendar Days From Initiation to Final Approval for Each Major Process Step Required to Activate a Phase III Study

	No.	Median (days)	Range (days)
Initial development			
Concept development	8	193	77-309
CTEP concept review*	13	126	28-562
Study development			
Protocol development	13	477	266-1,200
CTEP protocol review*	13	277	83-467
Forms/database development	13	434	259-1,183
CDE compliance*	7	240	83-361
Grant development	5	222	169-302
Regulatory affairs development	6	350	113-496
FDA review*	4	100	43-157
Central institutional review board review*	13	111	46-320
Total days from initial concept receipt to study activation†	8	784	537-1,130
Total days from CALGB executive review to study activation	13	580	295-1,248



19 MONTHS!

Now the trial is ready for your site

- How long will it take you to get it activated and get your first patient on?

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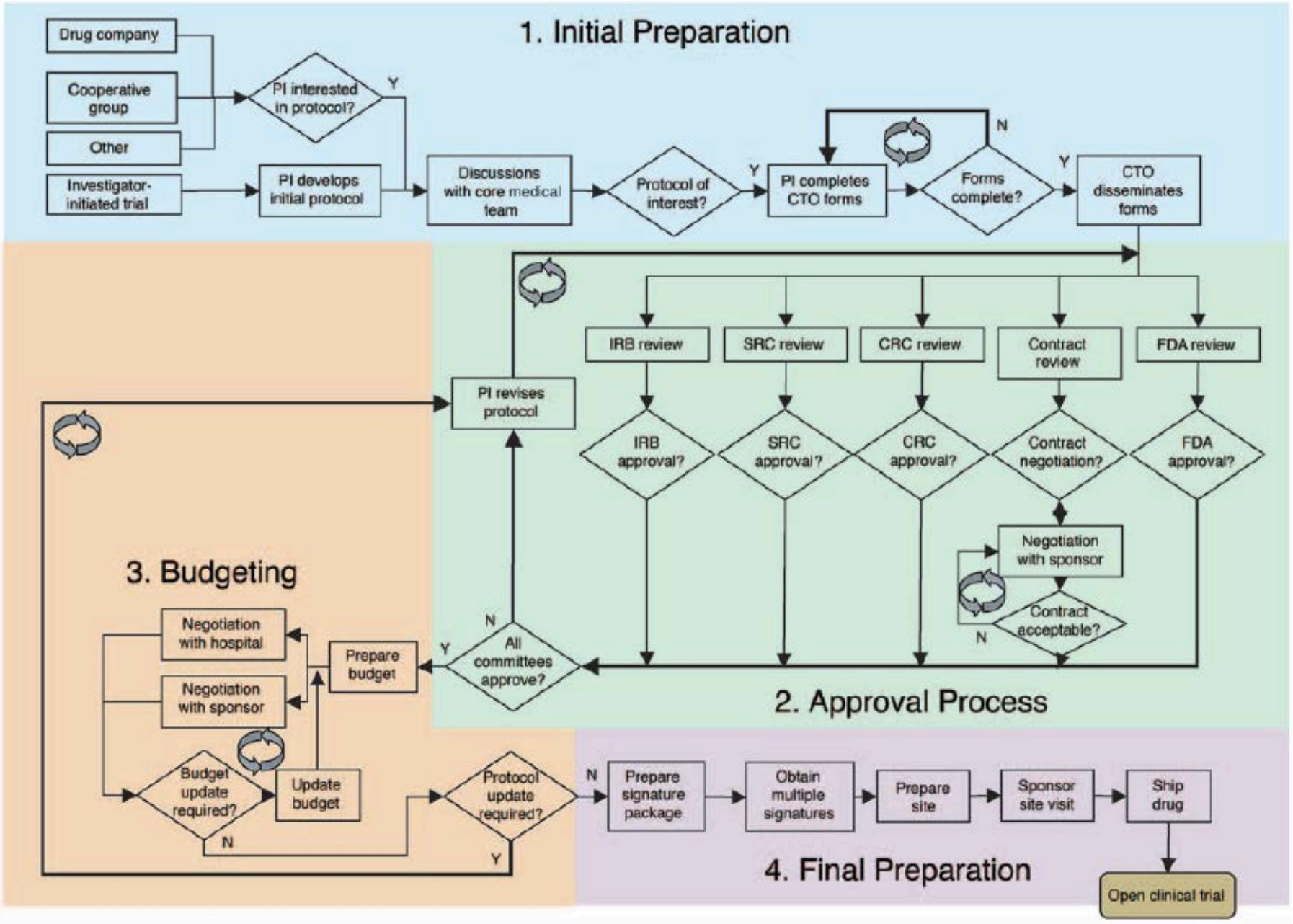
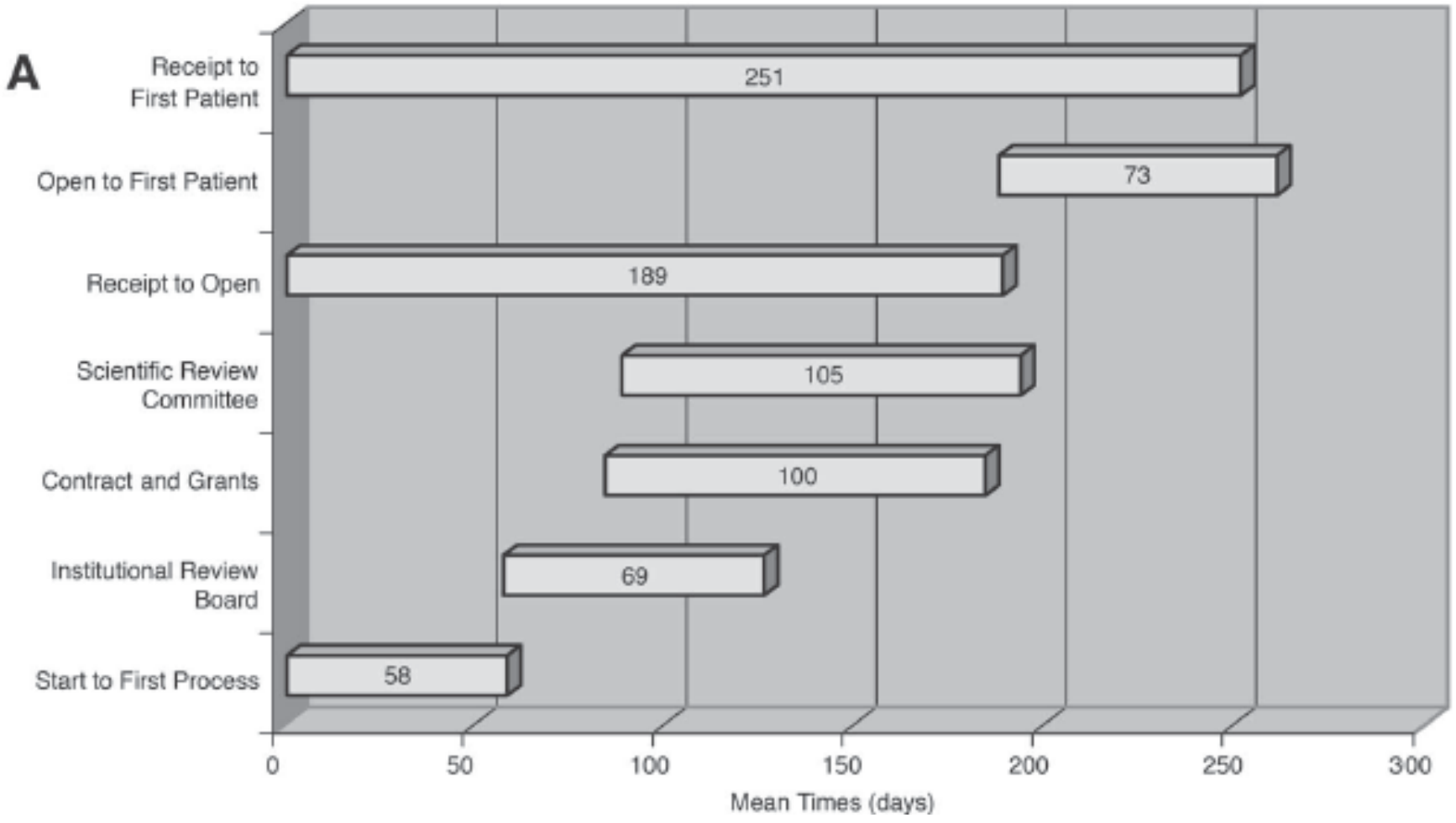
JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Invisible Barriers to Clinical Trials: The Impact of Structural, Infrastructural, and Procedural Barriers to Opening Oncology Clinical Trials

David M. Dilts and Alan B. Sandler


1. Initial Preparation
Drug company
Cooperative group
Other
Investigator-initiated trial
PI interested in protocol?
Y
PI develops initial protocol
Discussions with core medical team
Protocol of interest?
Y
PI completes CTO forms
N
Forms complete?
Y
CTO disseminates forms
IRB review
SRC review
CRC review
Contract review
FDA review
PI revises protocol
IRB approval?
SRC approval?
CRC approval?
Contract negotiation?
FDA approval?
Negotiation with sponsor
Contract acceptable?
N
N
All committees approve?
Y
2. Approval Process
3. Budgeting
Negotiation with hospital
Negotiation with sponsor
Prepare budget
Budget update required?
Update budget
N
Protocol update required?
Y
N
Prepare signature package
Obtain multiple signatures
Prepare site
Sponsor site visit
Ship drug
4. Final Preparation
Open clinical trial

