FOR THE RECORD

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Apotex receives second FDA warning

The United States Food and Drug Administration (FDA) has issued a second warning letter in a year to Toronto, Ontario-based generic drug manufacturer Apotex Inc. for lapses in good manufacturing practices.

The violations cause Apotex drug products to be considered "adulterated" within US regulations "in that the methods used in, or the facilities or controls used for, their manufacture, processing, packing, or holding do not comform to, are not operated or administered in conformity" with Current Good Manufacturing Practice (CGMP), states the FDA's Mar. 29 letter to Apotex Inc. President Jack M. Kay (http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/ucm207508.htm).

As a consequence, the FDA informed Kay that it would "recommend withholding approval of any new applications or supplements listing your firm as a drug product manufacturer" until such time as corrective action is taken.

"In addition, failure to correct these violations will result in FDA continuing to deny entry of articles manufactured at Apotex Inc., Toronto, Canada, into the United States," the warning letter added.

The FDA had issued a similar warning letter on June 25, 2009, with respect to manufacturing breaches uncovered at a Dec. 10–19 inspection of an Apotex facility in Etobicoke, Ontario.

The latest FDA letter adds that while Apotex recalled about 659 batches of different products as a result of the Etobicoke inspection, there was evidence of "serious and repeat violations" and Apotex's response to the manufacturing problems has been "inadequate and lacks sufficient corrective actions."

The new warning letter regards breaches uncovered during a July–August 2009 FDA inspection of an Apotex facility located at 150 Signet Drive in Toronto, during which "several violations that are identical" to those found during the inspection of the Etobicoke facility were discovered.

"These identical CGMP violations demonstrated a lack of adequate process controls and raised serious questions regarding your corporation's quality and production systems," the warning letter states.

The violations included contamination of a diabetes drug with an "active pharmaceutical ingredient" and unspecified "charred materials." Other violations included contamination found within an antihistamine, as well as failure "to have an adequate equipment cleaning and maintenance procedure or program to prevent contamination that would alter the safety, identity, strength, quality, or purity of the drug product beyond other established requirements."

The FDA letter also states that the numerous violations cited "are not intended to be an all-inclusive statement of violations that exist at your facility."

Apotex did not respond to telephone inquiries about the FDA warning letter. — Wayne Kondro, *CMAJ*

Adverse reaction reports soaring

There was a 35% increase in domestic adverse reaction reports to the Canada Vigilance Program in 2009, Health Canada says in its annual report on the incidence of adverse reactions.

The department received 27 496 reports in 2009, of which 74.9% were deemed to be serious enough as to require in-patient hospitalization or prolongation of existing hospitalization, cause congenital malformation, result in persistent or significant disability or incapacity, be life-threatening or result in death.

The report indicates that there has been a steady increase of adverse reaction reports since 2001, when roughly 11 000 incidents were reported (www.hc-sc.gc.ca/dhp-mps/alt_formats/pdf/medeff/bulletin/carn-bcei_v20n2-eng.pdf).

Roughly 70% (18 301) of 2009 incidents involved pharamaceuticals, while 23% (5998) involved biotechnology products. There were 833 adverse reaction reports involving biologics, 516 involving natural health products, 379 involving radiopharmaceuticals and 34 involving cells, tissues and organs.

Health Canada says that 8428 of the adverse reaction reports were made by consumers and patients, while 6064 came from physicians, 4364 from other health professionals, 3853 from pharmacists, 2906 from nurses, 6 from dentists, 3 from naturopaths and 437 from other unspecified persons.

The report indicates that market authorization holders submitted 305 847 foreign adverse reaction reports in 2009, as compared with roughly 80 000 in 2001. — Wayne Kondro, *CMAJ*

AIDS funding promises broken

Wealthy nations are using the recent economic crisis to renege on promised AIDS relief, reports the International Treatment Preparedness Coalition, a worldwide advocacy group for people living with HIV.

In the report *Rationing Funds, Risking Lives: World Backtracks on HIV Treatment*, the coalition documents early warning signs resulting from the global pull back on AIDS commitment and blasts major donors, such as the Global Fund to Fight AIDS, Tuberculosis and Malaria and the United States President's Emergency Plan for AIDS Relief (PEPFAR), for stalling or flat-

lining promised funding (www.itpcglobal.org/images/stories/doc/ITPC_MTT8_FINAL.pdf).

The report points to increasing caps on the number of people enrolled in treatment programs, drug stock outs and the frequency with which government-run antiretroviral treatment programs turn patients away at the door as the fallout of domestic and external funding cuts in the wake of the global economic crisis.

