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## Drug safety in Canada:

### 2 steps forward, 1 step back

Enhancement of patient safety has become a priority for health care practitioners and organizations. Adverse medication events remain a major concern, as drug error is a significant cause of adverse outcomes for hospital inpatients.<sup>1</sup> Patients are particularly vulnerable to medication error during the perioperative period. The leading cause of malpractice suits for Canadian anesthesiologists is medication error, and misidentification of drugs is the most frequent underlying problem.<sup>2,3</sup>

Improved safety requires a team effort with a focus on patients' well-being.<sup>4</sup> Thus, it is disturbing that AstraZeneca has marketed in Canada a product that fails to meet the minimum labelling standard set out in the Food

and Drugs Act.

Bupivacaine is a potent, potentially lethal local anesthetic that is used for local infiltration and for spinal and epidural anesthesia. It is considerably more cardiotoxic than many other local anesthetics. The label on the bupivacaine Polyamp® ampoule sold by AstraZeneca does not include the generic name of the drug, but rather identifies the product only by the brand name, Sensorcaine (Fig. 1).<sup>5</sup>

The Food and Drugs Act states that “the inner and outer labels of a drug shall show (i) the proper name, if any, of the drug which, if there is a brand name for the drug, shall immediately precede or follow the brand name in type not less than one-half the size of that of the brand name; (ii) if there is no proper name, the common name of the drug.” The act also specifies that “No person shall sell a drug that is not labelled as required by these Regulations.”<sup>6</sup>

Clearly, the Sensorcaine packaging does not meet these legal requirements. This situation raises several disturbing questions. Why would an international pharmaceutical firm design ampoule labels with an emphasis on marketing rather than patient safety? How could this product bypass scrutiny by Health Canada and be introduced into Canadian hospitals? Once the

oversight was brought to the attention of AstraZeneca, why did the manufacturer not post warnings and apply additional adhesive labels to the ampoule until a new product, appropriately labelled, was available?

Physicians and health care providers must demand that the pharmaceutical industry “join the team” and make patient safety more important than marketing considerations.

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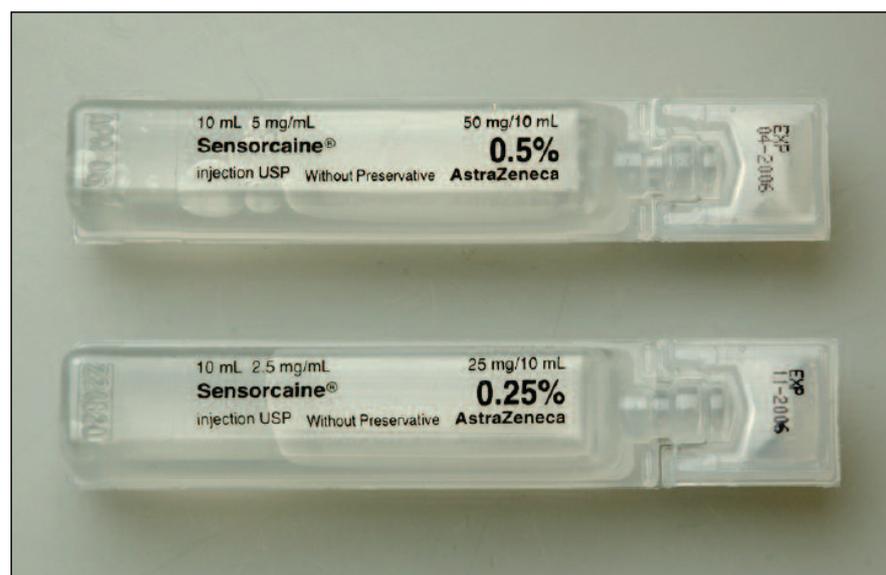
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[Response from the manufacturer:]

When the need to manufacture bupivacaine outside of Canada became a reality, our labelling capability was restricted to the manufacturing equipment at the new sourcing site. We



**Fig. 1:** Polyamp® ampoules containing bupivacaine are labelled with the company's brand name, Sensorcaine, rather than the generic name, bupivacaine.

made changes that we felt best accommodated the limitations of the labelling equipment and that we interpreted as acceptable for small labels. Of note, the generic name has always been included on the outer package.

