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Memorandum

To: Trialists

Fr: Curtis Meinert

Re: Please help Dear Lord

Registration of trials became a reality in 2000 with launch of ClinicalTrials.gov (herein CT.gov) by the NIH's National Library of Medicine.

Prior to registration the only means of tracking trials was via publication – an obvious biased subset since only a fraction are published.

The requirement came as a result of the Food and Drug Administration Modernization Act of 1997 (FDAMA). Technically, it pertains only to trials done under FDA regulations, but the push has been for registration of all trials, whether or not under FDA control.

The International Committee of Medical Journal Editors (ICMJE) gave registration a push in 2004 with the edict that

> *member journals will require, as a condition of consideration for publication, registration in a public trials registry. Trials must register at or before the onset of patient enrollment. This policy applies to any clinical trial starting enrollment after July 1, 2005. For trials that began enrollment prior to this date, the ICMJE member journals will require registration by September 13, 2005, before considering the trial for publication.* (JAMA **2004**; 292:1,363-1,364)

In 2007 requirements were expanded in the Food and Drug Administration Amendments Act of 2007 (FDAAA). The Act (for trials under FDA control) required investigators to post summary results to registrations within one year of completion of trials with penalties of up to $10,000 a day for every day late beyond the one year time period. But again the push has been for posting results for all trials, whether or not under the control of the FDA.

Trialists have been pushed to register by sponsors, by the FDA, by the public as an ethical obligation, by meta-analysts concerned with publication bias, and by threats of hefty fines for failure to report results on registration sites. So, with those urging, demands, and threats, what is the impact on compliance to the registration requirement?

All we can do is make "educated" guesses and hope the profile for trials not registered is the same as for registered trials. Unlikely.

There are lots of reasons to want to know about registration uptake, but making those assessments are akin to astronomers looking for color shifts as they gaze into the cosmos trying to determine if the universe is expanding or collapsing. We need research on compliance to registration requirements.

During the Ministerial Summit on Health Research in November 2004, participants called for "a network of international clinical trials registers". The following year the WHO launched its International Clinical Trials Registry Platform (ICTRP) of regional networks; now 17.

CT.gov is a partner registry with the WHO ICTRP, but does not share data with the ICTRP. This divide is one of the reasons why there are no studies comparing characteristics of trials registered on CT.gov with those registered on WHO regional sites.

Regional registrations have local appeal, but they erode the purpose of registration. Registration is predicated on the assumption that all trials, regardless of where registered, will be counted. That is difficult with 17 sites, each with its own data system. As a result most analyses are limited to registrations on CT.gov because of its data system. The downside is that CT.gov account for less than 60% of all registered trials, meaning we are left guessing about the other 40%.

The table below gives counts of trials registered on CT.gov and the 17 ICTRP sites. Blanks denote registries where we were not able to get counts.

Note that counts in the table below are for trials, exclusive of observational studies.

Some sites allow for registration of observational studies, but the registration mandate is for trials. There are no requirements for registration of observational studies. The primary value in registering them is for people looking for observational studies to join.

If we are to reap the benefits of registration, we need a single unified system – not 18.

The opportunity for a single system existed when CT.gov was launched but faded when the WHO created a competing system of regional registries in 2006 with launch of the International Clinical Trials Registry Platform (ICTRP); now having 17 registries.

The 17 registries and CT.gov should be merged into one file, with English as the base language. The International language of aviation is English for obvious reasons. The same should apply to trials since they have a common scientific basis regardless of where done.

How many registries do we need before the powers that be recognize the current system needs to be fixed?

The longer we go, the more difficult it will be to create a single universal system.

Please help Dear Lord!

Trials registered on CT.gov and on the 17 sites in the WHO registration platform

	Name/website	Trials*	% of total	As of date
	CT.gov	305,388	55.27%	26 Oct 2021
	WHO registration platform			
1	Australian New Zealand Clinical Trials Registry (ANZCTR)	18,769	3.40%	26 Oct 2021
2	Brazilian Clinical Trials Registry (ReBec)	5,133	0.93%	26 Oct 2021
3	Chinese Clinical Trial Registry (ChiCTR)	51,762	9.37%	26 Oct 2021
4	Cuban Public Registry of Clinical Trials (RPCEC)			
5	EU Clinical Trials Register (EU-CTR)	41,039	7.43%	26 Oct 2021
6	German Clinical Trials Register (DRKS)	7,049	1.28%	26 Oct 2021
7	India Clinical Trials Registry (CTRI)			
8	Iranian Registry of Clinical Trials (IRCT)	30,103	5.45%	26 Oct 2021
9	ISRCTN Registry (ISRCTN)	21,268	3.85%	26 Oct 2021
10	Japan Primary Registries Network (JPRN)	52,304	9.47%	26 Oct 2021
11	Pan African Clinical Trial Registry (PACTR)	2,782	0.50%	26 Oct 2021
12	Peruvian Clinical Trial Registry (REPEC)	1,948	0.35%	26 Oct 2021
13	Republic of Korea Clinical Research Information Service (CriS)	4,892	0.89%	26 Oct 2021
14	Sri Lanka Clinical Trials Registry (SLCTR)	210	0.04%	2017; PMID: 29322622
15	Thai Clinical Trials Registry (TCTR)			
16	The Netherlands National Trial Register (NTR)	9,774	1.77%	26 Oct 2021
17	Lebanese Clinical Trials Registry (LBCTR).	107	0.02%	26 Oct 2021
	Total	552,528		

* Exclusive of observational studies; trials only