

An interview with Philip A. Pizzo, MD, dean of the School of Medicine at Stanford University.

## Championing transparency in clinical trials

By Cori Vanchieri

**A**s public trust in medical research plummeted with revelations of selective reporting of results in studies that linked Vioxx (rofecoxib) with fatal heart attacks and antidepressants with teen suicide, the movement to register clinical trials has gained momentum. Dr. Philip A. Pizzo chaired a committee at the Institute of Medicine (IOM) in an attempt to move the agenda for clinical trial registration forward, striking a balance among the competing interests of industry, journal editors, and the public. A year later, he reflects on the progress made.

### **Community Oncology: Why do you feel that registration of clinical studies is so important?**

A number of surveys have demonstrated that more than half of our faculty and universities have some kind of interaction with industry, either through consulting, speaking, or serving on boards or other advisory groups. A commentary appeared in the journal *Nature* in 2005 that assessed—with more than 3,000 respondents and a 52% response rate—how scientists presented their views. Strikingly, nearly a third admitted that they might have in some way changed the reporting of their data based on the funding source. To me, this is unfortunate.

In this year's IOM workshop report, *Developing a National Registry of Pharmacologic and Biologic Clinical Trials*, we wrote that if clinical trials were systematically registered at their

inception, followed by the posting of summary results for the study, and if that information was easily accessible, then the full range of clinical evidence on an investigative therapy would become part of the public record. And once a drug has been approved, the registry provides a complete record that can serve as input for decisions by guideline developers, insurers, and those who monitor quality of care in the United States.

### **You were on the side of full disclosure in an open registry of clinical trial details and results. What were the sticking points during the IOM deliberations?**

The two main issues were whether exploratory trials, or early-phase studies, would be included in a registry, and whether all data fields would be listed up front, or whether some could be “blinded” for a period of time. Industry officials argued that, in order to protect their commercial interests, certain data points—such as a description of the intervention, and primary and key secondary outcomes—should be kept in a so-called “lockbox” until sometime after the study was completed. To me, the lockbox seemed to be something that would move us further away from a perception on the part of the public and the consumers that we are being transparent and honest in having all the information accessible. Our governing goal should be to convey information that engages public trust. Conveying some, but not all, information doesn't cut it.

**The International Committee of Medical Journal Editors really moved things along with its edict requiring that researchers register their trials before enrollment begins if they want to publish in the journals. But they excluded exploratory studies and decided to allow some veiling of data to protect “proprietary company information.” They also decided not to require results posting. Were you disappointed?**



**Philip A. Pizzo, MD**

I certainly recognized that some compromises needed to be made to move the process forward, but I was pushing for more action. In particular, I felt that the reporting should include earlier exploratory trials, and I also felt that secondary endpoints should be included.

**It looks like the World Health Organization has sided with you. In late May, the WHO decided to require registration of even**

**exploratory studies and not to support the lockbox concept. It seems that results reporting is the last matter to be tackled.**

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Leaving out results was an expedient effort to move the process forward, but it was an artificial one. Reporting the results is quite important. However, it seemed to me—and others—that had we addressed results reporting with the criteria for the registry, we might not have advanced very far. Clearly this needs to be an iterative process, and more work is needed.

**Let’s shift gears now to talk about enrollment in clinical trials. You spent the first part of your career as a pioneering pediatric oncologist at the National Cancer Institute, studying treatments for children with cancer as well as the first young patients with HIV. Why is enrollment among children with cancer so much higher than among adults with cancer?**

Clinical trials in pediatric oncology have become the standard of care for more than 30 years. Because childhood cancer is relatively rare, no single center can enroll enough

patients to produce meaningful results from clinical trials, short of very limited phase I or pilot studies. So from the outset, centers around the country came together to form large, collaborative, multicenter studies, first by two groups—the Pediatric Oncology Group and the Children’s Cancer Study Group—and now a single group, the Children’s Oncology Group. Nearly all children with cancer are treated in major centers because of the nature of the care they receive and also because that is where pediatric oncologists are located. It is quite unusual for pediatric oncologists to be in private practice or to operate outside a major center. The track record of these large cooperative studies has transformed pediatric oncology. Parents have come to understand that clinical trials in childhood cancer are the rule rather than the exception, and they have accepted this as a standard of care.

**There have been plenty of initiatives over the years to try to get adult enrollment up above its low rate of 5% or so. Why have none made a difference? What should researchers do to boost enrollment in research studies?**

The culture is quite different. Most oncologists are in private practice, and, as such, they are more likely to want to tailor therapy to their patients, partly as a means of proving their value, rather than by engaging in clinical trials. Progress in most adult

cancers has been slower, so clinical trials cannot be viewed as a standard. In addition, the competition over patients has led some oncologists to bias patients against clinical trials, presenting them as experimental therapy rather than a standard therapy.

**What should community oncologists do to support clinical research for their adult patients?**

They need to start by believing that clinical trials will improve outcomes and by presenting them to their patients in a positive light. Community oncologists also need to make clinical trials the course of choice rather than route of exception. To make them truly feel part of the clinical trial organization, community oncologists also need to get credit for their contributions. But at its heart, the most important change needs to be a cultural one, beginning with the recognition that patient outcomes are better simply through participation in a clinical trial, which is true. This, I hope, would lead community oncologists to offer trials to their patients as a first line of treatment rather than a last resort.

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See also Washington Update in this issue: “The pressure is on for full disclosure in clinical trials reporting,” page 455.