



# Canadian Adverse Reaction Newsletter

Volume 22 • Issue 3 • July 2012

[www.health.gc.ca/carn](http://www.health.gc.ca/carn)

## In this issue

|   |   |
|---|---|
| LigaSure vessel sealing system and torn vessels | 1 |
| CARN is "going green"                           | 2 |
| Adverse reaction and incident reporting — 2011  | 3 |
| Summary of advisories                           | 6 |

## Scope

This quarterly publication alerts health professionals to potential signals detected through the review of case reports submitted to Health Canada. It is a useful mechanism to stimulate adverse reaction reporting as well as to disseminate information on suspected adverse reactions to health products occurring in humans before comprehensive risk-benefit evaluations and regulatory decisions are undertaken. The continuous evaluation of health product safety profiles depends on the quality of your reports.

## Reporting Adverse Reactions

### Canada Vigilance Program

Phone: 866 234-2345

Fax: 866 678-6789

Online: [www.health.gc.ca/medeffect](http://www.health.gc.ca/medeffect)

## Did you know?

To receive the **Newsletter** and health product **advisories** free by email, **subscribe** to the **MedEffect™ e-Notice** at [www.health.gc.ca/medeffect](http://www.health.gc.ca/medeffect)

## LigaSure vessel sealing system and torn vessels

### Key points

- Health Canada has received reports of incidents in which LigaSure instruments were sticking to tissue or clamping onto tissue and not releasing.
- Excessive sticking can lead to tearing of tissue after sealing and can interfere with the proper functioning of the instrument.
- Health care professionals should be aware of this limitation of LigaSure vessel sealing systems and are encouraged to report adverse incidents to Health Canada.

The LigaSure Dolphin Tip (formally called LigaSure V) laparoscopic vessel sealer/divider (LS1500) is a single-use class II medical device (IV being the highest risk class). The device is intended for use with a manufacturer-approved power source to seal vessels 7 mm in diameter or smaller, and to produce hemostasis in arteries, veins and tissue bundles.<sup>1,2</sup> The instrument can also be used to seal pulmonary vasculature but only when used with the ForceTriad Energy Platform generator.<sup>1</sup> The LS1500 model (first marketed on Dec. 4, 2003) is one of 6 LigaSure laparoscopic instruments marketed in Canada by Covidien.

As of March 2012, Health Canada

received 24 reports of incidents suspected of being associated with the use of the LigaSure V instrument. Incidents described in the reports included stripped insulation, malfunction of the device, pieces of the device falling into the body cavity requiring retrieval, and inadequate sealing by the device. Nine of the reports described a problem of the tip of the instrument sticking to tissue or the instrument jaws clamping on tissue and not releasing, which often required physical manipulation or cutting the device off the tissue to release it. One of the 9 cases was included in the 2011 annual report of the Paediatric Death Review Committee and Deaths Under Five Committee published by the Office of the Chief Coroner, Province of Ontario.<sup>3</sup> The reported incident described the death of a 7-month-old infant who underwent surgical correction of a cystic lesion in his lung (intralobular sequestration of the left lower lobe) using the LigaSure V instrument and the LigaSure vessel-sealing generator. The patient's death from hemorrhagic shock was related to tearing of the pulmonary vein because of tissue sticking on the jaws of the device despite cleaning efforts.<sup>3</sup> In another reported incident, the device's propensity to stick to tissue led to blood loss but was described as insignificant and resulted in no further complication to the patient. The remaining 7 reports

mentioned no injuries or ill effects to the patient.

The issue of increased stickiness and difficulty in releasing the jaws of the device from tissue extends to other LigaSure devices as well. For example, as of March 2012, Health Canada received 18 reports of incidents suspected of being associated with the use of the LigaSure ATLAS instrument. Although some of the reports described incidents involving device damage or malfunction, 10 of the 18 reports were related to the stickiness of the tip or difficulty in releasing the jaws of the device. In one case, the device stuck to the tissue, resulting in a torn vessel, a blood transfusion and admission of the patient to the critical care unit. Another 3 reports described minimal bleeding because of the tip sticking, but no patient harm was reported. The remaining 6 cases reported no patient injury or serious deterioration in health.

