Half of trials supporting FDA applications go unpublished

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Over half of all supporting trials for FDA-approved drugs remained unpublished 5 years after approval, says new research published in this week's *PLoS Medicine*. The most important trials determining efficacy, and those with statistically significant results and larger sample sizes, are more likely to be published.

Ida Sim and colleagues from the University of California San Francisco searched the medical literature to determine the publication status of all 909 clinical trials that supported the 90 new drug approval applications approved by the US Food and Drug Administration (FDA) between 1998 and 2000. Although 76% of the pivotal trials (typically large Phase II or III trials designed to provide evidence on the overall risks and benefits of a drug) had been published in medical journals—usually within 3 years of FDA approval—only 43% of all of the submitted trials had been published.

The researchers also found evidence of selective reporting of the results from these trials. For example, Sim and colleagues report that a pivotal trial in which a new drug works better than an old drug is more likely to be published than a trial in which the new drug does no better. This is a form of publication bias that may lead to an inappropriately favorable record in the medical literature of a drug's true risk-benefit profile relative to other standard therapies, and can lead to preferential prescribing of newer and more-expensive treatments, say the authors.

These new results provide a baseline for monitoring the effects of the

FDA Amendments Act 2007, which was introduced to improve the accuracy and completeness of drug trial reporting. Under this Act, all trials supporting FDA-approved drugs must be registered when they start and the results of all the outcomes declared at trial registration as well as specific details about the trial protocol must be publicly posted within a year of drug approval on the US National Institutes of Health clinical trials.gov site.

In July the *PLoS Medicine* editors published an editorial discussing the FDA Amendment Act and what it means for medical journals: The PLoS Medicine Editors (2008) Next Stop, Don't Block the Doors: Opening Up Access to Clinical Trials Results. PLoS Med 5(7): e160 doi:10.1371/journal.pmed.0050160

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