Activating & Opening Oncology Clinical Trials: *A Process & Timing Study*

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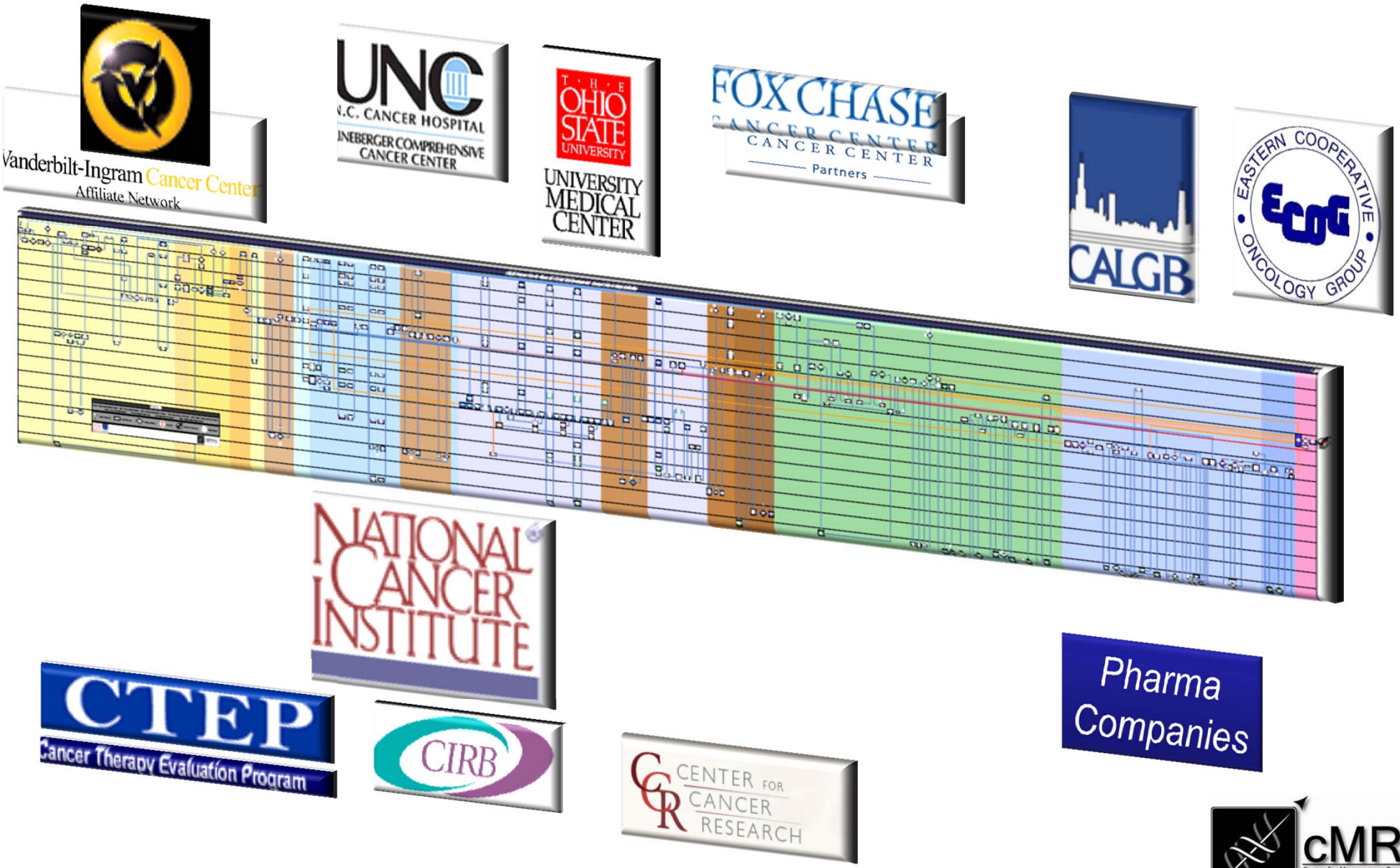
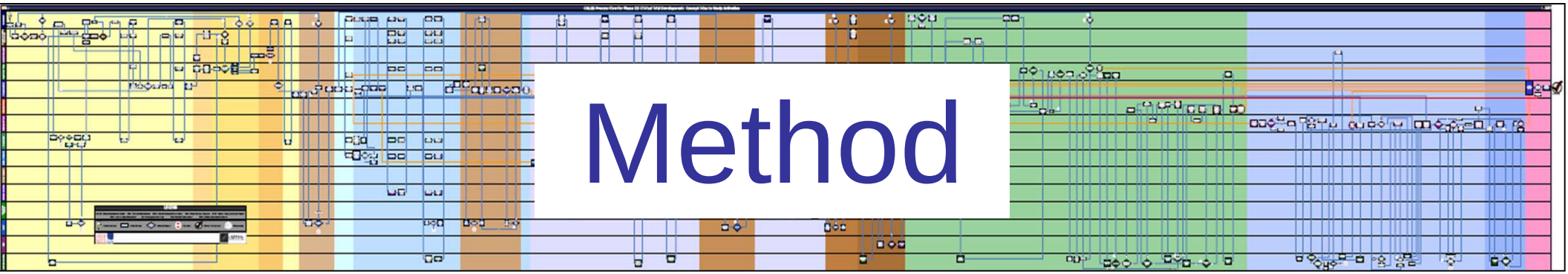
Thank you to the study sites