Importantly, when we received concerns, we took measures to change the label. These included informing the Institute for Safe Medication Practices about the absence of the generic name on the Polyamp®, and working with our colleagues to make equipment modifications enabling the inclusion of the generic name. With regard to existing stock, we investigated the option of attaching pre-printed labels to the Polyamp®. This was considered unacceptable, as it could have compromised the safety of the product due to potential leaching of adhesive through the Polyamp® into the solution.

AstraZeneca collaborated with the Health Products and Food Branch Inspectorate to manage the existing product and the introduction of product with revised labelling. In addition, we alerted customers and Drug Information Centres regarding the introduction of product with revised labelling and the option to exchange existing stock. We also destroyed all of our stock with the previous labelling and replaced returned inventory with newly labelled product.

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## Corrections

In recent Analysis article,<sup>1</sup> the second figure illustrating the cases of invasive pneumococcal infection among adults 65 years and older was incorrect. The correct figure, Fig. 1, is included here.

### REFERENCE

1. Kellner J, Church DL, MacDonald J, et al. Progress in the prevention of pneumococcal infection. *CMAJ* 2005;173(10):1149-51.

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In a recent commentary,<sup>1</sup> it was stated that Health Canada uses the World Health Organization Good Clinical Practice (GCP) guideline. In 1997, Health Canada adopted the GCP guideline developed by the International Conference on Harmonization.<sup>2</sup> In notifying us of the error, Jean Saint-Pierre, coordinator at the Good Clinical Practice Unit at Health Canada, stated that the Health Products and Food Branch Inspectorate has been conducting GCP inspections on clinical trials. These inspections assess the level of compliance with GCP of qualified investigators conducting trials. Two summary reports of findings made during these inspections are publicly available.<sup>3</sup>

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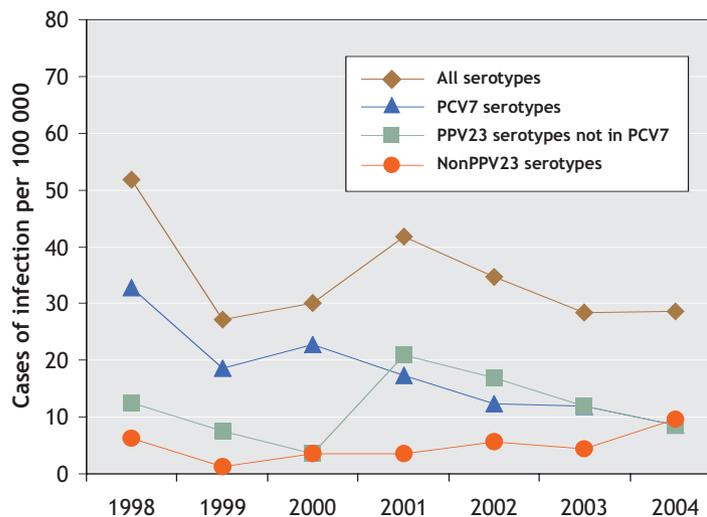
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In a recent editorial on clinical practice guidelines,<sup>1</sup> it is stated that, according to the Common Drug Review, the cost of insulin glargine is 5 times as much as generic insulin. According to the Canadian Expert Drug Advisory Committee, the comparative prices for insulin glargine and NPH insulin of \$5.50 and \$1.60 per 100 units, respectively — that is, just over 3 times the cost of generic insulin.<sup>2</sup> We thank Mike Tierney, Director, Common Drug Review, for bringing this matter to our attention.

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**Fig. 1:** Cases of invasive pneumococcal infection per 100 000 among adults 65 years and older according to year and serotype group. Data from CASPER Surveillance, 1998–2004 ( $\chi^2$  or Fisher exact test for comparisons). When compared with the combined rate between 1998 and 2001, the rate in 2004 decreased by 62.7% to 8.5 (95% CI 3.7–16.7) for PCV7 serotypes ( $p = 0.007$ ); the change of 23.9% to 28.6 (95% CI 18.9–41.7) for all serotypes was not significant ( $p = 0.24$ ), nor was the change of 24.1% to 8.5 (95% CI 3.7–16.7) for PPV23 serotypes that are not in PCV7 ( $p = 0.59$ ). The increase of 163.9% to 9.5 (95% CI 4.4–18.1) for nonPPV23 serotypes was significant ( $p = 0.03$ ).