tough new standards for industry-sponsored research,[1] and the extensive efforts the University has made to mediate a resolution of her issues.

Olivieri's claims about the publicity surrounding the allegations by the Medical Advisory Committee [MAC] of the Hospital for Sick Children are misleading. The substance of the allegations was never publicized in the University of Toronto Bulletin. The MAC's referral of these matters for investigation ran 9 lines on page 2 of the Bulletin with a 15-point headline.[2] The story on the University's dismissal of the complaints ran 28 lines on page 3 of the Bulletin with a 30-point headline.[3] It included my criticism of the hospital for publicizing the referral, a criticism repeated in *CMAJ*.[4] Then-university president J. Robert S. Prichard confirmed to the University's Academic Board that the matter had been referred, after the referral had already been publicized. As Olivieri knows, a statement dismissing the MAC allegations was later read into the formal record of the Council of the Faculty of Medicine.

Olivieri protests that the CEO of the pharmaceutical company with which she became entangled is suing her for $10M. In a fair and rational world, there would be no litigation surrounding this dispute. That said, the suit in question was initiated well after Olivieri had published her study and publicized her views of the drug. It arose from Olivieri's statements about the company's CEO. Moreover, a check through public court records shows that Olivieri has herself initiated lawsuits against officers of Apotex, academic colleagues, the hospital, the University, and media outlets, for claims in excess of $20M.

Olivieri's comments about her personal legal costs side-step her role in initiating proceedings. They also demean the involuntary contributions to her legal costs made by over a thousand nonclinician colleagues who pay mandatory dues to the University of Toronto Faculty Association [UTFA]. In fact, the UTFA has spent hundreds of thousands of dollars on legal fees and services for Olivieri and her supporters.

Olivieri seeks discipline against 2 colleagues "who advanced demonstrably incorrect testimony against me." But at times in this bitter dispute, Olivieri herself has advanced "demonstrably incorrect" allegations against others, including an allegation of forgery that was subsequently retracted publicly. Less understandable is her recent breach of confidential misconduct proceedings, causing dissemination of misinformation about a distinguished and neutral colleague.

On the efficacy and safety of L1, Olivieri wrongly assumes that the University has or had an official view. The drug's worth is for clinicians, researchers, and regulators to determine.

Olivieri alludes to deferoxamine therapy as "somewhat onerous"; "all this fuss," it seems, is about an intravenous pump infusion that must be given nightly to children. Not only is the need for an alternative obvious, but Olivieri's own L1 studies were directed to that end. I am therefore baffled by her personalized response to my comment that energy spent on this dispute could be better directed at research into other treatment options for the thalassemias.

In sum, Nancy F. Olivieri's letter sadly illustrates why a definitive resolution is needed to bring closure, if possible, for Olivieri and her allies, and underscores why the involved institutions are indeed moving on.

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Independent inquiry

Although we applaud the coverage[1-3] given in the Feb. 19, 2002, issue of the case of Nancy Olivieri, Apotex, the Hospital for Sick Children and the University of Toronto, the editorial "Questions of Interest"[4] may have left your readers with serious misapprehensions.

The first of these concerns the independence of our Committee of Inquiry. When it became clear that a committee of inquiry into this case was needed, the Canadian Association of University Teachers (CAUT) was the only external body prepared to commission such an inquiry and to provide it with full independence. Because CAUT had taken a position on some matters arising in the case, and because this organization by definition serves the interests of university teachers, we agreed to serve on the committee only on the provision that we could be independent of CAUT or of any other person or organization. At the outset, we stipulated special arrangements to ensure our independence. CAUT agreed to these, and also undertook to have our report published exactly as submitted and in its entirety. Our report was delivered to CAUT on Oct. 26, 2001, at the same time as it was released to the public; the association had no advance copy. It is also worth noting that none of us sought appointment to this committee; we agreed to serve because of the important issues it raised, and did so for 2 years without remuneration.

Second, with respect to the participation of the various individuals involved in the case, we agree that it would have been ideal to have an inquiry in which all parties participated. However, it must be noted that the administrations of the University, the Hospital and Apotex declined our invitation to participate. The potential disadvantage of their nonparticipation was substantially offset by the access that we

had to a large quantity of relevant correspondence and documents originating from the administrations of the university and the hospital, Apotex, and other nonparticipants. These thousands of documents included the 1998 Naimark Report commissioned by the hospital and its documentary base. We also had access to key Apotex and hospital documents not available to the Naimark Review. We therefore believe we had a comprehensive set, from both sides, of relevant information regarding all players in the dispute. The central conclusions of our report were independently corroborated by the Dec. 19, 2001, report issued by the College of Physicians and Surgeons of Ontario,[5] who had the participation of some of those very individuals who declined to participate in our inquiry.

We would encourage your readers to read our report, along with the supplement discussing events since October 2001; both can be accessed at www.dal.ca/committeeofinquiry. Contrary to the suggestion in your editorial, the rights of "the study subject who volunteers in research" are judged to be a centrally important issue in our report; indeed, they drive the wide-ranging recommendations that we hope will be taken up by all of those responsible for the well-being of research participants in Canada.

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Alzheimer's disease and herpes

Herpes simplex virus type 1 (HSV1) is present in latent form in the brains of a high proportion of elderly people[1] and is a risk factor for Alzheimer's disease in carriers of the type-4 allele of the apolipoprotein E gene (apoE-e4). ApoE-e4 is also a risk factor for cold sores.[2,3] We have suggested that when HSV1 is reactivated in the nervous system the resulting damage is greater in apoE-e4 carriers than in people who carry the other apoE alleles. We recently detected antibodies to HSV1 in cerebrospinal fluid, substantiating our detection of HSV1 by polymerase chain reaction and showing that it does indeed reactivate (unpublished data). A clinical trial testing a synthetic amyloid peptide as immunotherapy for Alzheimer's disease was recently halted because 4 patients developed inflammation of the brain; in "some" of these 4 patients, a virus was detected in the cerebrospinal fluid.[4]

The results of René Verreault and colleagues[5] raise the intriguing possibility that viruses other than HSV1 may directly influence Alzheimer's disease. Nonetheless, their findings could equally well be explained by an indirect effect: HSV1 reactivation can be triggered by inflammation, and vaccines would presumably prevent inflammation by preventing infection with the target virus, thus indirectly preventing HSV1 reactivation. Their study also supports the possibility that vaccination against HSV1 itself might prevent Alzheimer's disease; such vaccination is feasible now that the age at which primary infection occurs is rising. In fact, we have shown that vaccination of HSV1-infected mice with mixed HSV1 glycoproteins prevents establishment of latency in the brain.[6]

Finally, it would be interesting to know if the trend detected by Verreault and colleagues is dependent on the apoE-genotype. Such dependence has also been found for patients with herpes simplex encephalitis[7] and for subjects infected with HIV but who have not yet developed AIDS.[8]

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Spinal manipulation versus mobilization

The commentary by Edzard Ernst[1] alerts health professionals to the possible complications of cervical manipulation. However, we feel that the commentary would have been even