Method

Part I: Process Mapping

- Extensive visits at each site to document processes, loops and decisions:
  - *Say*…..: What they say they do
  - *Should*: What policies and procedures say they should do
  - *Do*……: What study chart reviews show they actually do
- Creation of process map

Part II: Process Timing

- Identify calendar time for total process and major steps, and potential influencers of the time

Part III: Accrual Data

- Investigate actual accrual results of the studies

- Dilts DM and Sandler AB (2006) "The Invisible Barriers to Opening Clinical Trials, *J Clinical Oncology,* 24(28): 4545-52
- Dilts DM, Sandler AB et al. (2006) "Processes to Activate Phase III Clinical Trials in a Cooperative Oncology Group: The Case of Cancer and Leukemia Group B," *J Clinical Oncology,* 24(28): 4553-57.

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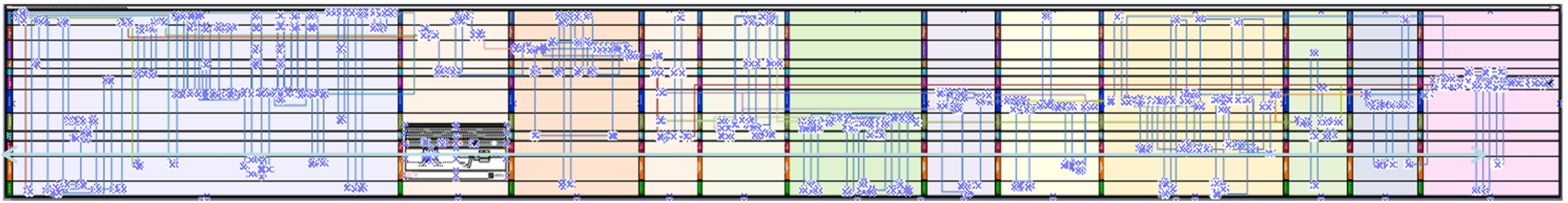
Detailed Process Maps

CCC-1



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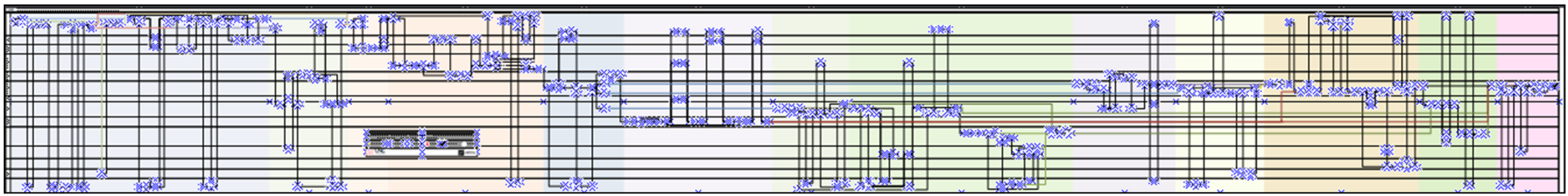
CCC-2



