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Memorandum

To: Trialists

Fr: Curtis Meinert

Re: Clinical trials by phase

My piece on 19 February entitled "Clinical trials and the NIH" generated a rich discussion. One of the questions raised had to do with what is happening to long-term trials. Some insight to that question can be garnered from counts on ClinicalTrials.gov classified as phase 3 or 4 trials defined on the site as follows:

Phase 3: Studies that gather more information about safety and effectiveness by studying different populations and different dosages and by using the drug in combination with other drugs.

Phase 4: Studies occurring after FDA has approved a drug for marketing. These including postmarket requirement and commitment studies that are required of or agreed to by the sponsor. These studies gather additional information about a drug's safety, efficacy, or optimal use.

Table 1: Percentages of trials by funding that are phase 3 or 4 trials

		NIH funded			Other funded		
	Total registered	No.	Phase 3 or 4	% phase 3 or 4	No.	Phase 3 or 4	% phase 3 or 4
2006	9,325	1,377	276	20.04	8,054	3,650	45.32
2007	11,128	1,247	207	16.60	9,987	3,704	37.09
2008	13,948	1,328	230	17.32	12,735	4,499	35.33
2009	13,721	1,166	212	18.18	12,655	3,820	30.19
2010	13,819	1,117	177	15.85	12,800	3,873	30.26
2011	14,204	1,056	149	14.11	13,243	3,946	29.80
2012	15,461	1,008	136	13.49	14,547	3,954	27.18
2013	16,187	1,047	114	10.89	15,217	3,862	25.38
2014	18,170	1,040	90	8.65	17,228	4,080	23.68

Table 2: Percentages of drug trials (phase 1, 2, 3, or 4) that are phase 3 or 4

		NIH funded			Other funded		
	Total registered	Phase 1, 2, 3, or 4	Phase 3 or 4	% phase 3 or 4	Phase 1, 2, 3, or 4	Phase 3 or 4	% phase 3 or 4
2006	9,325	1,094	276	25.23	6,594	3,650	55.35
2007	11,128	904	207	22.90	7,740	3,704	47.86
2008	13,948	900	230	25.56	9,527	4,499	47.22
2009	13,721	826	212	25.67	9,151	3,820	41.74
2010	13,819	790	177	22.41	8,836	3,873	43.83
2011	14,204	718	149	20.75	8,993	3,946	43.88
2012	15,461	614	136	22.15	9,117	3,954	43.37
2013	16,187	600	114	19.00	8,674	3,862	44.52
2014	18,170	538	90	16.73	9,887	4,080	41.27

Table 3: Percentages of all trials that are drug trials (phase 1, 2, 3, or 4)

		NIH funded			Other funded		
	Total registered	All trials	Phase 1, 2, 3 or 4	%	All trials	Phase 1, 2, 3 or 4	%
2006	9,325	1,377	1,094	79.45	8,054	6,594	81.87
2007	11,128	1,247	904	72.49	9,987	7,740	77.50
2008	13,948	1,328	900	67.77	12,735	9,527	74.81
2009	13,721	1,166	826	70.84	12,655	9,151	72.31
2010	13,819	1,117	790	70.73	12,800	8,836	69.03
2011	14,204	1,056	718	67.99	13,243	8,993	67.91
2012	15,461	1,008	614	60.91	14,547	9,117	62.67
2013	16,187	1,047	600	57.31	15,217	8,674	57.00
2014	18,170	1,040	538	51.73	17,228	9,887	57.39

The percentages of trials classified as phase 3 or 4 has fallen to about half of what they were in 2006, whether NIH or other funded (Table 1). Likewise, the percentages of drug trials (phase 1, 2, 3, or 4) that are classified as phase 3 or 4 has fallen (Table 2). Also, the percentages of trials that are drug trials (phase 1, 2, 3, or 4) have fallen (Table 3) suggesting a shift of emphasis in the trials enterprise.

The results are consistent with diminished size and length of followup for trials over the time interval covered, assuming phase 3 and 4 trials involve larger sample sizes and longer periods of followup than phase 1 and 2 drug trials. Not a direction we should be heading.