Commentary: Drug companies must report clinical trial results, even when they won't lead to a product

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Drug companies sponsoring human trials of possible new medications have ethical responsibilities to study participants and to science to disclose the results of their clinical research -- even when product development is no longer being pursued, says a commentary co-authored by a leading UC Davis drug researcher published online today in *Science Translational Medicine.*

In the commentary, titled "Disclosure of Clinical Trial Results When Product Development is Abandoned," Michael Rogawski, chair of the Department of Neurology in the UC Davis School of Medicine, says that far too little attention has been given to the failure to reveal study results for drugs or medical devices for which development has been terminated.

Rogawski, an international authority on the development of drugs for epilepsy, says companies most commonly stop development of an investigational drug when clinical trials fail to show evidence of efficacy or if unacceptable adverse events occur. However, in some cases development is terminated because regulatory agencies require additional studies and the company sponsoring the trial is unwilling to comply. Companies may also terminate a program because of a lack of resources or because of a "reevaluation of the market opportunity."

Many sponsors do publish the results of their clinical trials even when

there are no plans to market the product being tested, but there is no legal requirement that they do so. With little incentive to devote resources to an abandoned project, publishing often goes by the wayside. In this situation "scientific information on the efficacy — or lack of efficacy — and safety — or lack of safety — of the investigational agents is not available to the research community, and the opportunity to learn from unsuccessful clinical trials is eliminated," Rogawski says.

For example, Rogawski says that it is assumed that the mouse models used to identify new drugs to treat epilepsy have high predictive value, because every marketed antiepileptic drug has demonstrated activity in the screening models. But "this assumption could be erroneous, because we do not know if there are drugs that were effective in the models but did not exhibit efficacy or had unacceptable side effects in clinical trials and were therefore terminated by their sponsors."

Similar concerns have been identified in psychiatric drug research, leading to the conclusion that "translational medicine cannot approach its full potential if negative drug developments are unpublished."

Commentary co-author Howard J. Federoff, a neuroscientist and dean of the School of Medicine of Georgetown University in Washington, D.C., said disclosing negative results from drug and device trials benefits everyone.

"Disclosing negative results from drug and device clinical trials benefits the entire scientific spectrum," Federoff says. "Such reporting would lead to greater patient safety, improve treatment research strategies, and allow a more efficient use of limited resources. The HHS has within its power the authority to require such reporting and doing so would positively impact health outcomes."

Rogawski says that in 2007 Congress enacted a law requiring clinical

researchers to post the detailed results of most clinical trials on the publicly accessible ClinicalTrials.gov database, whose original purpose was to assist patients in finding clinical trials. However, there is a loophole in the law that allows sponsors to delay submission of the data until the drug or medical device is approved for marketing by the Food and Drug Administration (FDA). If the product is not approved, the clinical trial results do not need to be made public. Under the authority of the FDA Amendments Act of 2007, the National Institutes of Health (NIH) is considering regulations to require reporting of the results for any registered trial even those that do not lead to an FDA-approved product.

Patients participate in clinical trials for many reasons, Rogawski notes, including the desire to contribute to medical knowledge, help the sick and benefit humanity. If sponsors diminish the opportunity for society to benefit from the altruism of research subjects, this subverts an implicit moral contract between sponsors and study participants.

Federoff adds: "Transparency in data sharing of trial results for products whose development has been abandoned will further improve translational science, engender trust among study participants, and optimize resource allocations for the pursuit of the most promising new therapeutics."

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