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Process Counts

Comprehensive Cancer Centers

		CCC-1*	CCC-2	CCC-3	CCC-4
Process Counts	Process Steps	117	374	345	
	…Working Steps	64	292	272	
	…Decision Points	53	61	62	
	…Processing Loops	-	31	27	
	Stopping Points	19	21	11	
Process Steps by Type of Trial					
	Investigator Initiated	-	180	234	
	NCI Initiated	-	131	n/a	
	Cooperative Group Initiated	-	77	74	
	Industry Initiated	-	144	169	

Activation & Opening Time

Phase III Cooperative Group Trials

@ Cooperative Groups and Comprehensive Cancer Centers (CCC)

	n	*Median*	*Min*	*Max*
CALGB	13	784	537	1130
ECOG	28	808	435	1604
CCC- 1	58	120	27	657
CCC- 2	3	252	139	315
CCC- 3	4	122	81	179
CCC- 4	178	116	21	836

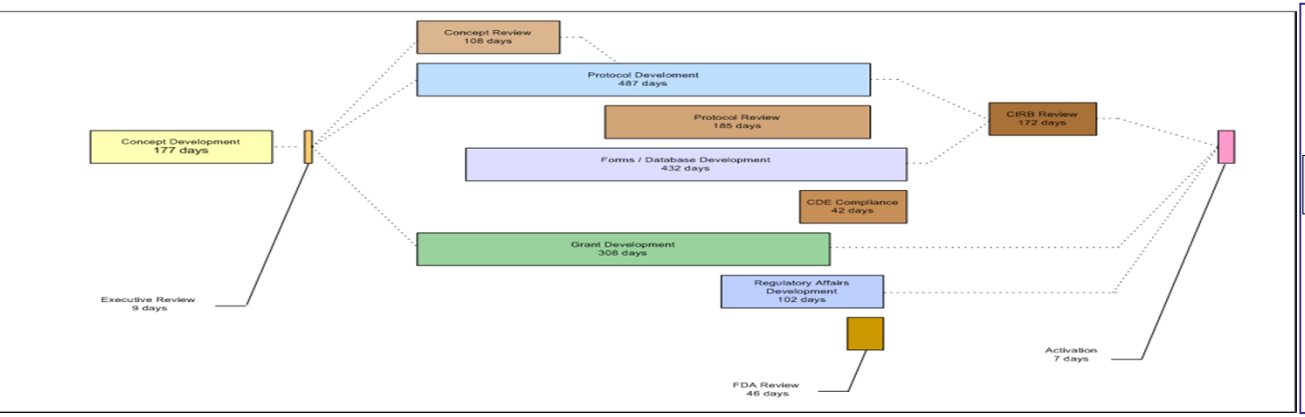
- Notes:
  - Receipt by *Group* or *AMC* to activation or opening
  - Time is calendar days, not work days
  - *These are lower bounds because only survivors were investigated*
  - *Total time to open a study is the addition of Group time + CCC time*

Days from Concept to Open *Investigator Initiated Trials (IIT)*

Comprehensive Cancer Center	*n*	*Median*	*Min*	*Max*
CCC-1	37	211	113	498
CCC-2	9	315	139	541
CCC-3	5	451	230	750
CCC-4	25	243	107	908

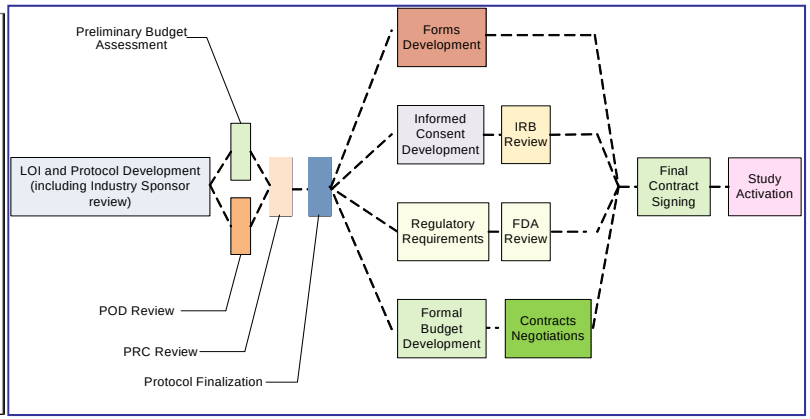
Total Processes to Open a Cooperative Group Study