There is evidence in the literature of the successful use of the LigaSure vessel sealing system during pediatric thoroscopic procedures involving pulmonary vasculature.<sup>4-6</sup> However, one published study, involving sheep, noted a tendency of the jaws of the

device to stick to tissue.<sup>7</sup> Irrigation and careful manipulation were required to release the sealed area unharmed.<sup>7</sup>

Many factors can contribute to increased charring and sticking of the tip to tissue. These factors include, but are not limited to, eschar in between the jaws due to a build-up of blood between the jaws, not using the device as per the instructions, using the device on a high-power setting or a large-power surge, and using the device beyond its intended use.<sup>3,7</sup>

There is a need to minimize the risk of tissue sticking to the instrument jaws, because excessive sticking can lead to tearing of tissue after sealing and can interfere with the proper functioning of the instrument.<sup>3</sup> Methods to minimize sticking include (a) keeping the jaws clean at all times; (b) cleaning the instrument more frequently when working in a bloody field; (c) decreasing the bar setting of the power source if consistent sticking is encountered;<sup>3</sup> and (d) having the sensor system calibrated at least once a year. In addition, experience with endoscopic manoeuvres within a small operative field, especially during thoroscopic lobectomy in

a small child, is recommended.<sup>8</sup>

Health care professionals are encouraged to report adverse incidents suspected of being associated with the use of the LigaSure vessel sealing system to the Health Products and Food Branch Inspectorate through the toll free hotline (1-800-267-9675).

---

Rana Filfil, PhD, Health Canada

## References

1. *LigaSure Dolphin Tip Laparoscopic Sealer/Divider [instructions for use]*. Mansfield (MA): Covidien; 2011.
2. *ForceTriad Energy Platform [user guide]*. Mansfield (MA): Covidien; 2011.
3. Office of the Chief Coroner, Province of Ontario. *Report of the Pediatric Death Review Committee and Deaths Under Five Committee*. Toronto (ON): Office of the Chief Coroner; 2011.
4. Albanese CT, Sydorak RM, Tsao K, et al. Thorascopic lobectomy for prenatally diagnosed lung lesions. *J Pediatr Surg* 2003;38(4):553-5.
5. Cano I, Antón-Pacheco JL, García A, et al. Video-assisted thorascopic lobectomy in infants. *Eur J Cardiothorac Surg* 2006;29(6):997-1000.
6. Rothenberg SS. First decade's experience with thorascopic lobectomy in infants and children. *J Pediatr Surg* 2008;43(1):40-5.
7. Lacin T, Batirel HF, Ozer K, et al. Safety of a thermal vessel sealer on main pulmonary vessels. *Eur J Cardiothorac Surg* 2007;31(3):482-5.
8. Kaneko K, Ono Y, Tainaka T, et al. Thorascopic lobectomy for congenial cystic lung diseases in neonates and small infants. *Pediatr Surg Int* 2010;26(4):361-5.

## CARN is “going green”

Starting with the October 2012 issue, the *Canadian Adverse Reaction Newsletter (CARN)* will be made available exclusively in an electronic format on the MedEffect™ Canada Web site. The paper format will no longer be available. As a result, *CARN* will significantly reduce its carbon footprint in an effort to be more environmentally friendly. The electronic version of the Newsletter will continue to feature topics related to serious or unexpected adverse reactions suspected of being associated with drugs, natural health products and medical devices marketed in Canada.

Visit the MedEffect™ Canada Web site at [www.health.gc.ca/medeffect](http://www.health.gc.ca/medeffect) to view or to subscribe to the Newsletter. The consolidation of health product safety information, including *CARN*, on the MedEffect™ Canada Web site is intended to promote centralized access to relevant and reliable information as it becomes available, in an easy to find, easy to remember location. A MedEffect™ e-Notice will be sent to all subscribers upon the release of a new electronic issue of *CARN*. Subscribers will also receive updates on health product advisories posted on Health Canada's Web site.

# Adverse reaction and incident reporting — 2011

## Canada Vigilance Program

The Canada Vigilance Program collects reports of suspected adverse reactions (ARs) to health products (pharmaceuticals, biotechnology products, blood products and biologics, natural health products, radiopharmaceuticals, and cells, tissues and organs). Further information about the program and its database can be found at [www.health.gc.ca/medeffect](http://www.health.gc.ca/medeffect).

### Domestic and foreign AR reports

In 2011, Health Canada received 41 923 domestic AR reports,\* of which 78% were considered to be serious.† Domestic AR reports received by product type are provided in Table 1. The 41 923 reports represent 28 675 AR cases. A case consists of all information describing the AR(s) experienced by one patient at one time and suspected of being related to the use of one or more health products; thus, an AR case will include an initial AR report as well as any subsequent additional information received as follow-up report(s).

