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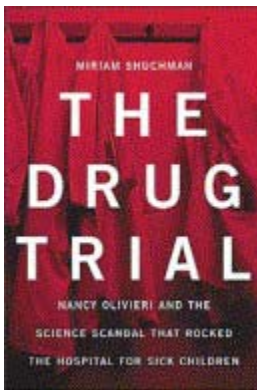
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### Perspectives

# Research conduct and the case of Nancy Olivieri

David Weatherall 

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“Survey the WHOLE, nor seeks slight faults to find.”

Alexander Pope, An Essay on Criticism (1711)

The spate of articles and books that highlight the dangers of the increasingly messy relationship between academia and industry continues unabated. Gag clauses, for example, provide industrial sponsors of clinical research, usually clinical trials, with complete control over what an investigator can publish. From 2001, the International Committee of Medical Journal Editors, which represents many leading journals, required that the responsible author of a study provides a written statement that he or she accepts full responsibility for its conduct, has full access to the data, and controls the decision to publish. But many of these requirements are still not being met in most clinical-trial agreements between

medical schools and industrial sponsors. A notable exception is the University of Toronto, Canada; since 2001, this institution has demanded comprehensive standards for all industry-sponsored clinical research. Its Dean is quoted as saying that some contracts are being lost as a result of these policies; “you are left with the sound of one hand clapping when you do this on your own, even in the country's largest medical school”.

One of the main reasons that Toronto put its house in order was its poor showing in the case of Nancy Olivieri, an expert on thalassaemia. In 1987, Olivieri began a study of the oral iron-chelator, deferiprone (L1), to find out if it might be effective in the control of iron loading in patients with severe thalassaemia who have regular transfusions. At first, the results were encouraging and she therefore initiated a company-sponsored trial to compare the efficacy of deferiprone with deferoxamine (desferrioxamine), a drug that was known to be effective in the control of iron loading but which has to be delivered by subcutaneous infusion. During the trial Olivieri noticed that a significant proportion of her patients seemed to be accumulating iron and that there might also be an unexpected side-effect. Hence she felt that her patients and the research community should be made aware of her findings. Despite threats of lawsuits by the company, she published her observations.

The University of Toronto and the Hospital for Sick Children, which at the time were in the process of negotiating a large donation from the same company, did not support Olivieri in her controversy with the company and, later, referred her to the Canadian College of Physicians and Surgeons for research misconduct.

They also tried to dismiss her from her post, although, mainly owing to the efforts of her colleagues, she was ultimately reinstated. During this unsavoury episode, which lasted for many years, Olivieri and the small group of clinical scientists in Toronto who supported her were subjected to continuous stress, including anonymous hate mail. In the end, she was completely vindicated by an independent 500-page report, and by the College of Physicians and Surgeons that found her conduct “exemplary”.

These reports apart, this case has been the subject of fully documented accounts in at least three books that deal with problems at the academia/industrial interface: Jerome Kassirer's *On the Take*, Sheldon Krimsky's *Science in the Private Interest*, and Marcia Angell's *The Truth About Drug Companies*. At first sight, therefore, it is difficult to see why there should be a place for yet another book on this topic, particularly so long after these unfortunate events; surely, all concerned should be left in peace to get on with their professional lives.

Miriam Shuchman's *The Drug Trial* takes a different, and to this reviewer inexplicable, approach to anything that has gone before. First, it gives a blow-by-blow description of the scientific disagreements and intrigues that bedevilled the development of deferiprone from its early beginnings in the UK, and which have raged unabated during the past 10 years. But there is nothing new in this; in any field of research there are controversies, personality clashes, and persistent doubters. This is how science evolves; it may take many years before the truth emerges, as it will in determining the role of deferiprone. The only difference in this case is that many of these disagreements were aired at scientific meetings that were attended by patients' parents and heavily influenced by commerce. But the really puzzling and disturbing feature of Shuchman's book is that, in retelling this story, she presents it in the form of a biography—or rather a pathobiography—of Olivieri and those who supported her. She includes anecdotal accounts, some of them hurtful, of her relationships with her parents, friends, staff, scientific colleagues, patients, and, apparently, anybody else who was willing to voice an opinion. In her “Note on Sources”, Shuchman admits that her book makes extensive use of off-the-record material. She writes, “many of the doctors and scientists who witnessed the events described here feared for their reputations if they were quoted, and some worried that they would be fired from their jobs or sued for libel”. Things have come to a sorry pass if scientists who tell the truth run the risk of professional dissolution; clearly, the current biographer's lot is not a happy one.

In summing up, Shuchman suggests that Olivieri's concerns about deferiprone may have heavily influenced the drug-licensing bodies in the USA and Canada such that many patients have been excluded from its benefits. But if one person's views can really influence these bodies to this extent, it is they that are at fault. Could it be that they have taken a more critical look at the literature than their counterparts elsewhere when assessing current research on deferiprone? Unfortunately, by ignoring Alexander Pope's advice to critics, Shuchman completely submerges the central message of this unfortunate affair. When a scientist had concerns about the efficacy of a drug, attempts were made by a company to prevent her disseminating this information. At the time, her university and teaching hospital did not have adequate processes in place, or the leadership required, to deal with this problem; a long and destructive controversy followed. But at least the outcome was a successful effort on the part of the University of Toronto to regulate clinical-research funding by companies, dissemination of the associated dangers to the scientific community, and a start, albeit not yet completely successful, at trying to regulate these potentially dangerous liaisons more effectively.

The current problems at the interface between clinical research and commerce are too important to be treated in a personalised, anecdotal, or inaccurate way. Those who wish to explore this worrying problem, and we all should, would be better advised to consult the several less emotive, better-documented, and broader-based accounts by Kassirer, Krimsky, and Angell. But at least Shuchman's retrospective is a warning to others who are contemplating taking a stand against commerce; if you do, those that you cross along the way may try to ensure that your lives are never quite the same again.

David Weatherall

[Liz.rose@imm.ox.ac.uk](mailto:Liz.rose@imm.ox.ac.uk)

### **Conflict of interest statement**

I am a research collaborator of Nancy Olivieri and supported the scientists in Toronto who helped her during the events covered by this book.

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Miriam Shuchman, *The Drug Trial: Nancy Olivieri and the Science Scandal that Rocked the Hospital For Sick Children*, Random House Canada (2005) ISBN 0-679-31084-3 Pp 451. CAN \$34.95..