Cooperative Group Processes



Median: 784 to 808 days*
Range: 435-1604 days

Comprehensive Cancer Center Processes



Median: 116 to 252 days*
Range: 21-836 days

* Depending Upon Site, based on the Phase III trials studied

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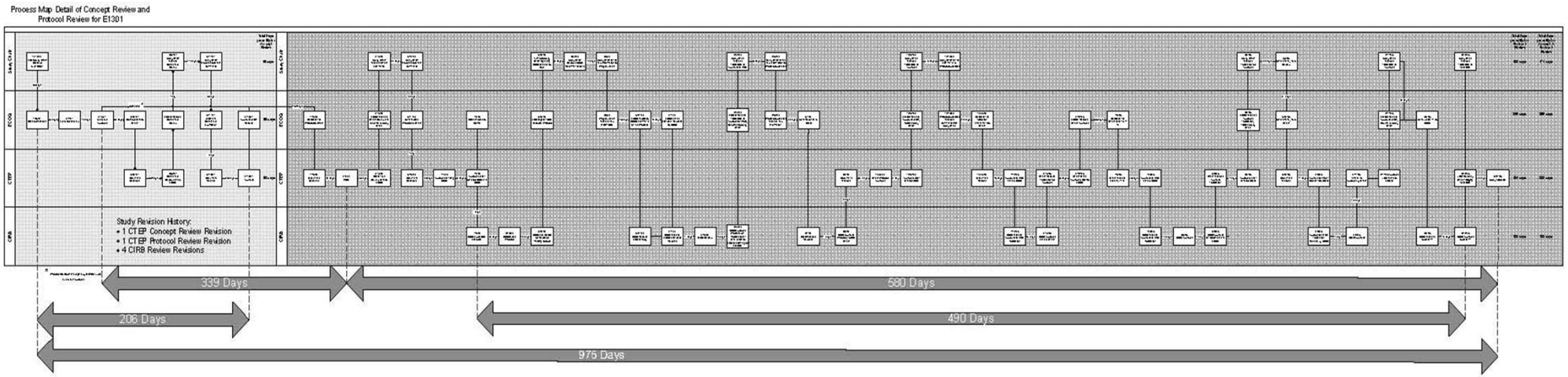
Example Of The Flow: *E1301*

	Concept Review Days	Protocol Review Days	Total Days
Study Chair	49	122	171
Cooperative Group	59	340	399
CTEP	98	184	282
CIRB	n/a	123	123
Total	206	769	975



