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Scientific Issues in the Registration of Clinical Trials

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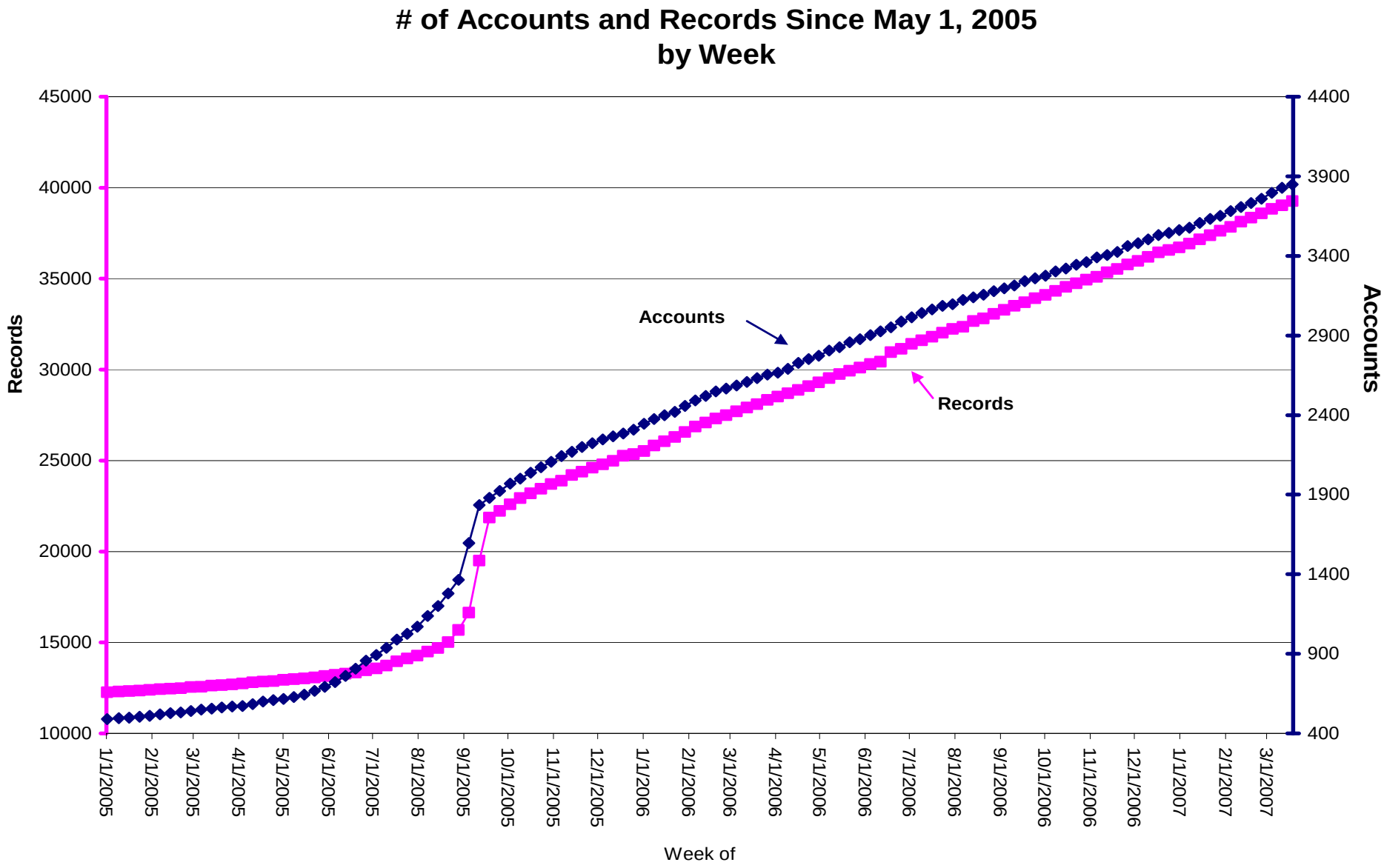
Table 1: Number and types of trials in ClinicalTrials.gov

Characteristics	Total Trials March 20, 2007
Total	38,739
Study Type	
Observational	5,619
Interventional	33,120
Provider Category	
Federal (including NIH)	14,926
Industry	10,533
University/Foundation/Other	13,280
Phase	
N/A	5361
I	5649
II	10,487
III	7,822
IV	3,786
Intervention Type*	
Drug	26,351
Device	1,918
Procedure	9,815
Behavioral, Therapy, Other	2,976

*** Not additive—trials may have more than one intervention type.**

Figure 1


# of Accounts and Records Since May 1, 2005
by Week
Records
Accounts
Accounts
Records
45000
40000
35000
30000
25000
20000
15000
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4400
3900
3400
2900
2400
1900
1400
900
400
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2/1/2005
3/1/2005
4/1/2005
5/1/2005
6/1/2005
7/1/2005
8/1/2005
9/1/2005
10/1/2005
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5/1/2006
6/1/2006
7/1/2006
8/1/2006
9/1/2006
10/1/2006
11/1/2006
12/1/2006
1/1/2007
2/1/2007
3/1/2007
Week of

Table 2:

