

Box 1: Vioxx timeline

- **May 18, 2000:** VIGOR trial paper submitted to *NEJM*
- **Aug. 2, 2000:** Merck & Co. submits information to the FDA about the VIGOR trial that includes the 3 additional myocardial infarctions (MIs)
- **Nov. 23, 2000:** *NEJM* publishes VIGOR study by Bombardier et al.
- **Feb. 8, 2001:** FDA posts a review of the VIGOR trial indicating 20 MIs
- **Jan. 31, 2002:** *Therapeutics Letter* concludes that COX-2 selective inhibitors are associated with a higher incidence of serious adverse events than nonselective NSAIDs and that rates of serious adverse events in all trials must be published
- **Sept. 30, 2004:** Merck voluntarily pulls Vioxx off the market after finding the drug doubled the risk of heart attack and stroke
- **Dec. 8, 2005:** *NEJM* publishes “expression of concern”

In the original article, the researchers, led by Dr. Claire Bombardier, the director of rheumatology at the University of Toronto, reported a relative risk of MI while taking rofecoxib of 4.25 (95% CI 1.4–17.4). Taking into account the 3 unreported MIs, the relative risk is 5.0 (95% CI 1.7–20.1).

Merck & Co. contends in a Dec. 8, 2005, statement that the MIs in question occurred “after the pre-specified cut-off date and therefore were not included in the primary analysis.”

A *NEJM* expression of concern (online Dec. 8, 2005; print 2005;353:2813-4) states that the editors first became aware of the additional infarctions in 2001 (see box 1), when additional data were made public by the FDA (www.fda.gov/ohrms/dockets/ac/01/briefing/367b2_03_med.doc), but until the memo emerged on Nov. 21, 2005, “we believed that these were late events that were not known to the authors in time to be included in the article.”

The expression of concern questions the validity of research and invites the authors to explain themselves. They had not done so as of this writing.

Bombardier and the *NEJM* declined to comment on the case. In a statement, the

editors said: “Once our concerns have been fully pursued and answered, we will publish the results.”

All this fuss is “somewhat surprising,” says Dr. James Wright, given that *NEJM* was aware of the 3 additional MIs when it saw the FDA posting 5 years ago (Feb. 8, 2001); that information was reiterated in Wrights’ *Therapeutics Letter* on Jan. 31, 2002 (www.ti.ubc.ca/PDF/43.pdf) and in *CMAJ* (2002;167:1131-7).

NEJM “should have reacted when the FDA put the information out there in February 2001. I don’t know if the drug would have been withdrawn sooner,” says Wright, who has been retained as an expert witness by 5 legal firms involved in Vioxx litigation.

Wright believes journals shouldn’t publish any research article unless they get all the data. “There should be standards.” — Barbara Sibbald, *CMAJ*

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China borrows Canadian know-how for new labs

Infectious disease experts from Winnipeg have signed a 3-year agreement with Guangdong Province in China to develop a network of high-security laboratories necessary to help contain outbreaks of diseases such as avian flu.

The agreement, signed in Novem-

ber, is the result of months of negotiations between government health officials from Guangdong and Winnipeg’s International Centre for Infectious Diseases (ICID), a private, non-profit organization that works with the University of Manitoba and the National Microbiology Laboratory, Canada’s only Level 4 containment facility, to promote research and commercialization in infectious disease control.

Guangdong Province, a heavily industrialized area of 100 million people on China’s southern coast, wants to establish up to 4 high-security labs, including at least one Level 4 containment facility. The Chinese want infectious disease experts in Winnipeg to provide expertise in design, construction and staff training.

“They really need people with knowledge, and Canadian expertise is without equal in this area,” said Terry Duguid, president and CEO of ICID.

China has been rapidly expanding its public health surveillance network in a bid to stem the spread of infectious diseases.

Lawrence Yu, chef de mission for the Guangdong delegation, said during a recent trip to Canada that Winnipeg’s laboratory is being viewed as a prototype in China. Yu said China became acutely aware of Canadian expertise in this area when researchers across Canada, including Winnipeg, contributed landmark surveillance and research to the SARS outbreak. — Dan Lett, Winnipeg

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Canapress

Expertise from Winnipeg’s lab (above) will be used to help contain outbreaks in China.