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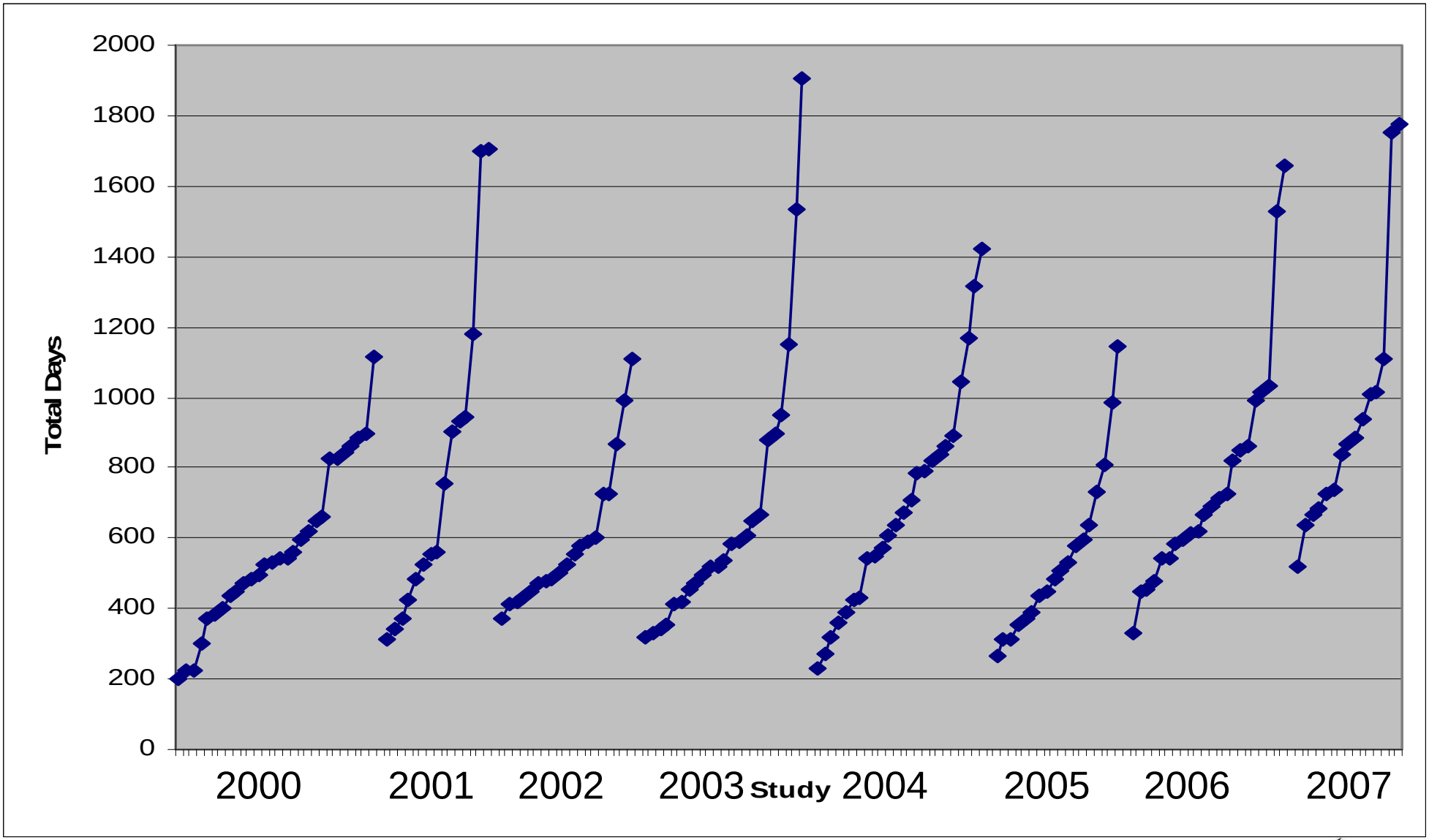
Time From Concept Receipt to Activation