"Providing access to AIDS treatment for 4 million people has been the most ambitious public health effort in history," says the coalition board member Gregg Gonsalves. "And after all this effort, we've got a few men in Washington [DC], in London [United Kingdom] and in Ottawa [Ontario] saying maybe it's time to do something else."

That's the same as "saying to millions of people: drop dead. Without treatment that is certainly their fate," Gonsalves earlier stated in a media release.

Created in 2001, the Global Fund was intended to provide US$10 billion per year to fight AIDS, tuberculosis and malaria. According to the report, that bold promise was not met; by 2008, donations topped out at only $3 billion per year (www.theglobalfund.org/en/pressreleases/?pr=pr_100308).

The report criticizes US President Barack Obama and UK Prime Minister Gordon Brown for failing to honor their country's promises to donate a fair share toward the Global Fund. Obama is also criticized for pledging US$50 billion to PEPFAR during his election campaign, but then flat-lining funding increases in 2010.

"I'm deeply disappointed in the president, because the US has found money for bailouts and huge stimulus bills over the past 12 months, and what we're asking comes down to promises made and promises kept," says Gonsalves. "A 2.2% increase isn't keeping that promise, because it's effectively making it impossible to put new people on treatment."

The report also singles out leaders of 46 African nations for failing to allocate 15% of their annual budgets toward health spending, as agreed in the Abuja Declaration of 2001. As of 2007, only Botswana, Djibouti, and Rwanda had met that target.

Private donations in the US and Europe have also declined. Between 2007 and 2008, US-based philanthropies decreased spending by about 3%, while funding for European HIV/AIDS charities dropped by 7%.

The report tracks the fallout in six nations: India, Kenya, Latvia, Malawi, Swaziland and Venezuela. It says consequences include severely limited access to antiretroviral treatments, shortages in physicians and nurses to provide treatment, and government reliance on outdated AIDS plans, as well as unreliable data on treatment needs.

"Nations with middle-sized economies and considerable epidemics will be able to hold back the flood, but the poorest countries are already being hit hard by this backtracking," says Gonsalves.

"If we don't pay now, we'll be paying soon," he adds. "Before the number of people in hospital beds goes up, before we see a rise in funerals, the damage will already be done."

Canada can play a major role in shifting the trend if Stephen Harper can be convinced to make universal access to treatment a priority at the next G8 meeting, Gonsalves says. "Living south of the border, we look to Canada for more progressive policies."

The report estimated that while some 4 million people have access to HIV treatment, another 6 million people still need it. — Lauren Vogel, Ottawa, Ont.

Children's health products recalled

The United States Food and Drug Administration (FDA) is advising consumers to stop using certain over-the-counter infant's and children's liquid health products manufactured by McNeil Consumer Healthcare as there may have been flaws in their manufacture.

The 40 products, which include infant and children's Tylenol®, Motrin®, Zyrtec® and Benadryl® (www.mcneilproductrecall.com/page.jhtml?id=/include/mpr_ndc_finder.inc), are distributed in Canada, the United States, Dominican Republic, Dubai (UAE), Fiji, Guam, Guatemala, Jamaica, Puerto Rico, Panama, Trinidad & Tobago and Kuwait.

All of the products have been voluntarily recalled by McNeil Consumer Healthcare "in consultation" with the FDA.

"The FDA recommends that consumers stop using these products," the agency stated in announcing the recall (www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm210441.htm).

"As a precautionary measure, parents and caregivers should not administer these products to their children," the FDA states. "Some of the products included in the recall may contain a higher concentration of active ingredient than specified; others contain inactive ingredients that may not meet internal testing requirements; and others may contain tiny particles. While the potential for serious medical events is remote, FDA advises consumers who have purchased these recalled products to discontinue use."

McNeil Consumer Healthcare stated in a press release that the recall was a "precautionary" measure (www.jnj.com/connect/news/all/McNeil-Consumer-Healthcare-announces-voluntary-recall-of-certain-OTC-infants-and-childrens-products).

"McNeil Consumer Healthcare is initiating this voluntary recall because some of these products may not meet required quality standards," the company stated in a press release. "This recall is not being undertaken on the basis of adverse medical events."

The firm added that it is "conducting a comprehensive quality assessment across its manufacturing operations and has identified corrective actions that will be implemented before new manufacturing is initiated at the plant where the recalled products were made."

The firm's Canadian branch stated in a release that the recall in Canada is "limited to Children's MOTRIN® and Infant's MOTRIN® liquid suspension products and Children's TYLENOL® Cough & Runny Nose liquid suspension only. No other Canadian product is impacted."

