

# Secrecy and the Health Protection Branch

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Information about drugs undergoing the regulatory approval process in Canada is shrouded in secrecy. The Health Protection Branch (HPB) of Health Canada considers confidential the information submitted by a manufacturer in requesting approval for a drug and at present does not publicly disclose that a product is under review. (In April 1998, the HPB proposed to list products under review on its Web site; this has still not been finalized.) Nor does the HPB have external advisory committees that meet in public to discuss drugs under consideration. The net effect is to deny health care professionals and consumers the right to make any intervention with the HPB before a drug comes to market.

After a drug has received approval for marketing, information about it is still highly restricted. The HPB will release information contained in the submission only with the consent of the sponsoring company. If consent is denied, that information remains confidential. The end result is that health care professionals may be unable to review and validate the information that the HPB used in deciding to allow a product to be sold.

This lack of access to health and safety data can be illustrated by my experience with regard to pediatric antidiarrheal agents. The World Health Organization (WHO) has concluded that these products have no place in the management of acute diarrhea in children.<sup>1</sup> This conclusion has been backed up by Public Citizen, a health research group in the US, which analysed studies identified through a MEDLINE search and the files of the US Food and Drug Administration (FDA).<sup>2</sup>

I wrote to the companies that make pediatric antidiarrheal products in Canada and asked them, among other things, to send me a copy of all the studies they had showing that their products were both safe and effective for the treatment of diarrhea in children. None of the 7 papers I received<sup>3-9</sup> met the methodological criteria outlined by the WHO for proving that antidiarrheal agents are effective.<sup>10</sup>

The fact that the manufacturers could not supply any methodologically sound literature to support the use of their products raised a question in my mind about the quality of the studies that had been submitted to the HPB to obtain approval for their use in children. Accordingly, in November 1996 I made a request to the Access to Information Centre of Health Canada for all studies that the HPB had that dealt with the question of the efficacy of a range of commonly used antidiarrheal agents. As of August 1998, or 21 months after my request was filed, I am still waiting for a final answer.

Does it really matter whether or not I was able to obtain the requested documents within a reasonable time? After all, inappropriate use of antidiarrheal medications is probably not a significant problem in Canada, and there have been very few reports in children in this country of adverse events associated with these products. In this case the lack of access to information is not critical, but the principle that health care professionals and the public should have access to health and safety data on drugs is one that needs to be established.

It is not hard to conceive of a situation in which lack of access to clinical information could be hazardous to patients' health. It often happens that after a drug appears on the market it becomes widely used for an indication for which it has not been approved. It is entirely possible that the manufacturer initially ap-



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plied to have its product approved for this use, but the application was rejected by the HPB because of inadequate proof of efficacy, concerns about safety or both. Under the current system the HPB's refusal to approve the drug for that indication and the clinical data supporting that decision would never come to light. Physicians could potentially keep using the product for the nonapproved indication for years.

Clearly, there are good reasons why manufacturing information should be protected by the HPB. This is proprietary knowledge that, if it became public, could adversely affect profits by providing competitors with an unfair advantage. In addition, personal data that enter the files of regulatory agencies such as the HPB can include the identity of individual patients and health care professionals as well as information on individual patients' diagnoses. Any such information that might lead to the identification of individual patients or health care professionals should not be disclosed to any party.<sup>11</sup>

However, concerns about confidentiality do not apply when it comes to health and safety data. There is no good evidence to show that the interests of companies would be harmed by the disclosure of this type of information; more specifically, confidentiality is not necessary to foster research and innovation.<sup>12</sup> On the other hand, nondisclosure has serious disadvantages for the HPB, health care professionals and the public. If information submitted to regulatory agencies is never disclosed, these data will never enter normal peer review channels and will therefore not be subject to scrutiny by independent scientists. Without this type of feedback HPB reviewers may be more prone to misjudge the accuracy or usefulness of the data submitted; moreover, the scientific atmosphere in the agency may be stifled and the professional growth of its staff severely inhibited.<sup>12</sup> Deprived of any independent access to information, health care professionals have no choice but to accept the HPB's judgement about the safety and effectiveness of products. In the case of well-established drugs this is probably not much of a concern, but it may be different with new drugs where experience is limited.

Finally, the public may be denied knowledge of the full health effects of products so that they can decide for themselves whether or not to use them. Even if most consumers would never take the time to read health and safety data, consumer-oriented journalists in consultation with scientific experts could use some of this information to inform the public of the risks and benefits of products.<sup>12</sup>

Issues of secrecy in drug regulation are being actively debated throughout the world. In 1996 the *International Journal of Risk and Safety in Medicine* devoted an issue to a review of the situation in countries such as the UK, Japan, Finland and Malaysia.<sup>13-16</sup> An editorial accompanying these

articles noted that "secrecy, together with its ugly sisters lack of transparency and lack of accountability, can distort and undermine the prime function of drug regulation which is to serve the public and protect health" and concluded that "those involved in drug regulation cannot properly serve the interests of those who use medicines if they are not subject to public scrutiny."<sup>17</sup>

Over the past few years many organizations have started a dialogue on the question of secrecy in drug regulation through a number of mechanisms. In September 1996 an International Working Group with members from the Brazilian Society for Drug Monitoring, the International Society of Drug Bulletins, the Dag Hammarskjöld Foundation and the Malaysian National Poison Centre met in Uppsala, Sweden, and issued a 10-point statement on transparency and accountability.<sup>11</sup>

In early 1997 the European Medicines Evaluation Agency (EMEA), the body responsible for centralized drug approvals in the European Union, initiated a consultation on improving access to information at a European level; this initiative culminated in a workshop at the end of October 1997. Although there are still many restrictions on the release of information, the consultation and workshop reflect a greater willingness to engage in a discussion than has yet been seen from the HPB. (Readers interested in the statement on access by the EMEA can find it on the agency's Web site: [www.eudra.org/emea.html](http://www.eudra.org/emea.html).)