In Canada, Market Authorization Holders (MAHs) are required to submit AR reports received in accordance with the requirements of the *Food and Drugs Act* and Regulations. MAHs are required to send, within 15 days, all reports of serious ARs that have occurred in Canada (domestic) and all reports of serious unexpected ARs‡ that have occurred outside Canada (foreign) to

the Canada Vigilance Program. In 2011, MAHs submitted 81.8% of all the domestic reports received. The remaining reports were received directly from the community and hospitals (Table 2).

The number of domestic AR reports was 27.3% higher in 2011 than in 2010 (Fig. 1). Most of the domestic reports received by both MAHs and Health Canada originated from health care professionals (Table 3).

In 2011, the number of foreign AR reports received from MAHs was 454 822 (Fig. 2). At this time, foreign reports are not included in the Canada Vigilance database.

### Sex and age

The distribution for the 28 675 cases by sex was 58% female, 37% male and 5% sex unknown. The distribution by age group was 6% pediatric (< 19

years), 51% adult (19–64 years), 26% elderly (≥ 65 years) and 17% age unknown.

### Suspect products

The top 10 groups of suspect products most commonly identified in AR reports are listed in Table 4. Anatomical Therapeutic Chemical (ATC) groups are classified according to the World Health Organization's ATC classification system ([www.whocc.no/atc\\_ddd\\_index](http://www.whocc.no/atc_ddd_index)). Several factors may influence the number of ARs reported for a specific health product or product type, such as length of time a product is on the market, volume of use, publicity of an AR, regulatory actions, method of data collection (reports submitted voluntarily v. organized data-collection systems). For example, ARs may be reported more frequently in organized data-collection systems (e.g., patient

Table 1: Number of domestic reports\* of adverse reactions by product type in 2011

| Product type                 | No. (%) of reports |
|------------------------------|--------------------|
| Pharmaceuticals              | 27 602 (65.8)      |
| Biotechnology products       | 12 419 (29.6)      |
| Blood products and biologics | 827 (2.0)          |
| Natural health products      | 680 (1.6)          |
| Radiopharmaceuticals         | 350 (0.8)          |
| Cells, tissues and organs    | 45 (0.1)           |
| Total                        | 41 923 (100.0)     |

\*Canada Vigilance receives reports for both initial and follow-up information concerning suspected adverse reactions.

\*This excludes AR reports received for product types that do not fall under the review of the Canada Vigilance Program, as outlined above. These reports were redirected to the appropriate AR reporting program.

†In the *Food and Drugs Act* and Regulations, a serious AR is defined as “a noxious and unintended response to a drug that occurs at any dose and that requires in-patient hospitalization or prolongation of existing hospitalization, causes congenital malformation, results in persistent or significant disability or incapacity, is life-threatening or results in death.”

‡In the *Food and Drugs Act* and Regulations, a serious unexpected AR is defined as “a serious adverse drug reaction that is not identified in nature, severity or frequency in the risk information set out on the label of the drug.”

registries, surveys, patient support and disease management programs) and may affect the pattern of reporting. It is not possible to compare the risk of health products based solely on numbers of AR reports. In addition, rare and serious reactions may not necessarily represent a large number of reported ARs.

## Adverse reactions

Table 5 displays the top 10 ARs reported to the Canada Vigilance Program, based on System Organ Class.<sup>§</sup> The most commonly reported ARs were general disorders and administration site conditions, which include disorders that affect several body systems or sites (e.g., drug ineffective, fatigue, fever, edema, pain, reactions at the administration site). The next most common ARs were gastrointestinal disorders.

## Conclusion

Health Canada would like to thank all who have contributed to the Canada Vigilance Program and encourages the continued support of postmarketing surveillance through AR reporting. The purpose of postmarket spontaneous reporting systems is the identification and

Table 2: Number of domestic reports\* of adverse reactions by source in 2011

| Source     | No. (%) of reports |
|------------|--------------------|
| MAH        | 34 307 (81.8)      |
| Community† | 6 451 (15.4)       |
| Hospital   | 1 108 (2.6)        |
| Other      | 57 (0.1)           |
| Total      | 41 923 (100.0)     |

Note: MAH = Market Authorization Holder.

\*Canada Vigilance receives reports for both initial and follow-up information concerning suspected adverse reactions.

