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Out in the open

Until recently, biotech and pharmaceutical companies have had little reason to heed calls for greater transparency in the disclosure data from their clinical trials. That all changed last year when New York State attorney general Eliot Spitzer filed a high-profile lawsuit against GlaxoSmithKline (GSK) alleging that the company had withheld trial data indicating that its antidepressant Seroxat (paroxetine) increased the risk of suicide in children. For some reason, the data revealing increased suicide risk were mysteriously absent from official GSK summaries of Seroxat's clinical performance.

As part of its settlement with New York State in September, GSK admitted no wrongdoing but agreed to post data on its website (http://ctr.gsk.co.uk/welcome.asp) from all of its clinical trials conducted after December 27, 2000. By this time, though, the impetus was growing for something altogether more ambitious: an official open register of research in which all drug companies would be required to disclose trial data. The World Health Organization announced it would create an international registry for trials. And the American Medical Association requested that the US government establish a public trials registry, advising institutional review boards to require trials registration. The editors of 11 medical journals also got in on the act, stating that from this July, they will require companies to disclose the launch of all drug studies as a condition of publication. Several bills were tabled in the US Congress aiming to make trial data disclosure mandatory; similar moves also got under way in the UK and Canada to ensure trials are registered and data made more widely available.

For its part, the pharmaceutical industry has been unusually keen to publicize its "commitment to transparency," perhaps in an attempt to head-off government legislation mandating trial data disclosure. Just last month, the International Federation of Pharmaceutical Manufacturers and Associations, along with three other industry associations covering Europe, the United States and Japan, announced voluntary principles for disclosing clinical information. These principles include a commitment to register details of trials at study initiation in a publicly accessible database (e.g., http://www.clinicaltrials.gov) with data submission no later than one year after a drug's approval "regardless of outcome."

This is all well and good, but voluntary principles are just that: voluntary. As long as drug companies have compelling business and competitive reasons not to participate in reporting clinical data, results that run counter to a company's commercial and competitive interests are unlikely to ever see the light of day. Put simply, voluntary principles are not going to solve the main problem: selective disclosure of trial data.

The pharma industry's decision to lodge company summaries of clinical data rather than raw data also is problematic. According to the Pharmaceutical Researchers and Manufacturers of America (PhRMA), company summaries are preferred "because data from clinical studies are often thousands of pages long." Of course, result summaries should be provided, but raw data is needed, too. In every other area of scientific endeavor, access to raw data associated with a study is a key criterion for publication. Without these data, there is no way of independently verifying and reproducing results. And for understanding the significance of clinical data, the devil very often is in the details of how raw data is statistically analyzed.

The decision not to post raw data also is puzzling given industry explanations for snail-paced progress in disclosing results. More than six months since the Seroxat debacle and three months after PhRMA launched its website (http://www.clinicalstudyresults.org) allowing the public "unprecedented access" to clinical data, unpublished trial results of just five drugs have been posted. PhRMA's reason: "it takes a long time to transform raw data from unpublished studies into an internationally recognized (ICH-E3) uniform summary format." So why not post the raw data in a standardized format in the meantime and submit the summaries requiring more lengthy analysis later?

So far, the biotech industry has remained conspicuously muted on this issue, although the Biotechnology Industry Organization is purportedly drawing up guidelines of its own. One explanation for the silence may be it hopes that big pharma will sort out the mess and in the meantime field the flak. But biotech companies need to take the issue of data disclosure seriously because their fortunes (and often survival) ride on the success of one or two drugs and because they could be at a competitive disadvantage. According to Michael Astrue of Transkaryotic Therapies in Cambridge, Massachusetts, biotech firms are more vulnerable than pharma because if bigger companies become aware of a biotech's programs "they could throw money [at the area] and beat you to the market." For this reason, it is critically important that data from 'exploratory trials' (e.g., most phase 1 and phase 2 trials) are omitted from any public registry plans. Once a project has entered phase 3, there is much less chance a competitor could steal in (and most biotechs have partnered up with pharma by this stage anyway).

Drug companies have a duty to provide patients and physicians with meaningful information about the medicines they develop and market. If they seek to publish the results of a clinical trial in a journal, then they should also be obligated to present all the data pertaining to that trial in a form accessible to researchers to enable independent data analysis. If companies cannot be trusted to supply negative data and physicians and researchers cannot access all the data, well, what then?

The answer is mandatory disclosure of all late-stage clinical trials, with penalties for companies that do not comply (even though that would be a significant practical and economic burden). If all firms were required to release late-stage data, there would be no commercial incentive for secrecy. And researchers, physicians and patients all would be better off for having complete information about the safety and efficacy of drugs in daily use.