Phase III Therapeutic Studies activated through CTEP 1/2000 – 6/2007†



By year

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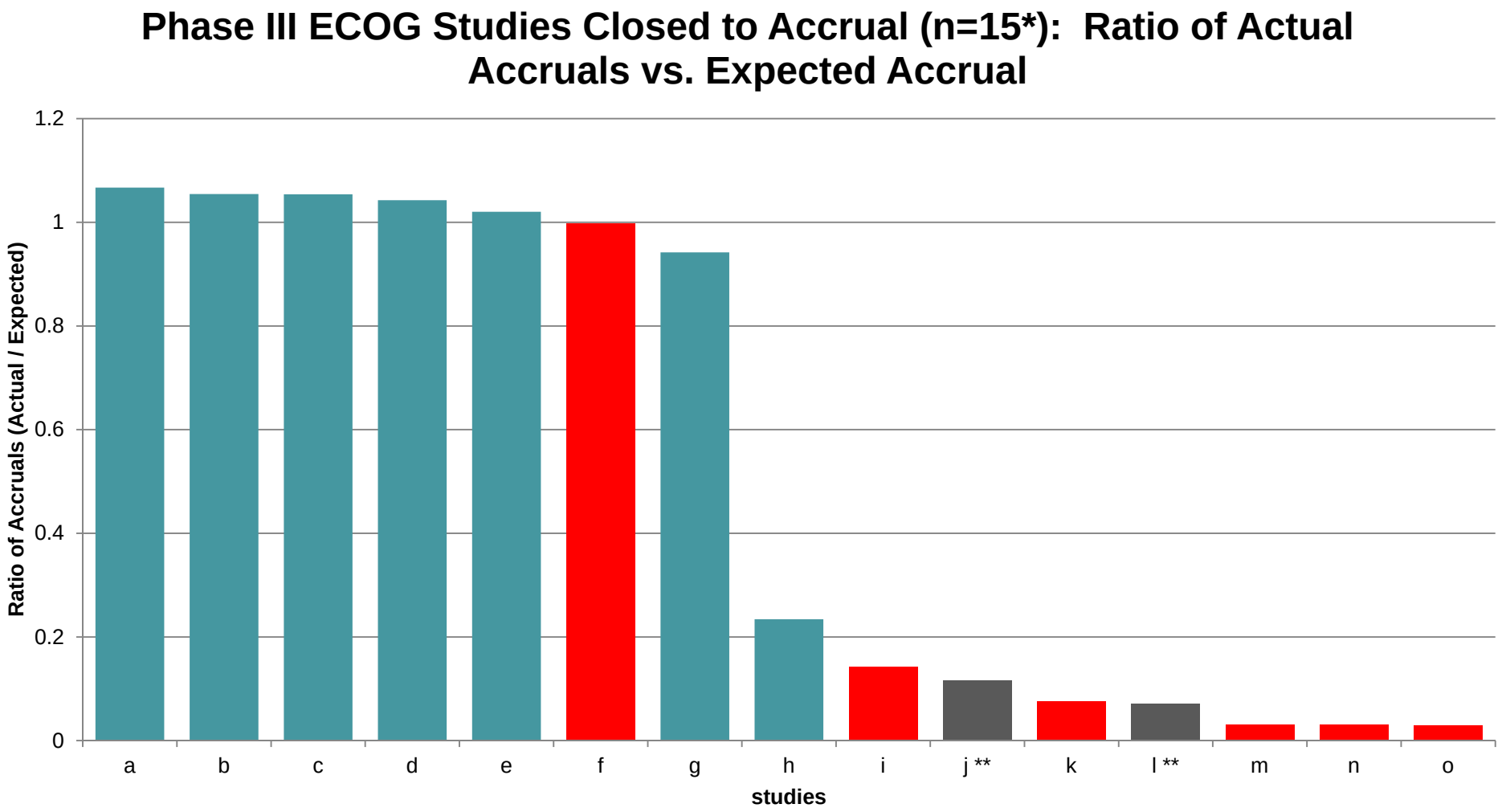
Actual Accrual Per Trial Ranges
Comprehensive Cancer Centers

Accrual Per Trial	***CCC-1***	***CCC-2***	***CCC-3***	***CCC-4***
0	20.6%	25.7%	27.7%	34.4%
1-4	33.0%	32.3%	30.3%	31.3%
5-10	19.3%	16.1%	22.7%	18.0%
11-15	11.0%	7.3%	8.4%	4.3%
16-20	3.7%	3.7%	3.4%	5.3%
>20	12.4%	15.0%	7.6%	6.8%

ECOG Phase III Accrual Performance



•All phase III studies activated and closed to accrual between 1/2000 – 7/2006
•Color Code:
- red : studies taking greater than the median time to open
- blue: studies taking less than the median time to open
- gray: studies closed due to reasons other than poor accrual

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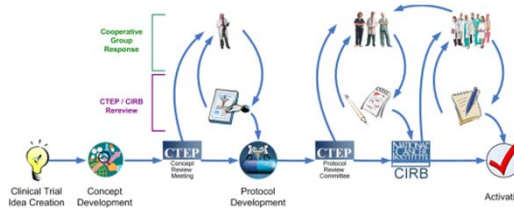
Initial Quick-Fix Recommendations

- Immediately start collecting & analyzing data
- "Just Say No"
  - Eliminate "entitlement culture"
- Stop tweaking
  - "Two strikes and you're out"
- Say what you mean & mean what you say

Simulation Results

* Simulation period defined over a period of 5 years (1825 Calendar Days)
* Note: Axes on the Timing Distribution Graphs are different



Initial Long Term Recommendations

- Start with a clean sheet of paper
- Develop and utilize standards
  - i.e., vary in critical scientific issues, not in administrative processes
- Use Focused Phase III Teams

Next Steps

- NCI intramural clinical trials program being studied
- CTAC Working Group forming
  - Results have been presented to Cancer Centers and Cooperative Groups
  - Collaboration and participation in the Working Group solicited
- Goal – cut clinical trial activation time in half