

Conference «Self-Regulation in the Pharmaceutical Industry – What can it achieve?» | April 21 2005 | Hilton Hotel Basel

## Clinical Research Sponsored by Pharmaceutical Companies (ABSTRACT)

Marcia Angell, M. D., Senior Lecturer in Social Medicine, Harvard Medical School

The pharmaceutical industry depends on clinical trials. Companies that wish to sell drugs in the U. S. must demonstrate to the Food and Drug Administration (FDA) that the drugs are safe and effective for their intended use, and this requires clinical trials. Drug companies also conduct many post-marketing studies to expand the use of drugs and buttress their marketing claims.

Since drug companies are for-profit businesses primarily responsible to their shareholders, they have a powerful incentive to make their drugs look good if they possibly can. Until a decade or so ago, that wasn't easy. Companies usually gave grants to independent university researchers who took full responsibility for carrying out the trials. Now, the companies have largely taken over that responsibility. They design the trials, analyze and interpret the data, and decide whether and in what form the results will be published. That gives them many opportunities to slant the research in favor of their drugs.

We have no way of knowing how often unfavorable results are suppressed altogether, but we know it happens. When a company seeks FDA approval for a drug, it is required to submit all the clinical trials done for that purpose, but it needn't submit studies of the drug not done to support an FDA application. Furthermore, the FDA will not release all the trial results it has in its possession without the consent of the companies. That means many clinical trials never see the light of day. Companies are, of course, eager to publicize favorable results, but unfavorable results remain hidden – often within the FDA, which in this regard seems to put protection of “proprietary” interests ahead of the public health.

We also need to ask whether we can rely on the favorable research that is published. I spent much of my professional life evaluating clinical trials for publication in the *New England Journal of Medicine*, and I can tell you there are many ways to design a trial to make a drug look better than it really is – in addition to the obvious one of comparing it with a placebo, when the relevant question is whether it is better than an older, cheaper drug.

For example, companies sometimes enroll only patients at low risk of side-effects, even though the drug is intended for use in more vulnerable populations. That way, it will seem to have fewer side-effects than it will when it comes into widespread use. Or a new drug may be compared with an old one administered at too low a dose. That makes the new one look more effective, and it can be promoted as being stronger. Sometimes unfavorable data are simply omitted from a publication. In one well-known case, a drug company published only the first six months of data from a one-year study in which the positive results disappeared in the second six months. There is now ample evidence that company-sponsored papers are more favorable to drugs than publicly-funded papers.

The theme of this conference is “self-regulation.” But self-regulation is what we have now – the status quo – and it is obviously failing. Indeed, how can we expect companies whose very survival depends on getting positive results in clinical trials to carry them out in a strictly impartial way? The notion of “self-regulation” is an oxymoron – a form of spin to try to ward off real regulation.

Real regulation has to come from the outside, and it should be aimed at separating commercial sponsorship from control over the research. Trials should not be designed by their commercial sponsors, but by independent researchers, and these researchers should take full responsibility for the results and for publication. All trials should be registered at inception in a publicly-administered database, with the salient results added after completion of the trial. In my book, “The Truth About the Drug Companies,” I propose an Institute for Prescription Drug Trials within the U. S. National Institutes of Health to oversee clinical research on prescription drugs. We need to make certain that human research serves a genuine medical purpose and that trials are properly designed, conducted, and reported. Clinical trials are too important to leave to companies that by their nature have overwhelming conflicts of interest.