

Are Canada's drug regulators working for you, or for the industry? Hamilton Spectator and Straight Goods, February 21, 2003,

By Dr. Gordon Guyatt

(Spectator headline: Regulators must not cozy up to drug companies)

You meet Paul Stolley, and you find a gentle, soft-spoken, older man with a delightful sense of humour. A perfect grandfather, or everyone's favourite uncle.

Yet, Stolley is one of the harshest critics of the U.S. Food and Drug Administration (FDA). The FDA decides whether there is enough evidence of benefit for drugs to go on the market, or enough evidence of harm to keep them off.

Stolley's complaint? Since 1992, the American government has required drug companies to pay a big part of the cost of the drug regulation process. Companies now pay almost half the FDA's cost of reviewing drugs. Stolley believes that the funding situation has made the FDA the industry's servant. "I think it's a shame how it has fallen down on the job. The FDA is in partnership with industry. It should be negotiating, not in partnership. Why is it in partnership? Because it's financially supported by industry."

What has led Stolley to his harsh conclusion? Stolley had an outstanding career as a health researcher. His credits include 8 years as Chair of the Department Preventative Medicine in Maryland, and a term as President of the American Epidemiological Society. In July 2000, he joined the FDA as a senior consultant.

Stolley's first job was to check out a recently approved drug called alosetron. A giant company, GlaxoSmithKline, markets the drug for "irritable bowel syndrome" or IBS.

People with IBS suffer from on-and-off diarrhoea, constipation, and abdominal pain. The condition is common. Depending on the definition, up to 20% of the population suffer from IBS. Most IBS is mild, a nuisance more than an illness. Not the sort of condition that warrants a drug with serious side effects.

In February 2000, the FDA approved alosetron for treatment of women with IBS who have diarrhoea as their main symptom. Several trials suggested that Alosetron helps this subgroup of patients. But the effect was modest. About 40% of the women taking placebo (a "sugar pill") improved. An additional 20% improved with alosetron.

Stolley was assigned to look at the drug because of alarming reports of side effects. These included severe constipation leading to a leak in the bowel, and "ischemic colitis" or severe bowel inflammation. Stolley raised a warning cry, and in November 2001, the company agreed to withdraw the drug from the market.

Almost immediately, however, the company lobbied for re-marketing the drug with restrictions. Stolley's boss at the FDA criticized Stolley for being too negative about alosetron, and told him it should be back on the market.

Feeling shut out of discussions, Stolley left the FDA six months ahead of schedule.

By April of 2002, serious complications of alosetron had led to 100 hospitalisations, 50 surgeries, and 7 deaths. An FDA committee of experts suggested that alosetron be put back on the market, but with severe restrictions.

The FDA decided to put the drug back on the market, but without the restrictions the committee had recommended. One member of the committee, Dr. Brian Strom, one of the world's leading experts on drug use, thinks the FDA made a bad decision.

"With alosetron, the risk-benefit ratio is not worth it," Strom has said, "unless the use can be restricted to those who really need it and who are likely to benefit from it which is a very, very small group."

Should Canadians care about this worrisome situation? Like the U.S., since the mid-1990s the Canadian government has been charging industry to pay for the drug regulation and approval process.

Critics of the Therapeutic Products Directorate (TPD), Canada's FDA-

equivalent, believe that the funding change has led to a similar inappropriate partnership between the drug manufacturers and the drug regulators here in Canada.

Critics point to an internal bulletin issued by a senior TPD official, Dann Michols, in 1997. Discussing whom the TPD should serve, Michols advised staff "the client is the direct recipient of your services. In many cases this is the person or company who pays for the service." The document gives the public secondary status of "stakeholder" or "beneficiary". Is there any evidence that TPD is putting industry interests ahead of the public? The TPD's attitude to direct-to-consumer (DTC) drug advertising suggests the answer is yes.

In this column 2 weeks ago I described how DTC advertising leads to more inappropriate prescribing, and escalation of skyrocketing drug spending.

In Canada, as in almost all industrialized countries, DTC advertising is illegal. TPD has become very lax in enforcing the ban, allowing advertisements that clearly violate the law.

Worse yet, TPD is seriously considering following the U.S. lead and allowing DTC advertising.

Roy Romanow's report recognizes the problem of TPD's conflict of interest. 'In effect," Romanow said, "a 'firewall' must be established between the industry's financial contribution and the Agency's work. Very stringent guidelines for pharmaceutical industry contributions should be in place to ensure the Agency's independence from the industry it regulates." Whoever pays the piper calls the tune. Should our drug regulators be putting the industry's needs above the public's health?

Not on your life -- or death.