more information about the safety and efficacy of the prostheses and supply a larger potential patient pool for conducting research, the report notes.

Inamed Corporation could not be reached for comment by press time, but a spokesman for Mentor Corporation issued the following statement about the panel report: "We believe in the scientific evidence supporting our products and look forward to Mentor's Memory Gel breast implants becoming an important additional option for women seeking breast reconstruction or augmentation in Canada."

Health Canada regulators will consider the panel report along with public comments and data from the manufacturer supporting its bid to get the products back on the Canadian market. A decision is expected in "a matter of months."

Dr. Supriya Sharma, associate director general of Health Canada's Therapeutic Products Directorate, said the recommendation for additional studies with regard to silicone bleed may affect the timing of any regulatory decision.

The report also recommended:

- Additional education for surgeons, since proper use is "crucial." The panel "very strongly recommends" that Health Canada provide these prostheses only to certified Royal College plastic surgeons who have been specifically trained in implanting them.
- Patient information should acknowledge that the implant is not a lifetime device and will likely need to be replaced, necessitating subsequent surgery.
- Labelling that is available before surgery as printed material and on a Web site. Contraindications should include clinical depression, eating disorders and desire to breast feed.
- Patient and physician information should advise that multiple surgical procedures on the breast may cause irreversible changes to the breast itself, and physicians should be advised that "strong consideration should be given to implant removal" in the case of multiple surgeries. — Laura Eggertson, *CMAJ*

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WTO's new rules allow poorest to import drugs

The World Trade Organization is planning to put into law a waiver originally drafted in 2003 that allows least-developed countries to import generic drugs in public health emergencies, such as the HIV/AIDS epidemic.

The waiver pertains to Article 31 of the WTO's Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS), which requires that drugs manufactured under compulsory licensing be sold predominantly in the domestic market of the countries that produce them. If it stood, that provision would restrict the ability of countries lacking production capacity to import cheaper generic copies of patented drugs.

WHO/Eric Miller

The new TRIPS agreement could allow countries to import generic drugs such as these antiretrovirals.

The amendment to Article 31 will come into force after ratification by two-thirds of WTO member countries — likely by December 2007. A statement attached to the agreement says that members will use the provision in "good faith" to deal with public health problems, not to meet industrial or commercial policy objectives.

The amendment "confirms once again that members are determined to ensure that WTO's trading system contributes to humanitarian and development goals," WTO Director-General Pascal Lamy stated in a news release.

But Médecins Sans Frontières says the 2003 waiver is cumbersome and inefficient: it requires each country to notify the WTO and to license the manufacture of generic drugs on a case-by-case basis. Once a generic manufacturer obtains a licence, it can produce only enough medication to supply a single country. There is no provision in the agreement that would allow international tendering to procure the medicines, "which is the most common and efficient way of purchasing drugs," says Carol Devine, acting program director for MSF.

So far, not one patient has benefited from the waiver, says Devine, who considers it "premature" to give it the force of law.

MSF intends to test the Canadian law by ordering drugs to treat patients in a country that should qualify under the definitions of the WTO agreement. But Devine fears there is so much red tape involved that getting a licence for a generic version, producing it and then having it approved by Health Canada will take years.

The International Federation of Pharmaceutical Manufacturers & Associations supports the amendment, saying it meets the needs of least-developed countries while preserving the agreement itself. — Laura Eggertson, *CMAJ*

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The vexations of Vioxx

The wave of litigation surrounding rofecoxib (Vioxx) has lapped ashore at the *New England Journal of Medicine* (*NEJM*), whose oft-cited study of the drug published in 2000 appears to contain incomplete adverse event information.

Merck & Co. pulled rofecoxib off the market on Sept. 30, 2004, after finding it doubled the risk of heart attack and stroke. There are now some 9200 lawsuits pending in the US against Merck & Co, based in Whitehouse Station, NJ.

In the midst of one such suit, on Nov. 21, 2005, a Merck & Co. memo dated July 5, 2000, emerged. It indicated that at least 2 authors of the *NEJM* article on the VIGOR (Vioxx Gastrointestinal Outcomes Research) study (2000;343:1520-8) knew 4.5 months before publication that 20 study participants suffered myocardial infarction (MI) after taking the drug — not 17 patients, as the *NEJM* article reported.

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/3672b2_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 November, 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.