Institute of Medicine's new drug safety report: implications for Canada

Does the most advanced economy in the world have adequate drug safety legislation to keep its citizens safe from the potential harmful effects of medicines? The Institute of Medicine (IOM), part of the National Academy of Sciences in the United States, doesn't think so. The IOM has issued a new report delivering one of the harshest post-rofecoxib (Vioxx) assessments yet of the US Food and Drug Administration's (FDA) drug safety system. According to the IOM, there are at least 1.5 million preventable adverse drug events in the US each year and the true number may be much higher.[1] This Sept. 22 report, *The future of drug safety: promoting and protecting the health of the public*, makes 25 recommendations focusing largely on clearer authority for the FDA and tougher safety legislation in the US. The recommendations include:

- tighter labelling requirements and advertising limits for newly approved medications
- clearer authority for the FDA and additional tools for enforcement
- better delineation of the FDA's role in gathering and communicating new information relating to marketed products' risks and benefits
- mandatory registration of clinical trial results and better public access to drug safety information
- a substantial increase in funding and staffing for the FDA to better augment drug safety monitoring activities.[2]

The overall context of this report comes from "the public perception that the drug safety system is in crisis" (page 15).[3] Even though government committees both in Canada and the US have examined the safety issues raised by the COX-2 inhibitors (including rofecoxib), this is the first set of concrete steps calling for federal action in the US to avoid future preventable drug catastrophes.

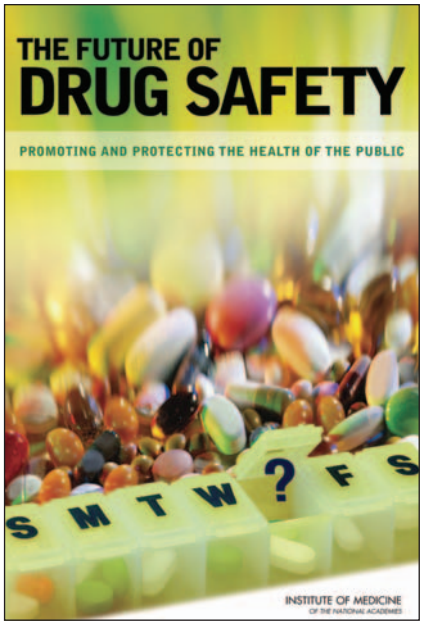
Rofecoxib was one of the world's best-selling arthritis treatments. Its abrupt withdrawal from the market in September 2004 due to the "increased risk of serious cardiovascular events, including heart attacks and strokes"[4] has most certainly affected public confidence in drug regulatory agencies around the world.

The main recommendation in this new drug safety report is that the FDA, operating under resource limitations and lacking legal authority to enforce drug safety, requires the money, manpower and congressional firepower to take its drug safety responsibilities seriously. The report notes that the FDA lacks sufficient federal authority to require post-marketing studies to assess and monitor risk to ensure drug products are used safely and appropriately. Far from being overzealous in its suggestions for better safety monitoring, the report notes that: "the limitations imposed should match the specific safety concerns and benefits presented by the drug product" (page 9).[3]

Dr. Bruce Psaty, from the University of Washington and one of the co-authors of the report, told the *CMAJ* that the FDA needs the "necessary levers to do the job, including penalties in hand — to force companies to finish their post-market studies." The report echoes this sentiment saying that such levers "should include fines, injunctions and withdrawal of drug approval" (page 134).[3]

It is too early to say what the implications of the IOM report are in the US, but the report may find some resonance with a number of current initiatives to improve drug safety in Canada. The National Pharmaceutical Strategy, for example, has recently reiterated that real world safety and effectiveness" is among its 5 key priorities.

According to Health Canada spokesperson, Alastair Sinclair, "although the IOM's report focused on proposed improvements to the regulatory system of the US Food and Drug Administration, many of its recommendations will be helpful in advancing Canada's own regulatory modernization agenda."



He told the *CMAJ* that the report comes at a time when Health Canada is planning "cross-country consultations to renew the Canadian federal drug regulatory system," part of what is called the Blueprint For Renewal (www.healthcanada.gc.ca/hpfb-blueprint). "This process will encompass discussions of the common issues experienced by federal regulators, many of those identified in the Institute of Medicine's report," he added.

Dr. Joel Lexchin, a professor at York University who has observed American and Canadian pharmaceutical policy for more than 2 decades, notes that any changes that will happen in Canada "pretty well depend on what the US chooses to do."

"We typically follow the Americans lead on these kinds of issues, yet it is unclear whether the IOM report will lead to the necessary legislative changes in the US," he says.

