SASKATCHEWAN COLLEGE OF PHARMACY PROFESSIONALS

Reference Manual

Vaccine Storage, Handling and Transport Guidelines

Companion Summary Statement to the National Vaccine Storage and Handling Guidelines for Immunization Providers (Public Health Agency of Canada, 2007)

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INTRODUCTION

Vaccination is a cost-effective method of protecting Canadians from preventable disease. Effective vaccine storage handling, and transportation is a key component of immunization programs; one where the pharmacist and pharmacy is involved in sharing the responsibility from manufacture to administration.

As biologic materials, vaccines could be subject to gradual loss of potency due to denaturation that may be accelerated under adverse conditions of transport, storage, and handling. Administration of unnoticed denatured vaccines may result in a failure to stimulate an adequate immune response, leading to reduced levels of protection.

Public Health officials involved in vaccination programs have expressed their desire to the Saskatchewan College of Pharmacy Professionals (SCPP) to see greater awareness on the part of Saskatchewan pharmacists pertaining to key principles involved in the transport, storage, and handling of vaccines. In response, we have developed this Companion Summary Statement highlighting sections of the National Vaccine Storage and Handling Guidelines for Immunization Providers that specifically outlines actions to be taken by pharmacists and staff in their pharmacies. By using this Statement, pharmacists will be incorporating best practices from the existing National Guidelines into their practice sites, thus helping assure effective vaccine administration. Each pharmacy is encouraged to evaluate and revise their procedures for both routine and urgent vaccine transport, storage, and handling procedures.

SCPP and public health officials recognize that pharmacies are only one link in the cold chain and that stakeholders at other links may also contribute to decreased public health due to compromises in vaccine compatibility. Other links in the chain, such as wholesalers who deliver their vaccines to pharmacies, are also being made aware of both the challenges of safe vaccine transport, storage, and handling and mandated to follow the National Guidelines as well. By strengthening all aspects of the cold chain, vaccine compatibility will be efficiently maintained.

IMPORTANCE OF THE NATIONAL VACCINATION GUIDELINES

The Public Health Agency of Canada has published two documents; the first is a Canadian Immunization Guide (Seventh Edition, 2006) and the second is the National Vaccine Storage and Handling Guidelines for Immunization Providers (2007). Both documents are referenced in the Companion Summary Statement and should be consulted for complete explanations and additional information. Access to these documents and their updates is available to the public on the Public Health Agency of Canada website at http://www.phac-aspc.gc.ca. If clarification of any of the policies or recommendations outlined herein or in the National Guidelines is necessary, consult the local public health office or immunization program.

THE COLD CHAIN AND WHY IT NEEDS TO STAY COLD

The cold chain refers to maintaining potency and integrity of a vaccine by ensuring optimal conditions during storage, handling, and transport. This process includes stakeholders, equipment, and facilities from manufacture to administration and is designed to ensure that proper storage temperatures and protection from light is maintained at every step. Exposure to excessive cold, heat or light results in a cumulative and irreversible loss of potency. The cold chain mandates that the optimum temperature for refrigerated vaccines remain between +2°C and +8°C, and that frozen vaccines remain at a temperature of -15°C or lower. Protection from

light is necessary for light sensitive vaccines. The pharmacist's role in the cold chain is to maintain its integrity by properly receiving, handling, and transporting vaccines, including the proper use and management of equipment, refrigerators, thermometers, temperature monitoring devices, transport coolers, insulation supplies, and ice packs.

COOL VS. COLD: WHAT'S THE DIFFERENCE?[1]

Category	International Storage and Shipping Requirements
Frozen	Maintained in a place where the temperature is between -10°C and -25°C
Cold	Any temperature not exceeding +8°C
Cool	Any temperature between +8°C and +15°C
Controlled room temperature	Thermostatically controlled temperature of +20°C to +25°C
Room temperature	Temperature prevailing in a working area; not thermostatically controlled
Warm	Any temperature between +30°C and +40°C
Excessive heat	Any temperature above +40°C

REFRIGERATOR COMPATIBILITY: KNOW YOUR REFRIGERATOR

It is important to understand the functions and components of your storage refrigerator to determine if the unit in your pharmacy meets the requirements for vaccine storage.

A purpose-built refrigerator, also known as a lab style unit, is the standard for storing large inventories of vaccines. Alternatively, a pharmacy may choose to use a food storage refrigerator as long as the unit has certain qualities that meet the standards for maintaining the cold chain. Ask your refrigerator supplier about the features of your unit in order to determine its suitability.

The requirements necessary to meet the standards for maintaining the cold chain are:

1. For combination freezer and refrigerator units, there must be a separate external freezer and refrigerator door.

2. The unit must be a frost free model, as this will ensure more uniform temperatures than manual/cyclic defrost models, and reduce the risk of freezing vaccines.

[1] Reed, Carla. Cold Chains are Hot! Mastering the Challenges of Temperature-Sensitive Distribution in Supply Chains; p.3. February 2005.

3. The unit chosen should be used solely for the purpose of storing vaccines. Other drugs requiring refrigeration or staff lunches should never be stored in the unit as these items can affect the spatial temperature differential, leading to temperature fluctuations within the unit.

4. The unit must maintain required vaccine storage temperatures through all seasons.

5. The unit must be large enough to accommodate fluctuations in vaccine supply due to demand, for example during influenza season.

6. The unit must have a calibrated thermometer inside each storage compartment.

7. The unit must be placed in a secure location away from unauthorized and public access.

There are many technical features of refrigerators that can affect the safe storage of vaccines. For further information, consult the complete National Guidelines. If your refrigerator also has an attached freezer, be aware that the unit cools the refrigerator by blowing cold air out of the freezer and into the refrigerator. Ensure you know where this vent is located on you unit and avoid placing vaccines directly under this vent where the temperatures are colder and near 0°C. Additionally, ensure you know where the thermostat inside the refrigerator is located as different models have different locations.

If a purpose built unit is used, be aware that the glass doors do not adequately protect light sensitive vaccines from denaturation. Additionally, the doors do not provide adequate insulation if there is ever a power interruption.

Jurisdictions in Canada report that use of bar fridges for vaccine storage are a leading cause of cold chain breaks because they are unpredictable at maintaining temperatures. Any style of small single door bar fridge is *not recommended* for vaccine storage.

To allow for proper heat exchange and cooling, equipment must be placed accordingly to allow for adequate air circulation around the unit. Ensure that the refrigeration coils on the back of the unit measure 10 cm away from the wall and that the wheels or levelling legs at the bottom of the unit sit 2.5 to 5 cm above the floor. Do not place the unit in direct sunlight, near a heat source, or along an outside wall where temperature can fluctuate.

STAFF ROLES: VACCINE COORDINATOR AND OTHER STAFF

All staff members who are in any way involved in the storage or handling of vaccines should be familiar with individual written pharmacy protocols as well as this document and the National Guidelines for Immunization.

Each site should designate one staff member to be the primary vaccine coordinator and an alternate staff member as a backup in the case of unavailability. The vaccine coordinator holds primary responsibility for maintenance of the cold chain by managing equipment, supplies, the vaccines themselves, and other staff. There should be posted documentation on the roles of the coordinator and additionally their contact information in case of an emergency situation. The role of the vaccine coordinator or back up is to:

1. Be responsible for daily temperature monitoring and documentation.

2. Deal with all situations as they pertain to the cold chain immediately when they occur, this includes being available for after-hours emergencies.

3. Have written policies for immediately dealing with breaches in the cold chain.

4. Be the designated person who takes and records daily temperatures, maintains and cleans the equipment, orders, ships, and receives all vaccines. They are also responsible for inspecting stock as it arrives and rotating or arranging stock in the refrigeration unit.

5. Know important information regarding the refrigeration unit that is used to store vaccines, particularly the various temperature zones in the different compartments, the air vent location, and how changes in ambient temperature affect the unit's internal temperature.

All staff members are to be familiar with and to be certain of the importance of maintaining the cold chain. It is especially important to have receptionists or front line staff aware of policies and procedures in place. Any staff member who notices a break in the cold chain is to report immediately to the vaccination coordinator.

STABILITY GUIDELINES: GENERAL RECOMMENDATIONS FOR SAFE STORAGE AND HANDLING

A. Temperature

Thermostats should never be relied upon to monitor temperature as they may not measure the temperature where the vaccines are stored. It is recommended that additional thermometers be placed inside the unit next to the vaccines on the storage shelf and that these thermometers are used for monitoring purposes. Room temperature should also be monitored at every refrigerator reading. To provide the best safety margin for temperature fluctuations within the +2°C to +8°C range, the refrigerator compartment should be set at +5°C which is mid-range and allows for suitable temperature fluctuations. The freezer should be set at -15°C or colder. The temperature of each compartment must be checked at least once in the morning when the door is opened for the first time and at the end of the day just before the door is closed for the last time.

B. Refrigerated and Frozen Vaccines

Heat sensitive vaccines experience an irreversible and cumulative loss of potency following many cold chain breaches whereas cold sensitive vaccines experience an immediate loss of potency following freezing.

Vaccines should always be placed on the middle rack in the center of the refrigerator or freezer and never on the side of the door or in the vegetable crisper bins.

C. How to Adjust Temperature

The temperature should be adjusted when it is outside the recommended range already or if over time the temperature trends demonstrate it to be moving toward the upper or lower temperature limit. Only the designated vaccine coordinator should adjust the temperature and if any additional staff notices the unit requires adjustment, they are to alert the vaccine coordinator. When adjusting the freezer temperature, take into consideration that this may potentially affect the temperature of the air venting into the fridge compartment. A warning sign

should be placed on the unit saying “DO NOT adjust refrigerator or freezer temperature controls.”
When adjusting the temperature, determine if it is necessary to remove all vaccines and store them appropriately. Check the temperatures inside the refrigerator and freezer and adjust the thermostat slightly. Adjustments should be done slowly; careful not to exceed the recommended temperature range. The temperature inside the unit may take about a half hour to stabilize at which time it should then be rechecked. As needed, continue to adjust the thermostat every half hour but be sure the temperature inside the unit has stabilized before returning the removed vaccines.

D. Factors Affecting Temperature Variation

There are many factors that can alter the temperature of vaccines inside a refrigerator or a freezer. The only way to be sure of temperature stability is to do twice daily testing and to record the data. Temperatures can vary in the storage unit based on the contents or load, the seasonal temperature, how often the door is opened or left ajar, and power interruptions. It is recommended not to open the door more than four times a day, as this exposes the vaccines to temperature variations and compromises light sensitive vaccines as well. Leaving plastic bottles of water along the side of the door rack, in the crisper area and along the walls of the refrigerator including storing frozen packs or ice trays along the walls and racks on the freezer door will help keep an even temperature in the compartments. This will prove beneficial when doors are opened during the day and it will also help keep temperatures stable longer if a power outage occurs.

E. Expiry

Any multi-dose vial without the first puncture date clearly marked on the vial or any uncapped vials must be discarded immediately in accordance with your company’s biomedical waste guidelines. Inventory management ensures appropriate use and minimization of wastage. Rotate stock to ensure product with shortest expiry date is used first.

EQUIPMENT AND MAINTENANCE

A. Thermometers

Not all thermometers are created equally! Thermometers have different calibrations and accuracies thus ask the manufacturer for the accuracy of your specific thermometer, ensuring it has a calibration accurate within +/- 1°C. The only thermometer recommended for domestic vaccine storage units are min/max thermometers that are properly monitored. A reputable thermometer supplier where these products are available is http://lgpharma.com/products/. These thermometers monitor the temperature constantly and can provide an idea of the length of time the unit has operated outside of the recommended temperature range. Min/max thermometers still must be checked twice a day. They record the current temperature as well as the min and max temperature since the last time it was reset. The thermometer must be reset each time a reading is taken in order to reset the min/ max function. You may want to consider an alarmed min/max thermometer regardless of if you store a large or small supply of vaccines in your unit in order to ensure there are no after-hours breaches in the cold chain that would go unnoticed until the next day. ALWAYS properly record and store the daily thermometer readings and have them available for audit if a cold chain incident occurs.

Thermometer placement is also essential! They should be placed in the center of the unit away from the walls, door or fan and adjacent to the vaccines in the vaccine box on the middle shelf.

B. Back Up Equipment

Always anticipate that vaccine storage equipment may fail. Arrange to have a backup generator available or another facility with proper equipment where the vaccines may be temporarily stored.

C. Daily, Weekly, Quarterly and Annual Equipment Maintenance Tasks

Regular maintenance of all equipment is recommended to maintain optimal functioning thus preventing equipment malfunctions. Recording that maintenance tasks were completed is as important as performing the tasks. If it was not documented, then it was not done! Always record the date equipment was installed, when repairs and routine cleaning tasks were done, the manufacturer's instructions for routine maintenance, and the contact information for the service provider.

The most important daily maintenance task is temperature monitoring and recording. This can be done more frequently, but minimally must be performed at the beginning of the day when the unit is opened for the first time and at the end of the day before leaving. During this time, also note and record the ambient temperature and ensure the doors to the unit are securely closed. Record the date and time of reading, the temperatures of all unit compartments and room temperature; all which must be signed by the vaccine coordinator. This information should be documented in a temperature log and charted on a graph, securely attached to the refrigerator unit. Cold chain breaches must be documented by the vaccination coordinator, indicating the time of the incident, the actions taken, and the outcome followed by the coordinator's signature.

On a weekly basis, the temperature logs should be reviewed and filed. The storage unit should be examined for a thick layer (greater than one centimetre) of frost. In this event, follow manufacturer's instructions for defrosting the unit, while taking necessary steps to ensure vaccine stability. Examine vaccines and multi dose vials for expiry dates and count remaining stock, updating inventory status.

Quarterly, the refrigerator is cleaned. All vaccines should be removed and stored properly while the walls and compartments inside the unit are wiped down with warm, mildly soapy water. The unit should then be dried and allowed to re-stabilize at the proper temperature range. This requires more frequent temperature monitoring; record the temperature every half hour for the next few hours until the temperature is stabilized. At this time the vaccines can be replaced but temperature monitoring must continue as frequently as every half hour for the rest of the day. The cooling coils at the back of the refrigerator unit readily collect dust. Other styles of refrigerators may have the cooling coils on the front of the unit near the bottom, close to the floor. To clean these coils, the refrigerator should be unplugged and the dust gently removed using a dusting cloth, vacuum, or brush. This should not take more than a few minutes, so the vaccines may remain in the refrigerator or freezer unit as long as the door remains tightly closed and are not opened. Door seals should also be inspected and checked at this time, ensuring they are not cracked and seal properly. Note: we do not recommend that you perform these duties on a Friday. If during cleaning any parts are accidentally damaged, a resultant break in the cold chain may not be noticed until the following Monday.

Equipment maintenance is done annually as outlined by the manufacturer. Thermometers should also be checked for accuracy using the slush test (see Appendix A); determine if batteries are functioning and that cables and probes are not damaged. Record all findings and actions and retain records for audit!

TRANSPORTATION TO OFFSITE LOCATIONS AND CLINICS

The cold chain must be maintained when pharmacies offer delivery services or drivers who will transport drugs or vaccines to patients or other clinics! Under these circumstances, a written protocol should be developed including how vaccines will be loaded in the vehicle, what storage and transportation materials to use, the quickest route to take and an estimated time en route. The vaccine coordinator should be the only personnel authorized to package and send vaccines.

Appropriate packing materials for temporary transport either from the pharmacy to a clinic or to another facility include:

1. Insulated containers or the shipping containers that the vaccines arrive in from the manufacturer or alternatively hard sided, plastic, insulated containers or Styrofoam coolers with at least two inch thick walls can be used. Thin walled Styrofoam coolers for recreational use, such as those purchased to hold beverages, are not acceptable.

2. Refrigerator packs.

3. Frozen packs (may be ice or gel, however gel packs may have a freezing point below 0°C and may pose a risk of freezing vaccines. Tap water filled ice packs are the safest type for maintaining the cold chain). NEVER use bagged or loose ice to transport vaccines.

4. Dry ice in situations where product must remain frozen.

5. Insulating barrier materials or materials used as barriers between the vaccine and refrigerated or frozen packs and as filler.

   NEVER use a cooler bag or lunch bag brought in by the patient.

The best way to accumulate the proper supplies is to save and use the packing supplies that the drug manufacturers send their vaccine shipments in. As long as the products are not damaged or destroyed or intended for one time use, this is an acceptable and recommended option.

Follow these steps when properly packing a vaccine in preparation for transport:

1. Document the time the vaccine is removed from the refrigeration unit for transport.

2. Pack the vaccine in layers: the bottom layer consisting of a refrigerated or frozen pack covered with an insulating material that acts as a barrier such as bubble wrap or crumpled brown packing paper.

3. Next place the vaccine and a temperature monitor inside and use more insulating materials to fill any remaining space, preventing the shifting of contents during transport. Temperature monitors must be properly placed next to the vaccine and not in contact with refrigerated or frozen packs.

4. Diluents may either be transported at room temperature or inside the same container as the corresponding vaccine. If the diluent is transported inside the cooled container with the vaccine, it must have been refrigerated at least 24 hours in advance so as not to

raise the temperature of the cooler and they must not be placed in direct contact with any refrigerated or frozen packs.

5. When packaging the products, consider the number and placement of refrigerated or frozen packs inside the container, the amount of vaccine being packaged, the size of the container, the outside temperature and the distance and time in transit. NEVER pack vaccines tightly as you need adequate air flow around the product to maintain the packages internal temperature.

6. Lastly, appropriate and visible labels should be applied to the outside of the container clearly identifying special instructions to refrigerate contents immediately upon arrival.

All transported vaccines should have a min/max thermometer inside the storage compartment next to the vaccine. Consider using a WarmMark or Freeze Watch indicator illustrated in Appendix B. These monitors are intended only for use when transporting vaccines and do not replace twice daily temperature readings. Once activated, the readings are irreversible. After transport, if vaccines are placed in another storage unit, it must meet the aforementioned criteria and temperature monitoring protocols. These monitors are available at lgpharma.com/products.

When a patient is transporting their own product, ask them to pick up the vaccine on the way to their appointment, discouraging removal from the pharmacy and storage at home. **NEVER encourage a patient to take the vaccine home and store it in an unmonitored home refrigeration unit.** If this cannot be avoided, provide the patient with the appropriate materials for transport or inspect their own supplies that they bring.

Take the opportunity to educate the patient about the principles and importance of proper storage of the vaccine. This is ABSOLUTELY NECESSARY. The patient needs to be educated on how to transport the vaccine in their vehicles.

When using personal vehicles to transport or deliver vaccines **NEVER place the vaccine inside the trunk, in direct sunlight, or directly in line with the air from the vehicle's air conditioner or heater**.

NEVER leave a vaccine unattended in the vehicle or use the vehicle to store the package. Upon delivery, the vaccine must be handed off directly to the appropriate personnel and a signature documenting the exchange should be recorded.

If a patient visits your pharmacy to pick up their vaccine immediately before their scheduled appointment at an office or clinic attached to the pharmacy, the vaccine coordinator must still package the product to ensure the cold chain is maintained. The vaccine does not need to be placed in a sealed box or container as if it were being transported off site; rather the vaccine may be placed in a sealed bag surrounded by a suitable barrier device and then packed with an ice or cooler pack in an insulated bag. This is to ensure that the cold chain is maintained even if the patient must wait longer than expected for their appointment at the clinic.

RECEIVING VACCINATIONS FROM SUPPLIERS

Consider stocking only a one-month supply or sufficient stock to meet seasonal and outbreak demands.

All staff including reception should be trained in the importance of immediately notifying the vaccine coordinator when a shipment arrives. Only the vaccine coordinator should accept and unpack the order. A visual inspection is necessary to determine if the integrity of the product

was maintained during transport and the temperature monitor included in the package should be examined.

When examining vaccine shipments for heat or cold damage, look for the following observations:

- Refrigerated packs should still be cold whereas frozen packs can be melted but must still be cold.
- Vaccines should not be in direct contact with refrigerated or frozen packs. They should be separated by an insulating barrier.
- Diluents should be cool or at room temperature.

Next, vaccines must be immediately unpackaged and safely transferred to the storage compartment. As the quantity of stock in the unit affects the temperature of the unit, frequent temperature monitoring should then take place. Stock should be rotated at this time.

If there is evidence of a potential cold chain break, immediately quarantine the affected vaccines storing them away from other vaccines but still under the same cold chain conditions. Immediately contact the local immunization office for instruction on what to do. Do not allow the vaccines to be dispensed, but also do not assume that the vaccine has retained its' potency.

After all stock is unpackaged and stored, update the inventory so that you always know the following information:

- Quantities of vaccines and diluents that have been received,
- Quantities of vaccines and diluents that have been administered, wasted, or expired,
- Quantities of vaccines and diluents that are currently in quarantine awaiting follow up directions,
- Vaccines and diluents that should be used first, and
- Vaccines and diluents that need to be ordered.

Keep the packing materials the vaccines were packaged in from the manufacturer, when appropriate, to use when vaccines are transported from your pharmacy.

When ordering vaccines, some general principles apply including the following:

- Order only enough stock to ensure that you have an adequate supply on hand based on your pharmacy's population needs.
- Order fewer quantities more often.
- Alert office staff when an order is placed so arrival can be anticipated.

TROUBLE SHOOTING, QUARANTINE, AND MANAGEMENT OF INAPPROPRIATE CONDITIONS

The following situations are representative of breaks in the cold chain and examples of how they should be managed.

A. An Equipment or Power Failure

Whoever discovers the failure is to take immediate action. Contact the vaccine coordinator and promptly ensure the proper management of the vaccines. This involves using a backup generator or transferring the vaccine supply to an alternate unit or facility first before attempting to identify or resolve the problem. Open the refrigerator or freezer doors only when absolutely necessary or once you have made all preparations for packing and transfer of vaccine to an alternative storage unit. The alternate storage unit must meet the aforementioned criteria and be monitored as if it were the primary storage unit.

The best offense is a strong defence so anticipate failures in advance and follow established directives. If a unit is out of commission for only a short period of time it is acceptable to store vaccines in an appropriately packed cooler as long as the temperature can be monitored and maintained. Have a min/max temperature monitor in the cooler and continue to record temperatures. This situation may need to be reassessed if the unit continues to be out of commission for a period of time longer than what was originally expected. Things to consider:

- Protecting the power supply. Avoid using power outlets activated by a wall switch.
- Invest in putting a safety lock or cover over the outlet and screw the cover into the wall.
- Post a warning sign next to the plug where it enters the wall stating “DO NOT unplug”.
- Label fuses on breakers.
- Consider an alarm system that is able to alert staff if a breach in the cold chain occurs after-hours.

B. Administration of an Expired or Compromised Vaccine

Immediately consult your public health office and immunization program for notification and advice. The patient must be notified and serological testing, revaccination, or further action may be suggested depending on the type of vaccine, duration, and temperature of exposure, and level of immunity acquired. However, each situation will be handled on a case by case scenario.

C. The Integrity of a Vaccine is Questioned

All staff personnel have the authority to question the integrity of a vaccine and report it to the vaccine coordinator. The coordinator will then contact the public health office or immunization program for advice.

D. There is a Problem with a Thermometer

First, attempt to replace the batteries. If this does not work, contact the manufacturer for recommendations on calibration or replacement and use another thermometer to monitor temperatures.

E. There is a Breach in the Cold Chain

A cold chain break is any circumstance where a biological is exposed to temperatures outside the +2°C to +8°C range. Immediately consult the regional immunization program and quarantine the products, marking them as “DO NOT USE”, but continue to store under appropriate conditions. Do not discard anything until instructed to do so.

F. Your Unit is Newly Installed or Repaired

The unit thermostat must be reset to the preconditioned temperature and stabilized before any vaccines can be returned. In this situation, allow for one week of twice daily fridge and freezer temperature recording before using the unit to store vaccines.

DRUG STORAGE REQUIREMENTS

Refer to the chart in Appendix C for recommendations and information on a selection of medications requiring refrigeration or related special storage conditions. This is not intended to be a complete or exhaustive reference, but rather to provide guidance on the stability and storage requirements of selected drug products including commonly used insulin preparations, DMARDS, antivirals, vaccines, and miscellaneous agents. Information gathered was collected using strategic search parameters, as well as reputable drug information databases.
For further questions on specific products, it is recommended that the drug manufacturers be consulted. This project was completed May 1, 2013 by Lindsey Usher, a senior pharmacy student, while completing a practicum with the Canadian Agency for Drugs and Technologies in Health (CADTH).

CONTACT INFORMATION

All pharmacies should post on the refrigerator up to date contact information for the following:

- Designated vaccine coordinators
- Written emergency protocols and emergency contact information
- Provincial, territorial, or local public health office and immunization programs
- Refrigerator/freezer manufacturer and maintenance company
- Sources for supplies of packing materials and thermometers
- Post manufacturer requirements for the storage of each vaccine and diluent.

GENERAL REFERENCE INFORMATION

1. The following documentation can be found on the Public Health Agency website at http://www.phac-aspc.gc.ca:
   a. Canadian Immunization Guide, Seventh Edition, 2006
   b. National Vaccine Storage and Handling Guidelines for Immunization Providers, 2007

2. Additional reference:
   a. Canadian Pharmacist's Letter, Vol. 24, No. 5, May 2008
   b. Saskatchewan Immunization Manual, Chapter 9, "Management of Biological Products": https://www.ehealthsask.ca/services/Manuals/Documents/sim-chapter9.pdf, October 2016

3. Temperature monitoring devices for storage and transport that are recommended within these guidelines are available at http://lgpharma.com/products/.

4. To obtain useful visual aids such as fridge magnets that can be posted as reminders in your pharmacy, contact Estelle Arseneault at the Public Health Agency of Canada at estelle_arseneault@phac-aspc.gc.ca

5. A vaccine temperature log may also be printed from the British Columbia Center for Disease Control website at http://www.bccdc.ca/resource-gallery/Documents/Guidelines%20and%20Forms/Forms/Immunization/Cold%20Chain/TemperatureFormSep2014.pdf

6. Ontario College of Pharmacists: "Protecting the Cold Chain," 2012 http://www.ocpinfo.com/regulations-standards/policies-guidelines/cold-chain/

Appendix A: The Slush Test

You can use this test to annually check the accuracy of your thermometer. Other tests should not be used as they are not considered to be reliable.

- Fill a plastic cup two thirds with cold water. Place the cup in the freezer until a fine layer of ice forms on top and a small section of ice forms within the fluid, which takes approximately two hours.

- If ice is present, this ensures the mixture is 0°C.

- Place the thermometer probe in the middle of the cup without touching the sides and observe the temperature after two minutes, at which time the temperature should have dropped to 0°C.

(Taken from the Canadian Immunization Guide – Seventh Edition – 2006)

Appendix B: WarmMark and Freeze Watch Indicators

From the Saskatchewan Immunization Manual Chapter 9, Page 19 – 20 “Management of Biological Products”: https://www.ehealthsask.ca/services/Manuals/Documents/sim-chapter9.pdf, May 2017.

3.5 Temperature Indicators

Temperature Indicator Cards are visual markers, sensitive to either warm or cold exposures. The SDCL uses WarmMark 2™ indicators that activate after exposure to temperatures greater than 10°C. The SDCL use Freeze Watch™ indicators with a threshold set point of 0°C.

3.5.1 WarmMark 2™ Time Temperature Indicators

The WarmMark™ indicators monitor temperature exposure, not product integrity. Their purpose is to signal when product integrity should be checked. WarmMark™ indicators are ideal for monitoring biological products which run the risk of being damaged when exposed to warmer-than acceptable temperatures during shipping and storage. WarmMark™ indicators are guaranteed to produce a highly accurate reading, within +/- 1°C of the response temperature. When exposed to temperatures beyond a certain threshold, the blue-dyed compound inside the WarmMark™. Indicator liquefies, and a blue colour moves through the indicators windows over a period of time. If the temperature remains above the response temperature, the colour gradually continues to move through the windows. If the temperature returns to below the threshold, the colour stops moving. In this way, you have an indication as to how long the product was exposed above the threshold temperature.

Directions for Use:

1. Peel the liner off the back of the indicator and adhere it to a clean, dry surface such as a piece of paper. This paper should also be conditioned at the appropriate temperature.
2. To activate, push the button on the indicator.
3. Place the indicator in the middle of the shipping contents, away from ice packs.
4. To detect if the product has been exposed to warmer than acceptable temperatures, observe the WarmMark™ indicator windows for any blue colouration. If the indicator remains white, there is no concern.
5. If the indicator windows show blue, place vaccine in a separate bag in the refrigerator, mark it DO NOT USE and contact the Ministry of Health for further instructions.

3.5.2 Freeze Watch™ Indicators

The Freeze Watch™ indicators monitor temperature exposure, not product integrity. Their purpose is to signal when product integrity should be checked. Freeze Watch™ indicators are ideal for monitoring biological products that run the risk of being damaged when exposed to freezing temperatures during shipment and storage. Freeze Watch™ indicators are available at two temperature levels, -4°C and 0°C, to accommodate differing product sensitivities. When exposed to sub-freezing temperatures, the liquid in the ampoule freezes, causing the ampoule to fracture and stain the indicator paper.

Directions for Use:

1. Attach the Freeze Watch™ indicator by peeling the release liner off the back and adhere the indicator to a clean, dry surface.
2. To detect if the product has been exposed to freezing temperatures, observe the Freeze Watch™ indicator. If the indicator paper is stained with color, your product has been

exposed. Place vaccine in a separate bag in refrigerator, mark it and contact the Ministry of Health for further direction. Saskatchewan Immunization Manual

3. If the indicator paper shows no color indication, remove indicator from the surface to which it is attached. Vigorously tap the bottom edge of the indicator three times on a hard surface. Tapping will not cause colour staining in an unexposed indicator. If the paper becomes stained, your product was exposed to freezing temperatures. Place vaccine in a separate bag in the refrigerator, mark it DO NOT USE and contact the Ministry of Health for further instructions.

Appendix C: Drug Storage Requirements

The following reference chart includes recommendations and information on a selection of medications requiring refrigeration or related special storage conditions. This is not intended to be a complete or exhaustive reference, but rather to provide guidance on the stability and storage requirements of selected drug products including commonly used insulin preparations, DMARDS, antivirals, vaccines, and miscellaneous agents. Information gathered was collected using strategic search parameters, as well as reputable drug information databases. For further questions on specific products, it is recommended that the drug manufacturers be consulted.

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Drug Name	Storage Requirements	Stability Once Out of Conditions	Additional Information
Diabetic Agents			
Insulins, except insulin detemir	Refrigerate at 2°C - 8°C	28 days at room temperature	Do not freeze
Insulin detemir (*Levemir*)	Refrigerate at 2°C - 8°C	42 days at room temperature	Do not freeze
Exenatide (*Byetta*)	Refrigerate at 2°C - 8°C	30 days at room temperature	Do not freeze; Protect from light
Liraglutide (*Victoza*)	Refrigerate at 2°C - 8°C	30 days at room temperature	Do not freeze; Protect from light and heat
Disease-Modifying Anti-Rheumatic Drugs (DMARDS)			
Adalimumab (*Humira*)	Refrigerate at 2°C - 8°C	Pen or pre-filled syringe can be stored at room temperature (up to 25°C) for a single maximum period of 14 days	Do not freeze; Protect from light
Certolizumab Pegol (*Cimzia*)	Refrigerate at 2°C - 8°C; Store up to 24 hours after reconstitution	Reconstituted vials for up to 2 hours	Do not freeze; Protect from light
Etanercept injection (Enbrel) -Syringes/autoinjectors	Refrigerate at 2°C - 8°C	Up to 4 days	Do not freeze; Protect from light; Do not shake; Expiry date should be reduced to four weeks after temperature excursion

Etanercept injection (*Enbrel*) -Powder for reconstitution	Refrigerate at 2°C - 8°C	Up to 7 days (not reconstituted) However, in-house stability data (UK Fridge Database) exists to support the storage of Enbrel at up to 25°C for a single period of up to 4 weeks	Do not freeze; Use within 14 days of reconstitution; Expiry date should be reduced to four weeks after temperature excursion
Golimumab (Simponi)	Refrigerate at 2°C - 8°C	The physical, biological and chemical integrity remained essentially unchanged when exposed to the following temperature cycling conditions and in conformance with specification for the pre-filled syringes: 1) -0.6°C - 0°C for no more than 3 cumulative days. 2) 0°C - 2°C for no more than 20 cumulative days. 3) 8°C - 10°C for no more than 20 cumulative days. 4) 10°C - 20°C for no more than 7 cumulative days. 5) 20°C - 25°C for no more than 1 cumulative day.	Do not freeze; Protect from light; Do not shake; Once the cumulative exposure has been reached, the product must be discarded
Infliximab (*Remicade*)	Refrigerate at 2°C - 8°C	Reconstituted diluted infusion solution is stable for 24 hours at room temperature (25°C); Unreconstituted powder: exposure to 3 freeze/thaw cycles at -20°C for 7 days **or** exposure to 50°C for 3 days; Followed by storage at 2°C - 8°C for 28 months, demonstrated **no adverse effect** on the biochemical or physical properties of the product.	
Antiviral Agents			
Interferon beta-1a (*Avonex*)	Refrigerate at 2°C - 8°C	Lyophilized powder vial: up to 25°C for 30 days; Pen and syringes can be stored at room temperature (between 15°C - 30°C) for up to one week	Do not freeze; Protect from light; Store in outer carton
Interferon beta-1a (*Rebif*)	Refrigerate at 2°C - 8°C	Prefilled syringes: up to 25°C for one month	Do not freeze
Peginterferon alfa-2a (*Pegasys*)	Refrigerate at 2°C - 8°C	Intact vial up to 14 days at room temperature; Pre-filled syringe: can be removed from refrigeration for ONE single period up to 7 days for storage up to 25°C without affecting shelf-life; Pre-filled pen: for transportation purposes it can be removed from the fridge for 8 days and 9 hours at up to 30°C and for 14 days at -20°C (max. 2 freeze-thaw cycles)	Do not freeze; Protect from light; Do not shake

Peginterferon alfa-2b (*Pegetron*)	Refrigerate at 2°C - 8°C	Stability data support storage at 30°C for 1 day maximum and 25°C for up to 14 days maximum	Use immediately after reconstitution
Miscellaneous			
Darbepoetin alfa (*Aranesp*)	Refrigerate at 2°C - 8°C	May be stored at room temperature for up to 7 days if in original carton; A single exposure to freezing temperatures down to -30°C for up to 48 hours does not affect the stability	Do not freeze; Protect from light; Do not shake
Diltiazem solution for injection	Refrigerate at 2°C - 8°C	May be stored at room temperature for up to 1 month; Following dilution to ≤1mg/ml solution is stable for 24 hours at room temperature or under refrigeration	Do not freeze
Dornase alfa recombinant (*Pulmozyme*)	Refrigerate at 2°C - 8°C	Single exposure to temperatures up to 30°C for up to 24 hours does not affect product stability	Discard if cloudy or discoloured
Epoetin alfa (*Eprex*)	Refrigerate at 2°C - 8°C	Can be stored up to 25°C for a single period of up to 3 days (manufacturer); Unlicensed stability data demonstrates all strengths in pre-filled syringes remain within current shelf-life specification when exposed to room temperatures (25°C) for up to 30 days; Discard if freezing occurs	Do not freeze; Do not shake
Etonogestrel/ethinyl estradiol vaginal ring (*NuvaRing*)	Prior to dispensing, refrigerate at 2°C - 8°C	After dispensing to the user, store for up to 4 months at 2°C - 30°C	
Glatiramer acetate injection (*Copaxone*)	Refrigerate at 2°C - 8°C immediately upon receipt	Can be stored at room temperature (15°C - 30°C) for up to 1 month	Do not freeze; Avoid heat; Protect from intense light
Latanoprost (*Xalatan*)	Prior to dispensing, refrigerate at 2°C - 8°C	Opened bottle may be stored at room temperature up to 25°C for up to 6 weeks (manufacturer); External data suggest Xalatan retains its quality and potency when cycled between 8°C, 25°C, and 40°C temperatures for 36 months; After 36 months, latanoprost was stable for 12 **additional weeks** when exposed to room temperature and conditions simulating patient use	Do not freeze
Octreotide (*Sandostatin, Sandostatin LAR*)	Refrigerate at 2°C - 8°C	Ampoules and vials: may be stored at room temperature (20°C - 30°C) for up to 2 weeks; Undiluted LAR vials: may remain at room temperature on the day of the injection but must be used immediately following reconstitution	Do not freeze; Protect from light

Vaccines			
Dukoral; Cholera, oral, inactivated and travellers' diarrhea vaccine	Refrigerate at 2°C - 8°C	Store at room temperature (<27°C) for up to 2 weeks on one occasion only; If the product has been frozen it should be discarded	Do not freeze; After reconstitution the vaccine should be used within 2 hours
Gardasil; Quadrivalent human papillomavirus (types 6, 11, 16, 18) recombinant vaccine	Refrigerate at 2°C - 8°C	Stable at up to 25°C for 72 hours	Do not freeze; Administer as soon as possible after removal from fridge
Prevnar; Pneumococcal 7-valent conjugate vaccine (diptheria CRM_{197} protein)	Refrigerate at 2°C - 8°C	Studies suggest potency of unopened vaccine is not significantly affected by exposure to temperatures between 8°C and 37°C for up to 1 week	Discard if frozen
Pneumovax 23; Pneumococcal 23-valent polysaccharide vaccine	Refrigerate at 2°C - 8°C	Multi-use vial may be stored in fridge for up to 48 hours after the first use, then discarded	Discard if frozen
Td Absorbed; Tetanus and diptheria toxoids adsorbed	Refrigerate at 2°C - 8°C		Discard if frozen
Twinrix, Twinrix Junior; Hepatitis A and hepatitis B vaccine	Refrigerate at 2°C - 8°C	Discard product if exposed to freezing; Off-label information indicates stable for 72 hours at temperatures between 8°C to 25°C	Do not freeze

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