†Consumer, patient and non-hospital-based health care professionals.

Table 3: Number of domestic reports\* of adverse reactions by type of originating reporter in 2011

| Reporter type        | No. (%) of reports |
|----------------------|--------------------|
| Consumer/patient     | 11 503 (27.4)      |
| Physician            | 10 052 (24.0)      |
| Nurse                | 7 319 (17.5)       |
| Health professional† | 6 674 (15.9)       |
| Pharmacist           | 5 418 (12.9)       |
| Dentist              | 7 (0.02)           |
| Naturopath           | 2 (0.005)          |
| Other                | 948 (2.3)          |
| Total                | 41 923 (100.0)     |

\*Canada Vigilance receives reports for both initial and follow-up information concerning suspected adverse reactions.

†Type not specified in report.

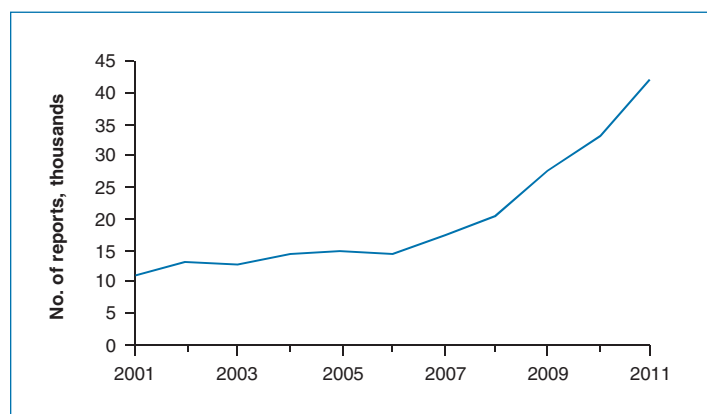


Fig. 1: Number of domestic reports of adverse reactions received by Health Canada from 2001 to 2011.

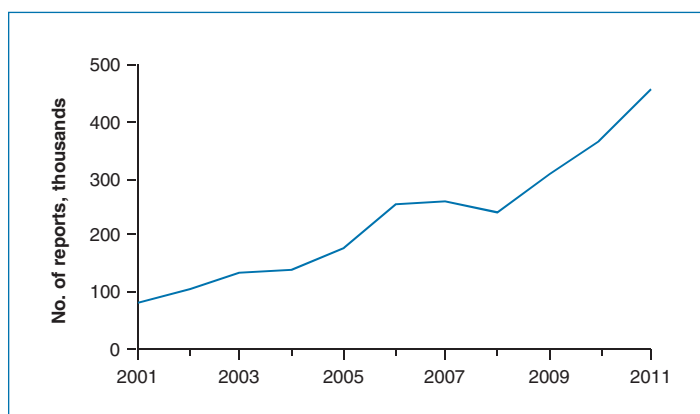


Fig. 2: Number of foreign reports of adverse reactions received by Health Canada from Market Authorization Holders from 2001 to 2011.

<sup>§</sup>Adverse reactions are coded using the Medical Dictionary for Regulatory Activities (MedDRA) Terminology. The terminology is organized in a hierarchical structure where the System Organ Class is the highest level of the hierarchy and represents the broadest concept of groupings. Further information about the MedDRA Terminology can be found at [www.hc-sc.gc.ca/dhp-mps/medeff/databasdon/meddra-eng.php](http://www.hc-sc.gc.ca/dhp-mps/medeff/databasdon/meddra-eng.php).

Adverse reactions (ARs) to health products are considered to be suspicions, as a definite causal association often cannot be determined. Spontaneous reports of ARs cannot be used to estimate the incidence of ARs because ARs remain underreported and patient exposure is unknown.



analysis of new safety information for health products. Any ARs suspected of being associated with the use of health

products can be reported to the Canada Vigilance Program ([www.health.gc.ca/medeffect](http://www.health.gc.ca/medeffect)).