(www.mcneilcanada.com/en/downloads/JJ_Release_on_April30.pdf). — Emily Panetta, Ottawa, Ont.

Ontario introduces health care accountability legislation

Linking hospital chief executive officer salaries to patient satisfaction and emergency wait times, the adoption of patient-based funding for larger hospitals and a requirement that hospitals "develop and post annual quality improvement plans" are among measures included in proposed Ontario legislation to bolster accountability in the province's health care system.

"We want our health care system to be focused on patient needs with health services supported by the best evidence and highest standards," said Ontario Minister of Health and Long-Term Care Deb Matthews in a press release (www.news.ontario.ca/mohltc/en/2010/05/improving-health-care-for-ontarians.html). "Improving quality of care not only means better patient care, it improves the value of our health care investment."

The Excellent Care for All Act, 2010 proposes that hospital CEOS — 14 of whom earned salaries higher than $500 000 in 2009 — would have their compensation and bonuses linked to their facility's ability to achieve performance targets that are established as part of their "quality improvement plans" (www.ontla.on.ca/bills/bills-files/39_Parliament/Session2/b046.pdf).

Each hospital would be obliged to establish a quality committee that would craft the plan and deliver an annual accountability report. As part of the process, hospitals would have to regularly conduct patient and employee satisfaction surveys, as well as ensure that a process is in place for handling patient complaints.

The patient-based funding system for larger hospitals, which will be introduced on Apr. 1, 2011, will see facilities reimbursed according to the number and type of patients that they see. Canadian hospitals have traditionally received money via a block-funding model, which grants annual lump sums. But many other countries — such as the United States and England — have implemented funding systems in which hospitals are rewarded on the basis of patient outcomes (called payment by results or pay for performance) or activity-based funding (*CMAJ* 2008; 178:1207-8).

The provincial government indicated it will be consulting with hospitals, local health networks and others in refining the precise payment system that will be used. "Among the issues to be considered is how to recognize hospitals with unique roles, such as academic health centres, as well as those serving small and rural communities."

The Ontario Hospital Association called the legislative proposals "an important next step in continuous quality improvement" (www.newswire.ca/en/releases/archive/May2010/03/c8080.html). — Emily Panetta, Ottawa, Ont.

RCMP restricts use of tasers

The Royal Canadian Mounted Police has moved to restrict the use of conducted energy weapons (CEWs) — more commonly known as tasers — by unveiling a policy that prohibits the use of the handheld weapons except in cases involving bodily harm or the clear threat of harm.

The policy limits the use of tasers "to situations where a subject is causing bodily harm, or the police officer believes, on reasonable grounds, that the subject will imminently cause bodily harm" (www.rcmp-grc.gc.ca/ccaps-spcca/cew-ai/operations-17-7-eng.htm).

Other revisions to the policy include:

- requiring officers to give a verbal warning, where tactically feasible, so the subject is aware of the imminent deployment of the CEW,
- requiring officers to request medical assistance, when feasible, prior to using the CEW in medically high-risk situations.
- adding further CEW-related record keeping requirements, and revising CEW testing procedures to determine if CEWs are operating within manufacturer specifications."

The RCMP said the policy revisions were made in to recommendations from the Commission for Public Complaints Against the RCMP, the province of Alberta's guidelines on CEW use and the Braidwood Inquiry into the Oct. 14, 2007 death of Polish citizen Robert Dziekanski at Vancouver International Airport after being shot by a taser (www.rcmp-grc.gc.ca/news-nouvelles/2010/05-03-cew-ai-eng.htm).

Ian McPhail, interim chair of the Commission for Public Complaints Against the RCMP called the moves "prudent" (www.cpc-cpp.gc.ca/nrm/nr/2010/20100504-eng.aspx). The commission added in a news release that discussions are ongoing in regard to RCMP adoption of other recommendations, "including the need for mandatory medical attention after every Taser use, as injuries may not be visible or apparent to the RCMP member, nor will the member necessarily be aware of any underlying medical conditions of the subject. There also remains the recommendation to generally limit the CEW to members with five years or more of experience (except those on specialized teams)." — Emily Panetta, Ottawa, Ont.

Better a hospital than a dumpster

Creating a drop-off zone for unwanted babies is preferable to them being "left in a dumpster," says the developer of a Vancouver, British Columbia-based initiative that will allow troubled women to anonymously abandon their newborn babies.

"It's not ideal. The ideal would be to know a little bit about the medical history for placement of the baby. But it's preferable to be in a safe place without that information then to be left in a dumpster," says Dr. Geoffrey Cundiff, head of the obstetrics and gynecology department at St. Paul's Hospital.