The Pharmaceutical Research and Manufacturers of America Senior Vice President Caroline Loew, agreed that

DOI:10.1503/cmaj.061437

the FDA needs better resources to carry out its drug review and surveillance functions. Among the recommendations aiming to modernize the surveillance system for drugs, she pinpointed in a press release that PhRMA supports "more efficient use of the adverse reaction reporting system; maximizing use of large health care data bases; and building more expertise around epidemiological studies."[5]

Others have suggested that many of the needed post-rofecoxib safety improvements are already happening at the FDA and that the drug safety system isn't as bad as some critics have suggested it is. Caroline Loew of PhRMA writes that "though there is always room for improvements, it would be a mistake to accept the notion that the FDA drug safety system is seriously flawed. After all, fewer than 3% of approved prescription drugs have been withdrawn from the American market for safety reasons over the last 20 years."

Others have challenged that assessment and say that the Institute's report doesn't go nearly far enough in recommending to the FDA measures to prevent future drug safety catastrophes. Dr. Sidney Wolfe, head of the Health Research Group at US Public Citizen told the *CMAJ* "the FDA has never done an autopsy on the mistakes it has made in approving drugs" and points to 13 specific cases in which he says serious mistakes have been made by the FDA, leading to large numbers of avoidable deaths and injuries.[6]

Given the potential magnitude of rofecoxib, major changes to drug safety regulation around the world, similar to how the world responded following the thalidomide disaster in the 1960s, might be called for. Yet Wolfe stresses that the US needs to get the lawmakers involved in making any new and substantive changes happen.

"Unless there is congressional oversight of the US Food and Drug Administration — which would change the balance between Congress and the FDA" — there will be no changes to the drug safety world in this country."

What the IOM report might mean for Canada is that, post rofecoxib, it is time to be rethinking the structure of drug safety and oversight activities at Health Canada. Some of the same criticisms of the FDA and its lack of oversight could apply to the Canadian context — especially in our need to have stronger and better funded post market activity.

Terence Young, President of Drug Safety Canada, says that as in the US, the Canadian drug regulatory apparatus needs legislative overhaul to improve drug safety. He outlines an overriding need for Canada to establish an independent drug agency that reports to parliament, not Health Canada. "Health Canada is like a leaky old wooden boat and we need a new icebreaker. Without a new independent drug agency the drug injuries and deaths will no doubt continue," he says.

Regardless of whether there will be substantial legislative changes on either side of the border, there are some simple pragmatic suggestions emerging from the report that could be immediately implemented by Health Canada or the FDA without changing any legislation. For example, arguments against loosening drug advertising legislation, currently being challenged in court on the grounds of freedom of speech could easily be fortified by the IOM recommendations, which suggest that drugs should not be advertised for their first 2 years on the market.

"Placing a black triangle symbol — as is currently done in the UK — on new drugs or new combinations for at least 2 years, is one of the recommendations that we could implement quite easily here in Canada" says Dr. Lexchin.

Alan Cassels
Victoria, BC

This article has been peer reviewed.

Competing interests: None declared.

REFERENCES

1. Institute of Medicine. Preventing medication errors. July 2006. Available: www.iom.edu/Object.File/Master/35/943/medication%20errors%20new.pdf (accessed 2006 Nov 9).
2. Institute of Medicine. Fixing drug safety system will require 'new drug' symbol on labels, major boost in FDA staff and funding, and increased public access to information [press release]. 2006 Sept 22. Available: www8.nationalacademies.org/onpinews/newsitem.aspx?RecordID=11750 (accessed 2006 Nov 9).
3. Institute of Medicine of the National Academies. The future of drug safety: promoting and protecting the health of the public. 2006. Available: http://fermat.nap.edu/books/0309103045/html/15.html (accessed 2006 Nov 9).
4. US food and Drug Administration. FDA News. FDA issues public health advisory on Vioxx as its manufacturer voluntarily withdraws the product. 2004 Sept 30. Available: www.fda.gov/bbs/topics/news/2004/NEW01122.html (accessed 2006 Nov 9).
5. PhRMA Statement on the IOM Drug Safety Report. 2006 Sept 22. Available: www.phrma.org/news_room/press_releases/phrma_statement_on_the_iom_drug_safety_report/ (accessed 2006 Nov 9).
6. Public Citizen. The Health Research Group. Statement before the Institute of Medicine Committee assessing the US drug safety system (HRG Publication #1759). Available: www.citizen.org/publications/release.cfm?ID=7411&secID=1666&catID=126 (accessed 2006 Nov 9).

Alan Cassels has been involved in drug policy evaluations and research focusing on the media's translation of pharmaceutical information for the past 12 years. He is with the School of Health Information Science at the University of Victoria.