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Memorandum

To: Trialists

Fr: Curtis Meinert

Re: Industry versus NIH drug trials: Registration, tabular results, and publications

This is the 3rd and last memo in this series. The first memo (distributed 14 November) dealt with the mix of trials done by industry and NIH. The second memo (distributed 29 November) provided information on sample size and time to completion of those trials. This memo provides information on registration, posting of results, and publications after completion.

Registration

The International Committee of Medical Journal Editors (ICMJE) requires that trials have to be registered before the start of enrollment to be eligible for publication; for trials starting after 1 July 2005. By that edict about 2/3rds of industry and NIH trials would be disqualified from publishing, as seen in the table below.

Counts are for completed drug trials with enrollment starting after 1 July 2005. Trials are counted as having been registered late if the date of registration is after the date of enrollment start.

	Industry-funded			NIH-funded		
	No. trials	Reg late	% late	No. trials	Reg late	% late
All drug trials	22,512	14,912	66.24	1,801	1,104	61.30
Phase 0	61	50	81.97	30	23	76.67
Phase 1	8,441	5,988	70.94	638	428	67.08
Phase 2	6,073	3,763	61.96	799	474	59.32
Phase 3	5,277	3,252	61.63	170	69	40.59
Phase 4	2,660	1,859	69.89	164	110	67.07

About 2/3rds of trials are registered after the start of enrollment. Allowing a 30 day grace period still means 18% of industry-funded trials and 27% of NIH-funded trials would be disqualified from publishing under ICMJE edict.

Clearly, registration is not the first thing trialists think of when planning trials. Even now, ten years after the edict, investigators are still lax registering before the start of enrollment. There were 3,559 drug trials registered starting enrollment in 2015 (3,291 industry and 268 NIH). Of those, 60% started enrollment before registration (1,984 industry and 159 NIH) and 40% were registered more than 30 days late (39% industry and 49% NIH). Fortunately, not even the editors signing the edict

stick to it and most of the 2,000 plus journals that have signed onto the policy do not pay heed to it when considering articles for publication.

Tabular results postings

Section 801 of the Food and Drug Administration Amendments Act of 2007 required operators of ClinicalTrials.gov to modify the registry to allow investigators to post results of completed drug trials. The Act required operators of the site to allow investigators to report:

Baseline characteristics;

Participant flow to indicate the number of participants at each stage of the trial;

and

Outcome data.

The Act requires sponsors or investigators to post summary results (identified in CinicalTrials.gov as "tabular results") within one year of completion of trials. The table below provides counts of postings by phase of trials for trials completed after 2007 through 31 December 2014. (Our dataset is through March 2016. The cutoff date of 31 December was chosen to allow at least a year after completion for postings.) Less than 50% of drug trials have postings.

	Industry-funded			NIH-funded		
	No. trials	Results posted	% posted	No. trials	Results posted	% posted
All drug trials	12,365	3,774	30.52	689	315	45.72
Phase 0	37	2	5.41	13	0	0.00
Phase 1	5,442	609	11.19	290	63	21.72
Phase 2	3,053	1,003	32.85	266	175	65.79
Phase 3	2,534	1,444	56.99	50	32	64.00
Phase 4	1,299	716	55.12	70	45	64.29

The Act carries provisions for up to $10,000 fines per day after the deadline for failure to post. Based on the counts observed, we could help balance our budgets by imposing the fine.

The trouble with postings (aside from the agony of fitting data into formats required) is two fold. First, it is unrealistic to assume data harvests are complete within one year of completion, especially in trials with event adjudication procedures after the trial is finished. Second, postings may remove incentives for publication.

Publications

There is a moral imperative to publish when a trial is completed and to do so regardless of the nature or direction of results. The imperative derives from the fact that research on human beings is undertaken with the promise of generating knowledge for the good of humankind. That commitment is violated when results are not published for repose in the world's medical libraries.

The NLM started indexing registration numbers in 2005, enabling the operators of ClinicalTrials.gov to troll for publications with CinicalTrials.gov registration numbers and to automatically post them to registration sites.

The counts below are of trials completed in 2005 through 2014 with one or more publications after the date of completion.

	Industry-funded			NIH-funded		
	No. trials	No. published	% published	No. trials	No. published	% published
All drug trials	20,090	2,091	10.41	1,591	611	38.40
Phase 0	59	7	11.86	26	10	38.46
Phase 1	7,492	416	5.55	569	236	41.48
Phase 2	5,423	658	12.13	708	250	35.31
Phase 3	4,688	703	15.00	142	58	40.85
Phase 4	2,428	307	12.64	146	57	39.04

The bad news is, as seen in the 2nd memo, it takes longer for the NIH to complete trials than industry, but the good news is that NIH investigators are much better at publishing results than their industry-funded counterparts.