Amendment to the Testimony of Thomas M. Greene, Managing Partner, Greene LLP
Before the House Energy & Commerce Subcommittee on Health
Hearing on Fostering Innovation to Fight Waste, Fraud, and Abuse in Health Care
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Before the submission of this amendment, my testimony did not directly address the 2007 FDA Amendments Act, which strengthened and clarified the language in the 1997 FDAMA which created a national clinical trials registry. However, FDAAA only requires some, but not all, clinical trials to be registered, certain designs are not included, and the legislation focuses on *approved* drugs, biologics and devices. Of course, if properly enforced, this legislation would address some of the concerns I have discussed (Part II Recommendation 1, pages 27-30). It is clear, however, that the spirit as well as the letter of the registry provisions in FDAAA have been subverted, and stronger measures are necessary to accomplish the goals of that legislation.[1]

The reporting of results for registered clinical trials lags far behind the target 100% compliance rate, subjecting the medical literature to "selective outcome bias" and other reporting biases. A 2012 study in the British Medical Journal concluded that only 22% of clinical trials registered on clinicaltrials.gov report the results of the clinical trial within one year, despite the FDAAA requirement to do so.[2] With regard to Phase IV post-marketing studies, which are the studies most relevant for health care fraud with

[1] Many of the issues I discuss in this amendment are also addressed in an editorial published in the Journal of the American Medical Association by Kay Dickersin and Drummond Rennie. *JAMA*. 2012;307(17): 1861–64.

[2] Prayle, AP, Hurley MN, Smyth AR. Compliance with mandatory reporting of clinical trial results on ClinicalTrials.gov: cross sectional study. *BMJ.* 2012;344: d7373.

regard to FDA approved drugs, only 31% of registered studies reported results.[3] Only last week, the former president of Pfizer Global Research and Development admitted these statistics are accurate.[4]

FDAAA includes a $10,000 a day fine for failure to report results to the clinicaltrials.gov registry,[5] but it is clear that few fines, if any, have actually been levied. The fines themselves may not be a sufficient incentive to comply with the letter of FDAAA, considering that the fine is a pittance compared to the possible profits a company might enjoy by flouting the regulations.[6] If the law specified that failure to make a timely filing of negative results would be deemed to constitute scienter in any subsequent fraud litigation by a private party, it is likely that pharmaceutical companies and their researchers would comply with FDAAA much more frequently.

Moreover, many clinical trials are still not registered with clinicaltrials.gov at all. In many cases, this is because the registry requirement only requires filing of results of clinical trials with at least one site in the United States. But most of the major pharmaceutical companies are multi-national and even those that have no overseas

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[3] Id.

[4] Last week, on Forbes Magazine's website, John LaMattina, the former president of Pfizer Global Research and Development, admitted that BMJ's statistics were correct and that the reporting of results of clinical trials "is lagging." http://www.forbes.com/sites/johnlamattina/2013/02/14/bad-pharma-maybe-but-goldacres-selective-use-of-data-is-wrong/ (page 2 of comments, last accessed February 26, 2013).

[5] 21 U.S.C. § 333(f)(3)(B).

[6] "[T]he fine for noncompliance is $10,000 a day, which sounds spectacular, until you realise that it's only $3.5 million a year, which is chickenfeed for a drug bringing in $4 billion a year. And what's more, no such fine has ever been levied, through the entire history of the legislation." Goldacre, Ben. (2013). *Bad Pharma*. New York, NY: Faber and Faber, Inc. pp. 53–54

presence still license and sponsor drugs developed in foreign countries. If a drug is to be marketed in the United States, then all clinical trials studying its safety and efficacy, not just those conducted in the United States, should be registered and results reported. Pharmaceutical research performed overseas is, in most cases, just as relevant to safety and efficacy issues as tests conducted in this country.

In addition, there is a significant difference between the simple registration of a trial, with or without the posting of summary results, and making the underlying patient-level data available so that the results can be verified and practitioners, decision-makers and researchers can draw their own conclusions from the full data set. I have dealt with this issue first hand; in the Neurontin litigation, we received full data sets from Pfizer's clinical trials through discovery. Because of this, we were able to get to the truth about Neurontin's efficacy for off-label indications. As an example, we were able to show that a clinical trial highly touted by Pfizer was irremediably compromised by the unblinding of patients. Without access to the underlying data, this sort of analysis would not have been possible. It should not require litigation for physicians to be able to analyze a study's purported results. Underlying data from clinical trials is also helpful to meta-analyses run by organizations like the Cochrane Collaboration, and withholding some data while releasing others can affect their conclusions immeasurably. Again, I saw this in Neurontin, where Pfizer's withholding of data from the Cochrane Collaboration obfuscated several of their reviews. As a result, the medical community and the patients they treat suffered.

For all of these reasons, I renew my recommendation that a stronger push be made to require the registration of all clinical trials at their early stages, so that the "selective outcome reporting" variety of publication bias no longer plagues the medical literature. Greater transparency is needed, so that physicians and medical researchers can accurately gauge the accuracy of the conclusions drawn by studies' authors. A bill proposed in the 112th Congress, the TEST Act proposed by Congressman Markey, would require that any trial that could be used to support an application for FDA approval be registered in Clinicaltrials.gov and that the results be reported in a timely fashion.[7] I urge this subcommittee to reconsider the proposals within that bill, and to otherwise revisit the issues raised by the inconsistent registration and reporting of clinical trials.

[7] Drazen, Jeffrey M. Transparency for Clinical Trials – the TEST ACT. N Engl J Med 2012; 367:863–64. "The TEST Act expands reporting requirements under existing federal law by broadening the scope to include all interventional studies of drugs or devices, regardless of phase (i.e., including phase 1) design (i.e., including single-group trials), or approval status (i.e., making no distinction between trials of approved vs. unapproved products); requiring all foreign trials that are used to support marketing in the United states to be registered; mandating results reporting for all trials within 2 years after study completion (including trials of unapproved drugs or devices); and extending results reporting to include the deposition of consent and protocol documents approved by institutional review boards."