The "angel's cradle" initiative allows a mother to put a baby in a bassinet in a private area of the hospital, press an alarm with a 30-second delay and then leave. Hospital staff would recover and treat the infant and

then hand it over to the Ministry of Children and Family Development to long-term care and likely, adoption.

Should a mother want to reclaim her maternal rights and responsibilities, she would have to negotiate with the ministry, Cundiff says. "The ministry is going to pursue what's best for the baby and the mother. If the mother's circumstances change and she's healthy, that could be the best situation for the baby."

Cundiff says he borrowed the notion of an angel's cradle from the so-called "foundling wheels" of 12th-century Europe, which saw the installation of wooden cribs or baby hatches in churches and convents for mothers to safely abandon their infants. "I like to read history and I had been reading about foundling wheels. I thought that's actually a good idea," he says.

The proposal was rapidly supported by the hospital's senior board. "We spent a lot of time trying to think about the ethical and legal ramifications," Cundiff says. "A lot of the work focused on taking the concept to authorities, Child and Family Development, and also internally within our institution — speaking to physicians in the emergency department, the nursery care unit and [hospital] security."

Cundiff adds that using the angel's cradle might be the best option for an unfit mother in desperate circumstances. "There are women who will abandon their babies out in the community. There's a reason they're not using their resources — maybe they don't know about them, or maybe they don't want to come forward," he says. "There's a need for anonymity, and we felt this was an approach to reach those women and make them aware of the other options."

Cundiff stresses that the program seeks to inform mothers of their options — providing contact information for adoption agencies and government services — before leaving a child. "All of our literature, even the sign on the door, provides other options," he says. "But if they're going to abandon their baby, then we want them to do it in a safe place." — Emily Panetta, Ottawa, Ont.

Progress being made on Millennium Development Goals

Although progress is being made in many nations toward achieving the World Health Organization's eight health-related Millennium Development Goals, some nations are "falling behind," the WHO says in an update on efforts to tackle ill-health by 2015.

"Often the countries making the least progress are those affected by high levels of HIV/AIDS, economic hardship or conflict," the WHO says in a fact sheet, Progress towards the health-related Millennium Development Goals (www.who.int/mediacentre/factsheets/fs290/en/index.html).

Evidence of progress toward achieving the goals includes indicators that fewer children are dying and fewer are underweight. As well, fewer people are contracting HIV, more people have access to safe drinking water and more women have access to help during childbirth.

Although five years remain to the 2015 deadline for achieving the targets, improvements in some areas have already been "striking," the WHO says. "The percentage of underweight children [under the age of five] is estimated to have declined from 25% in 1990 to 16% in 2010, HIV infections dropped 16% between 2001 and 2008 and the percentage of the world's population with access to safe water has increased from 77% to 87%, enough to reach the MDG target."

Nevertheless, challenges remain, WHO adds. In some countries, "progress has been limited because of conflict, poor governance, economic or humanitarian crises, and lack of resources. The effects of the global food, energy, financial and economic crises on health are still unfolding, and action is needed to protect the health spending of governments and donors alike."

With regard to the millennium development goal of halving the proportion of people who suffer from hunger, for example, the WHO notes that undernutrition remains "an underlying cause in about one-third of all child deaths. Over the past year, rising food prices coupled with falling incomes have increased the risk of malnutrition, especially among children" (www.who.int/whosis/whostat/EN_WHS10_Part1.pdf).

Moreover, "in some countries, the prevalence of undernutrition has increased, and worldwide stunted growth still affected about 186 million children under five years of age in 2005."

Similarly, there are regional and national variations in achieving the millennium development goal of a 67% reduction in child mortality from 1990 levels. "In 2008, the total annual number of deaths in children under five years old fell to 8.8 million — down by 30% from the 12.4 million estimated in 1990. Mortality in children under five years old in 2008 was estimated at 65 per 1000 live births, which is a 27% reduction from 90 per 1000 live births in 1990."

But the greatest reductions occurred in the wealthiest households and in urban areas. The progress has not been matched "in countries facing economic crises or conflicts. Low-income countries would need to increase their annual average rate of decline from 1.9% to 10.9% in order to achieve the target. Reducing child mortality increasingly depends upon tackling neonatal mortality; globally about 40% of deaths."

The report also suggests there have been improvements in child health interventions, including "the use of insecticide-treated nets to prevent malaria; efforts to prevent mother-to-child transmission of HIV; and vaccination against hepatitis B and Haemophilus influenzae type B pneumonia." — Emily Panetta, Ottawa, Ont.

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