Characterizing Sponsor-Imposed Restrictions on Disclosing Results of Clinical Trials

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Objective

To characterize the types of sponsor-principal investigator (PI) results disclosure restrictions reported to ClinicalTrials.gov (*as required by law*) to improve the existing categorization scheme.

Introduction

Concern about undisclosed conflicts of interest and associated withholding of trial data is growing. An FDA Amendments Act (FDAAA)[1] provision mandating public disclosure of agreements that restrict the PI's ability to disclose results became effective on September 27, 2008.

As part of its implementation of this provision of FDAAA, ClinicalTrials.gov (http://ClinicalTrials.gov) includes categories regarding sponsor review and embargoes (*see* Figure), which are based on published results of surveys of trial sponsors and organizations that conduct trials[2]. These "default" embargo categories address agreements where sponsors can only review results communications during the embargo period but cannot require any changes or extensions.

If the categories do not apply, "Other" can be selected and an optional 500-character text field may be used to describe the agreement, such as provisions allowing the sponsor to require changes, ban the communication, or extend an embargo.

Figure. Algorithm for Characterizing Restrictions and Sample Display at ClinicalTrials.gov

Certain Agreements:

Principal Investigators are **NOT** employed by the organization sponsoring the study.

There **IS** an agreement between Principal Investigators and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

The agreement is:

☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **less than or equal to 60 days**. The sponsor cannot require changes to the communication and cannot extend the embargo.

☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **more than 60 days but less than or equal to 180 days**. The sponsor cannot require changes to the communication and cannot extend the embargo.

Other disclosure agreement that restricts the right of the PI to discuss or publish trial results after the trial is completed.

☑ **Restriction Description:** Individual investigators are restricted from disclosure of results until 24 months after the completion of the Study at all participating research centers. Sponsor can review results communication prior to public release and can embargo communications regarding trial results for a period that is more than 60 days but less than or equal to 180 days.

Design

We evaluated the sponsor-imposed restriction data elements reported for 594 registered clinical studies with results posted at ClinicalTrials.gov on August 17, 2009. All full-text descriptions provided for the "Other" category were assessed, coded, and reviewed by two authors.

Results

Overall, of the 513 studies for which PIs were not employees of the sponsor, 415 (81%) indicated a restriction (*see* Table 1):

- 35 (8%) impose embargoes ≤60 days,
- 72 (17%) impose embargoes >60 days and ≤180 days, and
- 308 (74%) described "Other" restrictions.

Across all restricted studies, the majority (405/415) were sponsored by Industry. Of the 396 "interventional" studies reporting restrictions, there were 150 (38%) phase 1-2 trials and 237 (60%) phase 3-4 trials.

Of the unrestricted studies, the majority (67/98) were non-Industry sponsored. Among the 89 "interventional" studies, there were 24 (27%) phase 1-2 trials and 42 (47%) phase 3-4 trials.

Table 1. Schematic of Restrictions by Funder and Study Phase (8/17/09)

	PI Employed by Sponsor	PI Not Employed by Sponsor				Total
		No Disclosure Restrictions	Type of Disclosure Agreement			
			Embargo		"Other"*	
			≤60 Days	>60 & ≤180 Days		
All Results	81	98	35	72	308	594
Primary Sponsor						
Industry	52	31	27	72	306	488
Non-Industry	29	67	8	0	2	106
Study Type						
Observational	1	9	6	0	13	29
Interventional	80	89	29	72	295	565
Phase 1 – 2	16	24	12	28	110	190
Phase 3 – 4	47	42	16	44	177	326
N/A	17	23	1	0	8	49

* No descriptive text was provided for 9 "Other" Disclosure Agreement Types

Within the "Other" category, the following were addressed (*see* Table 2):

(1) **After Multi-Site Results Disclosure** – Sponsor-prohibited disclosure of study results until the multi-site study results are disclosed (153/308), including those permitting disclosure by the PI if no publication occurs within a particular time limit after study completion (88/153);

(2) **Control of Content** – The rights of a sponsor to review, edit, or approve communications (298/308); and

(3) **Embargo with Content Restrictions** – Sponsor-imposed embargo for a specific period of time in conjunction with other "control of content" restrictions (182/308)

In general, sponsors used consistent, standardized text for their entries.

Table 2. Analysis of "Other" Sponsor-Imposed Restrictions (8/17/09)

"Other" Restriction Areas	Number of Trials (N = 308)	Number of Sponsors (N = 57)*
After multi-site results disclosure	**153**	**22**
No time limit specified	65	8
Time limit specified, after study completion	88	15
12 months	60	8
18 months	22	3
24 months	7	4
Control of Content	**298**	**55**
PI not permitted to disclose**	59	6
Sponsor written consent/approval	19	15
Sponsor can change confidential information only or delay disclosure (e.g., patent pending)	103	20
Sponsor review & comment, including "Good faith"/"mutually agreeable" resolution of differences	60	20
Unspecified**	57	7
Embargoes with Content Restrictions	**182**	**46**
≤60 days	135	28
>60 and ≤180 days	16	9
Unspecified amount of time	31	18
Extended Embargo for Confidential Information	**62**	**15**

*Subcategories are not additive: a sponsor may have several types of agreements **Not associated with an embargo time period

Discussion

Of the studies with sponsor-imposed restrictions on results disclosure, 74% (308/415) were not captured by existing embargo categories at ClinicalTrials.gov.

Limitations of this analysis relate to both the sponsor-provided text describing "Other" disclosure agreements as well as the categories to which we assigned this text. For example, non-specific language was difficult to code accurately and restrictions specified infrequently in the sample (e.g., interim results, press releases) were not captured by our categories.

Despite these limitations, our analysis suggests that additional categories would more accurately reflect common restrictions.

Conclusion

Developing and implementing additional categories of results disclosure restrictions could enhance transparency by providing consistent, comprehensive descriptions common to sponsor-PI agreements.

Background on ClinicalTrials.gov (http://ClinicalTrials.gov)

- Largest public (NIH-funded) registry with 78,000 interventional and observational clinical research studies
- Results reporting required by law— as of September 27, 2008 [1]
- Online submission of summary results: interactive and batch upload
- Public access to "basic results," of certain clinical trials

[1] FDA Amendments Act of 2007 (FDAAA), Section 801 (Pub L No. 110-85); FDA Modernization Act of 1997 (FDAMA), Section 113 (Pub L No. 105-115)

[2] For example, Gøtzsche PC, et al. Constraints on publication rights in industry-initiated clinical trials. *JAMA*. 2006 Apr 12;295(14):1645-6; Mello MM, Clarridge BR, Studdert DM. Academic medical centers' standards for clinical-trial agreements with industry. *N Engl J Med*. 2005 May 26;352(21):2202-10; Schulman KA et al. A national survey of provisions in clinical-trial agreements between medical schools and industry sponsors. *N Engl J Med*. 2002 Oct 24;347(17):1335-41.