The tribulations of community-based trials

Doctors and the medical profession are facing some troubling issues as clinical trials sponsored by the pharmaceutical industry migrate from academic settings into the community. The issue of industry-sponsored clinical trials is "a bit of a hornet's nest," says Dr. David Naylor, dean of medicine at the University of Toronto. He says that "staying on top of perverse incentives and hidden conflicts of interest" is like trying to hit "a constantly moving target."

While academic centres struggle to tighten safeguards to ensure the integrity and independence of the research endeavour — for example, the U of T has banned finders' fees — observers say most of the action has already shifted away from universities.

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Tom Ekers, president of CMX Research Inc., estimates that about 47% of trials sponsored by the drug industry in Canada are now based at academic centres, compared with about 60% just 7 years ago. (CMX, a site-management organization [SMO], conducts clinical trials at about 40 sites in Canada. Contract research organizations (CROs) typically use SMOs to organize networks of research sites.)

Ekers says the pharmaceutical industry is directing more clinical trial work to community-based doctors because "academics are paranoid about control" and academic research ethics boards are typically slow to approve trials. This is a handicap, given the pressure to get drugs to market quickly. Most clinical trials in the community are Phase 3 drug trials involving large numbers of patients.

However, the shift toward community-based trials raises a number of alarms about conflict of interest, patient safety and the public interest. Observers worry there is very little oversight or information about the private CROs, their internal ethics review boards and the for-hire non-institutional review boards that have facilitated this shift in locale.

Health Canada reports that 86% of clinical trials conducted in Canada in 2002 were industry sponsored, but it cannot provide information on where the trials took place. "We know more about trials involving animals than trials involving humans," says Professor Michael McDonald, founding director of the W. Maurice Young Centre for Applied Ethics at UBC.

McDonald, who raised concerns about the governance of such research in an October 2000 report for the Law Commission of Canada, notes that in clinical trials payments to physicians "can be quite high, and that can have a corrosive effect on the doctor–patient relationship."

The Tri-Council Policy Statement on Ethical Conduct for Research Involving Humans says doctors can receive reasonable professional fees for participating in trials. However, Timothy Caulfield, research director of the Health Law Institute at the University of Alberta, thinks that statement is vague, since compensation is often very generous.

In Canada, only the College of Physicians and Surgeons of Alberta (CPSA) requires non-university-based doctors to register their involvement in clinical trials. "We believe that research is part of the practice of medicine when it involves human subjects," explains Dr. Paul Flynne, the assistant registrar. All clinical trials in Alberta must be reviewed by one of the province's public ethics review boards; the CPSA's research ethics review board was set up to review protocols for trials involving doctors practising in the community. Elsewhere in Canada, community clinical trials may be reviewed by ethics boards internal to CRO's or non-institutional for-hire boards. Such boards have an inherent conflict of interest in that they are paid to make decisions that have financial implications for their clients, notes Trudo Lemmens, a University of Toronto professor specializing in health law. Alberta's requirement has been in force since 1998, but no other regulatory bodies have followed suit. The Ontario college says the issue is "not even on the radar."

The CPSA also requires doctors to inform patients that they are being paid for enrolling patients in trials. Caulfield says all doctors should do this because of informed-consent obligations.

Naylor says the migration of trials to the community means there is a greater chance doctor–investigators will have little control over how their research is interpreted and where it is published. It "only makes sense" for Health Canada to set rules for all human trials, regardless of where they take place. UBC geneticist Patricia Baird agrees, but is discouraged that Health Canada has removed itself from the oversight role. She worries that the "social contract that allows research on human subjects" is at risk. — *Ann Silversides*, Toronto