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Lockbox for Registered Trials of Unapproved Devices

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To the Editor

Prospective registration of clinical trials is a universally-recognized approach for mitigating selective reporting and publication bias.^{1,2} While a 2007 federal law largely increased incentives for registration, it prohibited publicly disclosing information about certain trials of devices that had not been approved by the US Food and Drug Administration.³ By law, these trials were required to be registered, but [ClinicalTrials.gov](https://clinicaltrials.gov) was forbidden from displaying the information publicly unless or until device approval by FDA (i.e., effectively placed in a “lockbox”). Consequently, lockbox trials do not satisfy the International Committee of Medical Journal Editors (ICMJE) registration policy or the ethical and scientific goals underlying registration and many ICMJE journals required registration of such trials in another database.⁴

As a consequence of a 2016 federal regulation (42 CFR Part 11)⁵ and statutory amendment, sponsors can now “opt out” from putting trials in the lockbox. Using data from [ClinicalTrials.gov](https://clinicaltrials.gov), we assessed the number of registered lockbox-eligible records, numbers and types of organizations providing such records, and numbers of records for which organizations elected to opt out of the lockbox.

We identified 380 records eligible for placement in the lockbox based on sponsor-submitted trial information as of January 4, 2018, with study start dates on or after January 18, 2017, the date on which the opt-out option was implemented. These records were provided by 273 unique organizations: 73.7% from industry, 25.3% from other sectors (e.g., universities, including three records listing funding from the National Institutes of Health), and 1.1% from other Federal agencies. Among these 380 records, 64.7% (246/380) were opted out and posted on [ClinicalTrials.gov](https://clinicaltrials.gov) while 35.3% (134/380) were placed in the lockbox.

Eleven organizations in the sample registered four or more lockbox-eligible records; 33.9% of these records (21/62) were opted out of the lockbox (Figure). Five organizations placed all of their eligible records in the lockbox and one organization opted out all eligible records.

These data indicate that many sponsors are choosing to make registration information about trials of unapproved devices publicly available. Overall, 64.7% (246/380) of records that were previously legally required to be in the lockbox are now publicly available. On the

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other hand, a third of organizations (90/273) placed at least one record in the lockbox. Journals, funders, and other interested entities are now able to hold trials of unapproved devices to the same registration requirements as for other trials without legal impediments to public posting.

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Figure.
Lockbox-Eligible Records Provided by the Top 11 Organizations