Table 2: Comparison of Select Trial Registration and Results Policies

Policy Name	Policy Type	Intervention Type	Policy Scope	Inclusion of Provisions for Results
FDAMA, Sec. 113 [20]	Federal Law	Drugs and biologics	Efficacy trials for "serious or life-threatening diseases or conditions" regulated by FDA	No
ICMJE Statement [13]	Publication policy	Any[1]	"Clinically directive"[2] trials; Defines criteria for "acceptable registries"	No
WHO ICTRP [16]	WHO policy	Any	"all medical studies that test treatments on patients or healthy volunteers"	Yes
AAMC Principles [45]	Recommendation	Any	"All trials meeting the ICMJE requirements"	Yes
Ottawa Group[4]	Recommendation	Any	"prospective controlled or uncontrolled research study evaluating the effects of one or more health-related interventions assigned to human participants"; Defines criteria for "acceptable registries"	Yes
PhRMA Clinical Trial Registry Proposal and Principles[46]	Recommendation	Drugs only	"all company-sponsored hypothesis-testing (non-exploratory) clinical trials conducted on drugs and biologics marketed in the US or intended for marketing in the US, regardless of disease studied or the location of the trial."	Yes
IOM Report: Drug Safety[17]	Recommendation	Drugs only	"industry sponsors…at a minimum, all Phase 2 through 4 clinical trials, wherever they may have been conducted, if data from the trials are intended to be submitted to the FDA as part of an NDA, sNDA, or to fulfill a postmarket commitment."	Yes
Maine State Law[47]	State Law	Drugs only	Trials of "prescription drugs in this State" (of Maine); includes "biological products"	Yes
Enhancing Drug Safety and Innovation Act [36]	Bill introduced in U.S. Senate by Sen. Enzi (WY)	Drugs only	Some "exploratory" and all "confirmatory" and fast-track trials regulated by FDA	Yes
Fair Access to Clinical Trials (FACT) Act[37]	Bill introduced in U.S. Senate by Sen. Dodd (CT)	Drugs, biologics and devices	Ongoing trials for "serious and life-threatening diseases and conditions" regulated by FDA except Phase I safety trials; registration prerequisite for IRB approval.	Yes
Prescription Drug Right-to-Know Act, New Jersey State Bill[48]	Bill before State legislature	Drugs only	"each clinical trial that the company conducts or sponsors for each prescription drug that the company sells, delivers, offers for sale or gives away in this State" (of New Jersey)	Yes

[1] Includes drugs, biologics, devices, surgical procedures, and behavioral treatments.

[2] "Clinical Directive" is defined as "trials whose primary purpose is to affect clinical practice."

Table 3: Procedures Used by ClinicalTrials.Gov to Verify and Enhance the Validity and Quality of Reported Data Elements

	Use of Organizational Accounts	Pre-Registration Check for Required Data	QA for Logic, Internal Consistency	Links Verified; Inappropriate Links Removed	QA Edits of Specific Entries	Reminders to Update	Check of 3 Recruiting Sites	Request IRB Letter	Specific Usability Assessment
VALIDATION:									
Does the trial exist?	3						3	3	
Are sponsorship and other administrative data correct?	3							2	
Are protocol items accurate?	1					2		1	
Is recruiting information accurate and up-to-date?						2	3		
QUALITY ASSURANCE:									
Are entries informative, appropriate and complete?		3	3		3	3			
Is controlled vocabulary used whenever possible?		3	3		3				
Are "add-on" links appropriate and "live"?				3					
Can users get needed info?									3
Is the search engine operating to meet users' needs optimally?									3

*Legend: Numbers in the table reflect the application and utility of each validation/QA procedure: 3-Very Useful; 2-Moderately Useful; 1-Minimally Useful.

Table 4a: Example of Duplicate Trials Identified in Clinical Trials.Gov

Trial Registry Unique Identifier	NCT00399139	NCT00086684
Title:	An Effectiveness and Safety Study of Pentosan Polysulfate Sodium for the Treatment of Interstitial Cystitis	Efficacy and Tolerability of ELMIRON
Official Title:	A Randomized, Double-Blind, Placebo-Controlled, Parallel Group Evaluation of the Efficacy and Tolerability of Two Different Doses of Elmiron for the Treatment of Interstitial Cystitis	Multi-Center, Randomized, Double-Blind, PBO-Controlled Parallel Evaluation of the Efficacy and Tolerability of ELMIRON
Condition Under Study:	Interstitial Cystitis	Interstitial Cystitis
Interventions:	Pentosan Polysulfate Sodium	ELMIRON
Sponsors:	McNeil Consumer & Specialty Pharmaceuticals, a Division of McNeil-PPC, Inc.	Johnson & Johnson Pharmaceutical Research & Development, L.L.C.; McNeil Consumer & Specialty Pharmaceuticals, a Division of McNeil-PPC, Inc.; Ortho-McNeil Pharmaceutical

Table 4b: Example of Trials in ClinicalTrials.Gov Appearing to be Duplicates, but Sponsor Reports Are Not

Trial Registry Unique Identifier	NCT00168298	NCT00168324
Title:	A Study of the Safety and Efficacy of a New Treatment for Macular Edema Resulting From Retinal Vein Occlusion	A Study of the Safety and Efficacy of a New Treatment for Macular Edema Resulting From Retinal Vein Occlusion
Condition Under Study:	Macular Edema associated with retinal vein occlusion	Macular Edema associated with retinal vein occlusion
Interventions:	Dexamethasone	Dexamethasone
Sponsors:	Allergan	Allergan