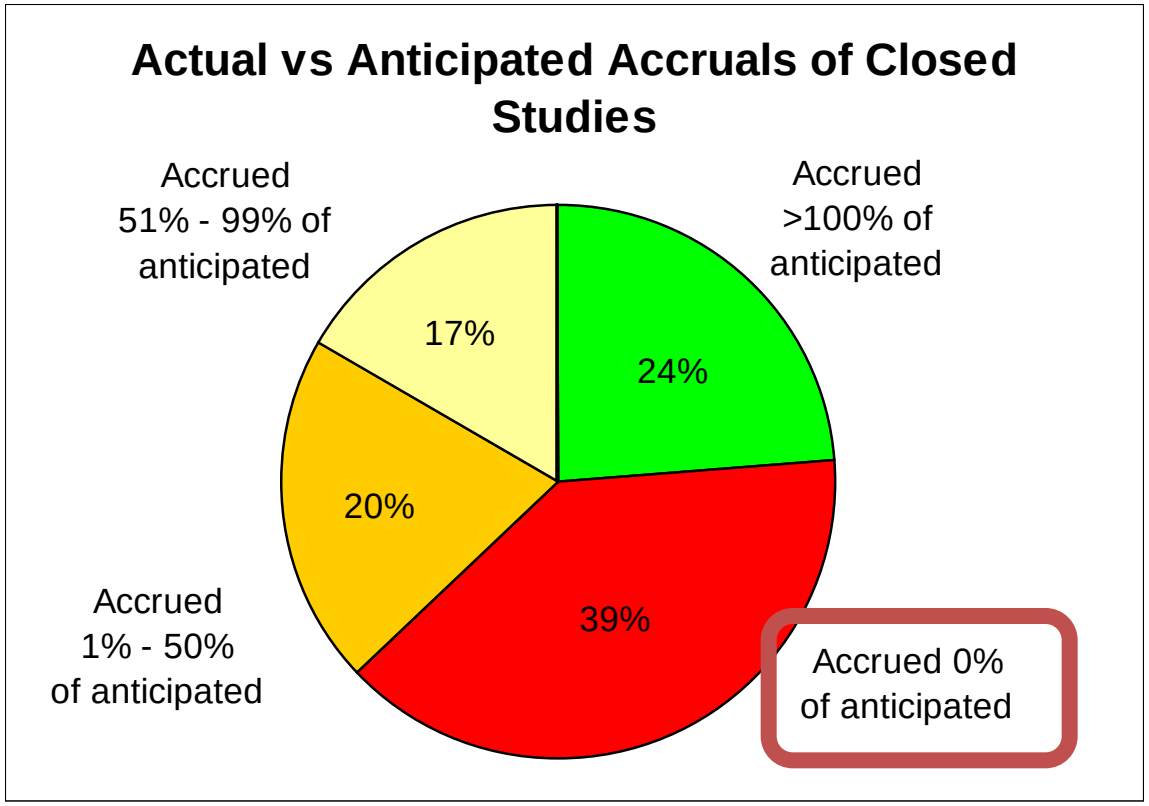

A
Receipt to First Patient
251
Open to First Patient
73
Receipt to Open
189
Scientific Review Committee
105
Contract and Grants
100
Institutional Review Board
69
Start to First Process
58
0
50
100
150
200
250
300
Mean Times (days)

Now you finally have it open!

- How well will you accrue?

Alberta Accrual Data

- 102 closed studies that had anticipated accrual data were reviewed



The average study accrued 55% of anticipated.

Alberta is not alone

Alberta:

24% of studies met or exceeded their accrual targets *(on average within 350 days from open date)*

39% of studies did not accrue any patients

From Literature:

Cheng et al. reviewed 765 NCI-CTEP sponsored studies

18.5% of these studies achieved their accrual targets *within the anticipated period*

*J Clin Oncol **28**:15s, 2010 (suppl; abstr 6001)*

Durivage et al. reviewed 2,864 cooperative group and industry sponsored studies at 14 centres

54.2% did not accrue any patients

*J Clin Oncol **27**:337s, 2009 (suppl; abstr 6557)*

Strategies

- Delegate actively, but …
- You are the driving force for your research
  - No one else will be
- Choose/develop trials that are very likely to succeed
  - Eligibility, departments impacted, budget, follow-up, correlative tests, competing studies, science

Strategies

- Identify and champion efficiencies within your centre's infrastructure
  - They are there
- Identify and eliminate "non-value-added" steps within your centre's infrastructure
  - They ARE there!
- Collaborate with others
  - "joy of shared wins", or "misery loves company"

Thank You/Questions