Table 4: Top 10 groups of suspect health products most commonly reported in 2011, by Anatomical Therapeutic Chemical (ATC) group\*

| Health product (ATC group)                              | No. (%) of times reported† |
|---|----------------------------|
| Immunosuppressants (L04)                                | 7 708 (23.3)               |
| Psycholeptics‡ (N05)                                    | 2 461 (7.4)                |
| Drugs for treatment of bone diseases (M05)              | 1 872 (5.7)                |
| Psychoanaleptics‡ (N06)                                 | 1 588 (4.8)                |
| Antineoplastic agents (L01)                             | 1 493 (4.5)                |
| Analgesics (N02)  | 1 424 (4.3)                |
| Agents acting on the renin–angiotensin system (C09)     | 1 286 (3.9)                |
| Antithrombotic agents (B01)                             | 1 058 (3.2)                |
| Antibacterials for systemic use (J01)                   | 1 045 (3.2)                |
| Pituitary and hypothalamic hormones and analogues (H01) | 825 (2.5)                  |

\*Solicited reports or organized data-collection systems (e.g., patient registries, surveys, patient support and disease management programs) may affect the total number of ARs reported for specific products or product types.

†One case may contain one or more suspect product(s). The total number of suspect health products reported was 33 063 in a total of 28 675 cases.

‡N05 psycholeptics: antipsychotics, anxiolytics, hypnotics and sedatives; N06 psychoanaleptics: antidepressants, psychostimulants, psycholeptics and psychoanaleptics in combination, anti-dementia drugs.

Table 5: Top 10 adverse reactions reported in 2011, by System Organ Class\*

| System Organ Class                                   | No. (%) of times reported† |
|--|----------------------------|
| General disorders and administration site conditions | 16 580 (20.8)              |
| Gastrointestinal disorders                           | 8 539 (10.7)               |
| Nervous system disorders                             | 7 484 (9.4)                |
| Investigations                                       | 5 539 (7.0)                |
| Psychiatric disorders                                | 4 970 (6.3)                |
| Skin and subcutaneous tissue disorders               | 4 547 (5.7)                |
| Infections and infestations                          | 4 375 (5.5)                |
| Musculoskeletal and connective tissue disorders      | 4 286 (5.4)                |
| Injury, poisoning and procedural complications       | 4 045 (5.1)                |
| Respiratory, thoracic and mediastinal disorders      | 3 864 (4.9)                |

\*Medical Dictionary for Regulatory Activities (MedDRA) Terminology, version 13.1; reactions at preferred term level. Further information about the MedDRA terminology can be found at [www.hc-sc.gc.ca/dhp-mps/medeff/databasdon/meddra-eng.php](http://www.hc-sc.gc.ca/dhp-mps/medeff/databasdon/meddra-eng.php).

†One case may contain one or more reaction(s). The total number of ARs reported was 79 571 in a total of 28 675 cases.

## Medical device incidents

Medical device incident reports are collected by Health Canada and are entered into the Medical Devices System database. A major component of Health Canada's Medical Devices Program involves the collection, review and follow-up of incidents related to medical devices, which are reported to Health Canada via the submission of mandatory and voluntary problem reports. Manufacturers and importers are required to submit mandatory reports as per sections 59 to 61 of the Medical Devices Regulations. Voluntary reports are submitted mostly by health care professionals and patients/users. Effective Oct. 3, 2011, the responsibility for the collection and entering of mandatory problem reports for medical devices was transferred from the Health Products and Food Branch Inspectorate to the Canada Vigilance — Medical Device Problem Reporting Program.

In 2011, a total of 9228 reports were entered into the Medical Device System database. Of these reports, 8199 (88.9%) were domestic mandatory reports, 611 (6.6%) were foreign mandatory reports, and 418 (4.5%) were domestic voluntary reports.

Information on mandatory and voluntary reporting of medical device incidents can be found on the Health Canada Web site ([www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php](http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php)).

Marielle McMorran, BSc, BSc(Pharm);  
Duarte Rodrigues, HonBSc, RAQC, Health Canada

## Quarterly summary of health professional and consumer advisories

(posted on Health Canada's Web site: Feb. 28, 2012 – May 20, 2012)

