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Communicable Disease Control Manual

Chapter 2 : