

Protecting the Cold Chain

By Barbara Cadotte
Senior Policy Advisor, OCP

A cold chain is a temperature-controlled supply chain for products such as pharmaceuticals, vaccines and blood products that require a specific temperature range during distribution and storage.

The cold chain is necessary to preserve the potency of substances while they are in transit. In addition to temperature, products may also be sensitive to variations in humidity and light, and it is appropriate to include these in the category of those products requiring a cold chain. Products that have not been maintained at the appropriate temperature and under the appropriate conditions are considered to be unsafe for use.

This article will provide an overview of the legislative and policy framework that governs the safety and security of temperature-sensitive products and a brief introduction to the cold chain journey, including the issues associated with the 'last mile.' Some best practices for protection of cold chain products in the pharmacy are identified as well. As this is an issue that falls within the accreditation requirements for pharmacies in Ontario, information on the inspection process will also be included. Tips on implementing good cold chain practices appear in the side bar to this article.

LEGISLATIVE AND POLICY FRAMEWORK

An increasing number of medications require cold chain protection and it is expected that the number of pharmaceuticals and biologics that require cold-chain monitoring will continue to increase over the next several years. All persons and companies who are involved in the storage and transportation of drug products, for either human or veterinary use, should be aware of their responsibilities to keep products safe. The federal *Food and Drugs Act and Regulations* set out the requirements for the labelling, storage and

transportation of temperature-sensitive drugs in Canada.¹ Health Canada has also provided guidelines to assist fabricators, packagers/labellers, distributors, importers and wholesalers to understand and meet their obligations when handling, storing and distributing such products.²

The *Drug and Pharmacies Regulation Act* establishes accreditation requirements for pharmacies in Ontario, including the requirement for a refrigerator in the dispensary maintained at a temperature between 2° and 8° Celsius to store drugs and other medications requiring refrigeration.³ The Designated Manager (DM) is responsible for ensuring that all drugs and medications purchased by a pharmacy for use or sale are of an acceptable standard and quality.⁴ The DM is also accountable for ensuring that there are appropriate policies and procedures in place to manage the cold chain once the pharmacy takes custody of the

product. Where there is a remote dispensing system operated by the pharmacy, the DM ensures that systems are in place to track the movement of drugs and other medications between and among the pharmacy and its remote dispensing locations.

THE COLD CHAIN JOURNEY

Environmental controls are key to maintaining drug safety, quality and efficacy.⁵ The cold chain distribution process officially begins when a product is released from a manufacturer's warehouse. From that point on, the cold chain is a complex series of multiple touch points, facilities, vehicles, modes of transportation, and personnel that ultimately ends with the administration of a medication to a patient.⁶ In the near future, this may occur at a pharmacy, but generally today this requires additional movement of the medication from the pharmacy to the place of administration, generally a physicians' office, other

facility or the patient's home. All temperature-sensitive pharmaceutical and biologic products (those that require refrigeration to avoid heat damage, and those that must avoid freezing) are at risk of temperature damage if handled improperly anywhere along this journey.

VACCINES

Vaccination is one of the most effective public health interventions for promoting good health and preventing disease, and pharmacists have always played a role in advocating for patient immunization by providing general information and educating patients on risks and benefits, as well as by hosting immunization clinics. In both Canada and the United States, the scope of pharmacist practice is moving toward medication therapy management and away from the traditional practice of only dispensing medications. Several provinces and states have already conferred

COOL VS. COLD: WHAT'S THE DIFFERENCE?⁷

Category	International Storage and Shipping Requirements
Frozen	-25°C and -10°C
Cold	Any temperature not exceeding 8° (in Ontario a pharmacy is required to have a refrigerator with a temperature between 2°C – 8°C)
Cool	Between 8°C and 15°C
Temperature controlled	Thermostatically controlled temperature of 20°C to 25°C
Room temperature	Temperature prevailing in a working area; not thermostatically controlled
Warm	Between 30°C and 40°C
Excessive heat	Above 40°C



upon pharmacists the authority to administer vaccines, and this scope of practice has been proposed for consideration in Ontario.

The issue of cold chain protection for vaccines is an important one; if vaccines are stored or administered at temperatures that are too high or too low, efficacy can be negatively affected and the patient may be inadequately protected or harmed due to the use of an ineffective vaccine.⁸ The optimum temperature for refrigerated vaccines is generally between +2°C and +8°C. For frozen vaccines the optimum temperature is -15°C or lower and there may be additional restrictions on their use. For example, the Zostavax® vaccine must be maintained at a temperature of -15°C or colder and, once it is reconstituted, must be used within 30 minutes.⁹ Protection from light and humidity is also a necessary condition for some vaccines.

VACCINE STORAGE

Maintaining vaccines at the appropriate temperature from the time they leave the manufacturer to the time of administration is a very important aspect of immunization delivery programs.¹⁰ In Ontario,

Public Health Standards outline the expectations for boards of health, including their mandate to ensure safe vaccine storage and handling procedures.¹¹ Publicly funded vaccine must be stored in refrigerators that have been inspected annually by public health units wherever they are, including physician offices, nursing agencies, etc. During the inspection, the health care providers' level of compliance with vaccine storage and handling requirements will be assessed and information and resources provided as required.¹² The inspector will review:

- i. Vaccine storage;
- ii. Vaccine storage and handling equipment;
- iii. Vaccine refrigerator temperatures;
- iv. Vaccine temperature log book;
- v. Vaccine handling;
- vi. Vaccine inventory; and
- vii. Availability of vaccine storage and handling resources material.

THE LAST MILE

There are many hand-offs in the process of moving a product from a manufacturer to the end user. The "last mile" of the cold chain refers to that point in time just

before the product is administered to a patient. Generally it is at this time that a product leaves the carefully controlled cold chain, and there is less control over the conditions in which it is kept. This can be a critical period, when temperature-sensitive products may be most vulnerable to degradation, particularly when medications are to be transported to a facility, a physician's office for injection at a future date, or provided directly to patients to be stored and administered in the home.¹³

The pharmacy should develop written standards of practice covering the process for shipping and transport as both a reference and staff training tool. To ensure that products retain their potency during that last mile, it is recommended that the pharmacist provide both written material and counseling about the risks related to transportation and storage.¹⁴ The pharmacist should provide the same advice and materials to clinics, long-term care facilities and physician's offices that are receiving batches of medications for administration, and to patients who are taking prescriptions home to be administered later.

BEST PRACTICES IN COLD CHAIN MANAGEMENT

There are several steps the pharmacy can take to help protect patients against unsafe or ineffective medicines due to cold-chain failure:

- Deal with reputable companies: these organizations will generally have agreements in place between the appropriate parties that outline the chain of storage and transportation conditions for the products that ultimately come to your door.¹⁵

- Conduct a regular review of the standard operating policies and procedures in place within the pharmacy to ensure that temperature-sensitive products are properly received, stored and dispensed, and ensure that key staff members are trained on their duties and receive the appropriate oversight and monitoring.
 - Protect deliveries from poor weather during unloading and examine containers to ensure there is no damage. Cold chain products requiring special monitoring will have temperature sensitive tags which should be checked before accepting at the pharmacy to ensure the cold chain was maintained during transportation.
 - The contents of a shipment should promptly be transferred to the appropriate, environmentally controlled storage area.¹⁶
 - The use of commercial grade equipment is recommended. The equipment must be well maintained, equipped with alarms and free from excessive frost build up.
- Frequent opening of the door can lead to temperature instability and no vaccines or medications should be stored on the door. There should be a back up power source in the event of a power failure and the door should be opened only when absolutely necessary. Very sensitive products should be kept in a separate refrigerator.¹⁷
- Ensure that the pharmaceutical packaging for home delivery meets the specifications needed for the product.¹⁸

Implementing Cold Chain Protection

All staff members must be trained in the importance of maintaining the cold chain and the implications of cold chain incidents, including what actions to take in the event of a breach (exposure of products to temperatures outside the standard storage conditions).

ESSENTIAL EQUIPMENT:

1. Dedicated purpose-built refrigerator for storing biological products;
2. Freezer;
3. Temperature monitoring devices;
4. Insulated containers (coolers);
5. Ice packs (frozen);
6. Gel packs (stored at biological refrigerator temperatures); and
7. Insulating material.

RECEIVING PRODUCTS:

- Identify products requiring cold chain protection and check for any signs of damage;
- If the product has a temperature monitoring device or indicator, determine that it is working properly and registering temperatures according to the label on the product;
- Identify controlled drugs and

substances subject to specific security requirements and ensure they are stored in accordance with legislative requirements.


STORING PRODUCTS:

- The product label should specify any special storage conditions; otherwise, confirm requirements against the product monograph;
- The refrigerator and freezer should be well maintained and kept free of frost buildup;
- To minimize temperature fluctuations caused by opening the door, the refrigerator should not be used to store anything other than products requiring cold chain protection;
- Do not store products on door shelves or crispers;
- Storage conditions should be checked, monitored and recorded:
 - Temperatures should be controlled and monitored using calibrated monitoring devices;
 - Records of temperatures and alarms, if any, should be maintained;
 - Humidity monitoring devices should be used in the appropriate locations;

- The monitoring equipment should include an alarm to alert personnel in the event that control is compromised;
- Calibration and functioning of all equipment should be checked on an annual or semi-annual basis;
- Regular maintenance protocols should be in place for all refrigeration equipment.

- An alternate storage or a backup power source should be in place in the event of a power failure;
- Rotate stock according to expiry date so that products closer to the date are used first.

TIPS TO SHARE WITH PATIENTS:

- An ice pack is only sufficient for short-term transport and should not be placed directly against the product;
- Keep the product in its original packaging during transport;
- Consider the length of time required to reach final destination, if not transporting the product directly home, it may be more appropriate to pick it up later;
- If overnight storage is needed, place the product in the center shelf of a refrigerator. 

A COLLEGE INSPECTION

The pharmacy is only one link in the cold chain, and pharmacy staff members have little control over what happens to a product prior to arrival at the door. However, the pharmacy has an obligation to ensure the appropriate practices are in place to receive, handle and store products once they are delivered to the pharmacy. The accreditation provisions of the Drug and Pharmacies Regulation Act provide the College with the authority to inspect pharmacies. Inspections focus on the operational requirements of the pharmacy, to ensure that the operation is safe and the public is protected, and to assist members to comply with legislated

requirements. Inspectors are also a resource for the pharmacy and can provide information and advice regarding the pharmacy's operations. With respect to cold chain management, an inspector will confirm that the refrigerator in the pharmacy meets the temperature requirements and that nothing other than drugs or medications requiring refrigeration are stored in the refrigerator. The inspector will also confirm that the contents are stored appropriately. Where the pharmacy operates a remote dispensing location, the inspector will confirm that the location has an alarm system that provides immediate notification to the DM of any alteration in the temperature of the location outside of the approved standards.

CONCLUSION

Most pharmacies manage the storage and handling of cold chain products appropriately and according to requirements established through legislation and policy. In order to protect the safety and efficacy of medications, and ultimately for the benefit of patient health and well-being, continuing vigilance of every link of the cold chain should be fully integrated into pharmacy practice. This article has provided an overview of some of the important elements leading to good cold chain practices; however every pharmacy needs to customize their practices to fit their patients and their needs. **PC**

REFERENCES

- 1 Health Canada. Food and Nutrition: Canada's Food and Drugs Act & Regulations. Retrieved at: http://www.hc-sc.gc.ca/fn-an/legislation/acts-lois/act-loi_reg-eng.php
- 2 Health Canada / Health Products and Food Branch Inspectorate. Guidelines for Temperature Control of Drug Products during Storage and Transportation. January 28, 2011. Retrieved at: http://hc-sc.gc.ca/dhp-mps/alt_formats/pdf/compli-conform/gmp-bpf/docs/GUI-0069-eng.pdf
- 3 Drug and Pharmacies Regulation Act, Ontario Regulation 58/11. Section 21(1)(e). Retrieved at: http://www.e-laws.gov.on.ca/html/source/regis/english/2011/elaws_src_regis_r11058_e.htm
- 4 Ontario College of Pharmacists. Medication Procurement and Inventory Management. Retrieved at: [http://www.ocpinfo.com/Client/ocp/OCPHome.nsf/web/Medication Procurement and Inventory Management?OpenDocument&PFV](http://www.ocpinfo.com/Client/ocp/OCPHome.nsf/web/Medication%20Procurement%20and%20Inventory%20Management?OpenDocument&PFV)
- 5 Health Canada / Health Products and Food Branch Inspectorate. Guidelines for Temperature Control of Drug Products during Storage and Transportation. January 28, 2011. Retrieved at: http://hc-sc.gc.ca/dhp-mps/alt_formats/pdf/compli-conform/gmp-bpf/docs/GUI-0069-eng.pdf
- 6 Prusik, Ted. 'Cure for the Common Cold Chain Break' Pharmaceutical Executive; Volume 31, Number 8, August, 2011. Retrieved at: <http://www.temptimecorp.com/Admin/UploadedImages/ContentDocument/Cure%20for%20the%20Common%20Cold%20Chain%20Break.pdf>
- 7 Reed, Carla. Cold Chains are Hot! Mastering the Challenges of Temperature-Sensitive Distribution in Supply Chains; p.3. February 2005. ©ChainLink Research 2002-2005. Retrieved at: http://www.gokodiak.com/Downloads/chainlink_coldchainsarehot.pdf
- 8 O'Donnell, Kevin and Patrick McGrath. The Changing Landscape for Vaccine Administration. July 13, 2011. Retrieved at: http://www.contractpharma.com/issues/2011-07/view_advanced-degrees/the-changing-landscape-for-vaccine-administration/
- 9 Merck-Frosst Canada Inc. (2011) Product Monograph: Zostavax®. Retrieved on the World Wide Web on October 28, 2011 at: http://www.merck.ca/assets/en/pdf/products/ZOSTAVAX-PM_E.pdf
- 10 Canada Communication Group. The Canada Communicable Disease Report (CCDR). Eleanor Paulson (ed) Minister of National Health and Welfare (1995). Retrieved at: <http://publications.gc.ca/collections/Collection/H12-21-21-11E.pdf>
- 11 Ontario Minister of Health and Long-Term Care. Ontario Public Health Standards 2008, p.8. Retrieved at: http://www.health.gov.on.ca/english/providers/program/pubhealth/oph_standards/ophs/progstds/pdfs/ophs_2008.pdf
- 12 Ontario Ministry of Health and Long-Term Care. Vaccine Storage and Handling Protocol, 2010. Retrieved at: http://www.health.gov.on.ca/english/providers/program/pubhealth/oph_standards/ophs/progstds/protocols/vaccine_storage_handling.pdf
- 13 Prusik, Ted. 'Cure for the Common Cold Chain Break' Pharmaceutical Executive; Volume 31, Number 8, August, 2011. Retrieved at: <http://www.temptimecorp.com/Admin/UploadedImages/ContentDocument/Cure%20for%20the%20Common%20Cold%20Chain%20Break.pdf>
- 14 Reed, Carla. Ibid. p. 1 Reed, Carla. Cold Chains are Hot! Mastering the Challenges of Temperature-Sensitive Distribution in Supply Chains; p.3. February 2005. ©ChainLink Research 2002-2005. Retrieved at: http://www.gokodiak.com/Downloads/chainlink_coldchain-sarehot.pdf
- 15 Health Canada / Health Products and Food Branch Inspectorate. Guidelines for Temperature Control of Drug Products during Storage and Transportation. p. 3. January 28, 2011. Retrieved at: http://hc-sc.gc.ca/dhp-mps/alt_formats/pdf/compli-conform/gmp-bpf/docs/GUI-0069-eng.pdf
- 16 Ibid, p. 7.
- 17 Ibid, p. 4.
- 18 Ziance, R., Chandler, C. and Bishara, R. Integration of temperature-controlled requirements into pharmacy practice. Pharmacy Today; Retrieved at: http://pharmacytoday.org/pdf/2009/Apr_CE_exam.pdf