| Date*            | Product  | Subject   |
|------------------|--|---|
| May 18           | Miracle Mineral Solution (sodium chlorite solution)                | New Web site selling the nonauthorized product  |
| May 10           | Spinbrush Pro Clean SONIC Recharge Toothbrushes                    | Recall: may overheat and cause fire, burn or shock  |
| May 7            | Cipralext (escitalopram)   | Updated information regarding dose-related heart risk   |
| May 3 & 8        | Benlysta (belimumab)   | Association with hypersensitivity and infusion reactions  |
| May 1 & 3        | Revlimid (lenalidomide)  | Association with increased risk of second cancers   |
| Apr 18           | Compliments Extra Strength Acetaminophen Gelcaps                   | Recall: labelling error — may cause serious harm to children  |
| April 16 & 19    | Actos (pioglitazone)   | Potential association with bladder cancer   |
| April 11 & May 9 | Metal-on-Metal Hip Implants  | Information for orthopedic surgeons regarding patient management following surgery  |
| Apr 5            | Benzocaine health products   | New risk statements to be added to product labels   |
| Mar 22 & 24      | Sandoz Morphine Sulfate Injection USP 2 mg/mL (1 mL)               | Urgent recall: potential presence of ampoules of Isoproterenol HCl Injection in boxes of Morphine Sulfate Injection                             |
| Mar 21           | Sandoz Morphine Sulfate Injection USP 2 mg/mL (1 mL)               | Some boxes may contain ampoules labelled as Isoproterenol HCl Injection   |
| Mar 19           | Apo-Ramipril 5 mg  | Recall of lot JR2178: intact but empty capsules   |
| Mar 19           | Finasteride (Proscar, Propecia) and dutasteride (Avodart, Jalyn)   | May increase risk of high-grade prostate cancer   |
| Mar 16 & 21      | Pradax (dabigatran)  | Updated labelling regarding kidney function assessment and use in patients with certain types of heart valve disease or artificial heart valves |
| Mar 12           | Power X  | Unauthorized health product removed from sale at BC's Chong Kun Dang Health Store because of possible serious health risks                      |
| Mar 12           | Rexall Extra Strength Sinus Relief Daytime and Nighttime Caplets   | Recall: labelling error misidentifying daytime and nighttime medications  |
| Mar 9 & 14       | Fluoroquinolone antibiotics (Avelox, Cipro, Cipro XL and Levaquin) | Worsening of symptoms in patients with myasthenia gravis  |
| Mar 9            | GemStar Bolus Cord   | Potential risk owing to device failure  |
| Mar 6            | EnTrust VR/DR/AT Implantable Cardioverter Defibrillators           | Medical device correction: more rapid than expected drop in battery voltage   |
| Mar 6            | Bios Diagnostics Rollator 56001                                    | Recall: potential manufacturing defect that could result in falls   |
| Mar 2 & 7        | Domperidone Maleate  | Association with serious ventricular arrhythmias and sudden cardiac death   |
| Mar 1            | Arm and Hammer's Spinbrush Powered Toothbrush                      | New safety information  |

Advisories are available at [www.health.gc.ca/medeffect](http://www.health.gc.ca/medeffect).

\*Date of issuance. This date may differ from the posting date on Health Canada's Web site.

## Canadian Adverse Reaction Newsletter

Health Canada

Marketed Health Products Directorate  
AL 0701D

Ottawa ON K1A 0K9

Tel: 613 954-6522

Fax: 613 952-7738

### Editorial Team

Patricia Carruthers-Czyzewski, BScPhm, MSc  
(Editor-in-Chief)

Christianne Scott, BPharm, MBA

Hoa Ly, BSc

Emir Al-Khalili, BA, BScPhm

Myriam Rivas, RPharm, BSc, MQA

Sophie Bourbonnais, BScPht

### Acknowledgement

We thank the following members of the Expert Advisory Committee on the Vigilance of Health Products for their review of material for this issue: Colleen J. Metge, BSc(Pharm), PhD; and Yola Moride, PhD, FISPE. We also thank Benjamin Pearson and Aleksandar Brezar, students in Health Sciences and Biopharmaceutical Sciences, respectively, for their participation in the production of the newsletter.

### Suggestions?

Your comments are important to us. Let us know what you think by reaching us at [mhpd\\_dpssc@hc-sc.gc.ca](mailto:mhpd_dpssc@hc-sc.gc.ca)

### Reporting Adverse Reactions

Canada Vigilance Program

Phone: 866 234-2345; Fax: 866 678-6789

Online: [www.health.gc.ca/medeffect](http://www.health.gc.ca/medeffect)

### Copyright

© 2012 Her Majesty the Queen in Right of Canada. This publication may be reproduced without permission provided the source is fully acknowledged. The use of this publication for advertising purposes is prohibited. Health Canada does not assume liability for the accuracy or authenticity of the information submitted in case reports.

Due to time constraints relating to the production of this publication, information published may not reflect the most current information.

ISSN 1499-9447, Cat no H42-4/1-22-3E

[Aussi disponible en français](#)