



Independent review adds to controversy at Sick Kids

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In brief

Editor's note: A truce was finally reached in the Dr. Nancy Olivieri–HSC dispute as this article went to press. Under it, Olivieri transfers to the Toronto Hospital and HSC pays \$150 000 of her legal expenses and withdraws all written complaints against her.

In the past 6 months, the controversial drug study headed by Dr. Nancy Olivieri at Toronto's Hospital for Sick Children (HSC) has become a lightning rod for scientists worried about the relationship between industry and academia. It's been discussed throughout Canada and internationally, garnering cover articles in *Macleans* and *Elm Street* and prominent coverage in US media outlets such as *Business Week* and in journals such as *Science*. The gist of the story in both the scientific and lay press is that while conducting clinical trials on an experimental drug for thalassemia, Olivieri became worried that the drug (deferiprone, or LI) could harm patients. The trials were sponsored by a Canadian drug firm, Apotex. When Olivieri told company officials about her concerns, they reminded her that she'd signed a contract requiring her to keep research results confidential. She argued that she had to make the results public to protect patients, and alleged that the hospital did not support her in the dispute. The company said it could take legal action against her if she published without permission, but she published anyway (*N Eng J Med* 1998;339:417-23).

In December, an independent review commissioned by the HSC board called Olivieri's allegations into question. The review, led by Dr. Arnold Naimark, a past president and former dean of medicine at the University of Manitoba, alleged that Olivieri was at fault and allowed hospital executives to shine — perhaps for the first time since this story broke last August. Naimark's report alleges that Olivieri failed to provide adequate protection for the patients who were her research subjects and ascribes that failure to her concern for her own liability.

The review says that confidentiality clauses in Olivieri's "personal consulting" contract with Apotex conflicted with her obligation to report serious adverse drug reactions to the research ethics board (REB). It also states that she failed to have her contract with Apotex reviewed by

the hospital and to mention that Apotex had agreed to pay her US\$30 000 per year plus travel expenses and US\$200 per diem while she was travelling, plus an additional \$5000 for each patient studied. The review asserts that the resulting conflict of interest for Olivieri, combined with her "interest in protecting herself legally . . . caused her . . . to delay reporting to the REB."

The Naimark review's most damning evidence against Olivieri alleges that she knew by late 1996 or early 1997 that the experimental drug might cause a serious adverse reaction — liver toxicity — but that she did not present her evidence to the REBs at Sick Kids or at the Toronto Hospital, where patients were taking the drug during clinical trials. Naimark considers this a serious lapse in what he terms "the security system" designed to ensure the safety of research subjects.

But Olivieri contends that her findings at that point were preliminary and had not yet been fully evaluated nor peer reviewed. She says she did not want to go to the REBs until she and a pathologist had reviewed the slides of patients' liver biopsies, and she claims that they were performing this review into February 1997. Dr. Peter Durie, an Olivieri supporter, suggests that Naimark could have learned more about why Olivieri did not speak with the REBs earlier if he'd contacted her collaborators.

Naimark acknowledges that he didn't try to contact them. Instead, interviews with Dr. Gideon Koren and HSC's chief of pediatrics, Dr. Hugh O'Brodovich, form the basis for the review's account of Olivieri's decision about when to inform the REBs; Olivieri has been in sharp conflict with both individuals. The review also refers to a letter from Olivieri to O'Brodovich: "The only reason that the . . . research ethics boards were not informed prior to this time is that my legal counsel . . . has recommended that Apotex Pharmaceuticals be informed prior to any other body." Olivieri's lawyers were not contacted by Naimark to confirm or explain this, and Olivieri's description of her actions that winter seem to imply that her lawyers considered her findings preliminary.

"There's a conflict of interest there"

In contrast to his findings about Olivieri, Naimark



“found no evidence that patient safety was ever compromised by hospital management . . . ,” James Pitblado, chair of the Sick Kids’ board, said during a December press conference convened to release Naimark’s review. Instead, he said, the review found that hospital officials “acted promptly, and when Dr. O’Brodivich learned that Dr. Olivieri had concluded there was a possibility of liver toxicity in some of her patients, he moved very quickly to convene a meeting and deal with that issue. . . .”

Was the review unfair? Naimark was hindered because Olivieri and some of her key supporters, including her program head Dr. Brenda Gallie, declined to speak with him or provide relevant documents. “Dr. Naimark . . . just happens to have been the president of the University of Manitoba at a time when Apotex was a donor, so there’s a conflict of interest there,” Olivieri explained in an interview. “There’s an apprehension [about] bias. . . .”

Dr. Henry Friesen, head of the Medical Research Council of Canada, had attempted to ensure Olivieri’s participation by including her in the selection of 2 associates who were to help Naimark, but those efforts proved unsuccessful. “The possibility that we might participate [in an inquiry] was seen as a huge risk to [certain] individuals,” Gallie claims, “so they tried to take actions that would mean that we would not participate.”