We need only look south of the border for an example of a much more open system. In the US, third-party requests for reports of the clinical trials submitted with a new drug application are honoured within 10 working days and the company involved does not have a veto on the release of information. (Trade secrets such as a commercially valuable plan, formula, process or device as well as commercial or financial information are exempt from release.) In addition, the FDA releases a Disclosable Summary, formerly known as a Summary Basis of Approval, for newly approved drugs. These summaries include a pharmacology review, a toxicology review, a safety summary, a statistical review and the entire report on the clinical trials submitted by the sponsor as well as the FDA reviewer's comments on those trials. The only information routinely released by the HPB is the Official Product Monograph.

To compare these 2 types of documentation, consider the volume of information available for the product carvedilol. The Official Product Monograph in Canada is 16 pages long, whereas the Disclosable Summary from the US comprises 1009 pages. Finally, the review of many drugs in the US is referred to expert advisory committees for an opinion before a final decision is made by the FDA. These committees meet in public, and before the formal meeting begins there is a 1-hour period,



which can be extended, for public comment about the drugs being considered.

As a result of cutbacks in federal funding, the Therapeutic Products Directorate, the arm of the HPB charged with regulating drugs and devices, now receives about 70% of its financing from fees paid by pharmaceutical and other companies.<sup>18</sup> This situation has led to charges that the drug companies have too much influence over decisions made by the HPB and that public safety is being sacrificed for corporate profits. If the HPB is to assure the public that safety issues are of paramount importance in its decisions and that there is no conflict of interest, then it must start to provide rapid and open access to a much wider range of information.

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## References

1. World Health Organization. *The rational use of drugs in the management of acute diarrhoea in children*. Geneva: The Organization; 1990.
2. Ahmad SR, Lurie P, Wolfe SM. *Citizen's petition for a ban and/or relabeling of antidiarrheal drugs*. Washington: Public Citizen; 1993.
3. Dukes GE. Over-the-counter antidiarrheal medications used for the self-treatment of acute nonspecific diarrhea. *Am J Med* 1990;88(6A Suppl): 24S-26S.
4. Gupte S. Diphenoxylate hydrochloride (Lomotil) in chronic diarrhoea in children. *Indian Pract* 1974;27:339-41.
5. Karan S, Mukherjee V, Mukherjee L. Assessment of safety of Lomotil in infants. *Indian Pediatr* 1976;13:295-300.
6. Limaye AS. Comparison of Lomotil with Pectokab in furazolidone-treated infective diarrhoea. *Curr Ther Res* 1980;28:80-7.
7. Haqqani AH, Taqi S. Diphenoxylate hydrochloride in the diarrhoeal disease of children. *Pak Pediatr J* 1981;5:249-58.
8. Anderson J. Double-blind comparison of loperamide HCl and placebo in the treatment of acute diarrhea in children. *Adv Ther* 1984;1:14-8.
9. Chavarria AP, Loria-Cortes R, Carrillo-Henchoz JM. Control of pediatric diarrhea. *Adv Ther* 1984;1:115-9.
10. World Health Organization. *The rational use of drugs in the management of acute diarrhoea in children*. Geneva: The Organization; 1990. p. 68.
11. *Statement of the International Working Group on Transparency and Accountability in Drug Regulation*. Amsterdam: Health Action International; 1996.
12. McGarity TO, Shapiro SA. The trade secret status of health and safety testing information: reforming agency disclosure policies. *Harv Law Rev* 1980; 93:837-88.
13. Medawar C. Secrecy and medicines. *Int J Risk Safety Med* 1996;9:133-41.
14. Beppu H. The case of contaminated blood products in Japan. *Int J Risk Safety Med* 1996;9:157-9.
15. Ollila E, Hemminki E. Secrecy in drug regulation. *Int J Risk Safety Med* 1996;9:161-72.
16. Razak DA. Access to regulatory information in Malaysia — a preliminary study. *Int J Risk Safety Med* 1996;9:179-86.
17. Time to lift the veil of secrecy. *Int J Risk Safety Med* 1996;9:131-2.
18. Therapeutic Products Programme. *Overview of product licensing framework II*. Ottawa: Health Canada; 1997.

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## HOLIDAY REVIEW '98 CALL FOR OUTLANDISH PAPERS

Deadline: Oct. 1, 1998

Last December *CMAJ* published its first Holiday Review issue. We hope this will become an annual tradition, but that depends on you. Last year we presented the year in review, with writers from across Canada looking back at the advances within their specialties. This year, and we admit unabashedly that we've stolen the idea from our friends at the *BMJ*, we want to take a lighter approach. Here's what they look for: "The usual cocktail of the deadly serious, the poignant, the speculative, the frivolous, and the downright barmy."

We know Canadian physicians can be as barmy as the best of them, so we are throwing down the gauntlet. Give us your weird studies, your unsubstantiated research, your outrageous anecdotal evidence, tell us why you should have been a vet or an investment banker, document the undocu-

mented. To wit: one of the *BMJ*'s 1997 reports was entitled "Do overweight people remove their shoes before being weighed by a doctor? Consecutive study of patients in general practice." You get the idea. We are also looking for some poignant, practice-related articles.

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