Naimark says Olivieri’s refusal to participate does not invalidate his review. “The question I had was, is the nonparticipation so critical . . . that it would make the report useless?” he said in an interview. “In my opinion, it wasn’t.”

Others, such as Sick Kids’ epidemiologist Mary Corey, say the review was written “unequivocally from the point of view of the hospital administration.” Naimark points out that he studied many documents, including voluminous pages of Olivieri’s correspondence, although the review also relied heavily on undocumented evidence obtained during interviews with hospital, university and company officials. However, the reviewers did not attempt to confirm the facts provided in those interviews by asking individuals who had been named whether the information provided was accurate. Nor did the reviewers interview Olivieri’s research collaborators or mentors to try and get at her side of the story.

The resulting report, based on more than 40 interviews and over 500 documents, is, at best, incomplete. If it is accurate, despite its gaps, a lot of scientists who heard about the dispute and called on the hospital and the university to stand up for Olivieri’s right to publish got this story wrong, and numerous journalists, including this one, have been misled. However, if the review is a one-sided appraisal of events, then the scientists and journalists may have been closer to the truth.

Some claim that reporters fell victim to a media campaign orchestrated by Olivieri and her supporters, a

charge that Naimark reiterated. For several months communications consultant Michael Langlois has been providing free advice to Olivieri and her supporters about how and when to deal with reporters. Langlois has a decade of experience and says he has worked for HSC in the past. Did he perhaps prevent reporters from learning the true version of events? That seems doubtful.

“An unpleasant place to be”

One thing is certain: the Naimark review did little to settle the controversy at Sick Kids. Many say the hospital has degenerated into an interpersonal battleground, and the review confirms that “collegiality, friendship, civil discourse, trust and common courtesy have all been victims of the controversy.” But the review may have reignited that controversy. “It’s caused even more divisiveness in this institution and made it an even more unpleasant place to be,” Dr. Jeff Smallwood told Naimark when he met with HSC staff in January.

Events since the review’s release confirm Smallwood’s remark. The University of Toronto Faculty Association has filed a grievance against the university for failing to protect Olivieri’s academic freedom. Olivieri’s lawyers, including well-known Toronto attorney Clayton Ruby, have accused the hospital publicly of placing patients with sickle cell disease and thalassemia “at risk” and have insinuated that this may be because many of these patients are members of racial and ethnic minorities. Sick Kids has a long-standing reputation as a place where children from around the world are treated, regardless of ethnic origin, and hospital executives consider such insinuations slurs on HSC’s good name. Subsequently, HSC terminated Olivieri’s status as a program director and its executives instructed her supporters that their “actions over the past several months in relation to the LI/Apotex matter” involved “unacceptable conduct.” Senior HSC scientists who have been outspoken supporters of Olivieri were told to “ensure that [their] future conduct meets . . . requirements” of hospital policies. One policy requires all staff media interviews to be “arranged through Public Affairs.”

The Naimark review differs from other published accounts of this dispute in its portrayal of hospital actions taken in support of Olivieri. It states that 3 physicians — 2 HSC administrators and Dr. Arnold Aberman, dean of medicine at the U of T — contacted Apotex and asked that the company refrain from suing Olivieri. However, there is no written proof that this happened.

The review’s harshest criticisms are saved for Olivieri, but it does suggest that the hospital should have provided greater moral support during her battle with Apotex and should have responded earlier to calls for an external in-



quiry into the matter. The review also provides evidence that hospital administrators believed they could suppress news of the Olivieri-Apotex dispute, referring to an external review of Olivieri's division at the HSC that was cancelled after the outside reviewer who had been appointed raised the issue of the dispute with an administrator.

The controversy at Sick Kids offers a few lessons about how not to deal with scientific controversies. The main lesson? Don't expect that a controversy will disappear simply because your organization steers clear of people trying to talk to you about it. Unfortunately, the Naimark review also seems to provide some lessons about how not to conduct a public inquiry into a contentious dispute. For example, reviewers must try to ensure that people on all sides of the dispute will speak to them, and they must make a point of confirming hearsay facts with primary sources. To be fair, once the Olivieri group declined to participate, the cards were stacked against Naimark, but a federal or national body might have been asked to step in at that point.

The clinical trial conducted by Olivieri was partially

funded by the Medical Research Council of Canada (MRC), and the Sick Kids' controversy might fall within its purview, since it involves the question of whether human research subjects were placed at risk. Alternatively, the Health Protection Branch at Health Canada could have reviewed the study, since it involved an unlicensed, experimental drug. When a controversy arose in the US a few years ago about whether a study funded by the National Institutes of Health (NIH) placed participants at risk, the NIH director established an advisory panel to conduct an independent review of the study.

But it's not clear which, if any, federal offices here can play that role. The MRC cannot, says its ethics director, Dr. Francis Rolleston. "These [issues] are institutional responsibilities," he says. "If you have big brother in Ottawa looking after these things, that's not healthy."

The scientists who have watched events unfold at Sick Kids may beg to differ.

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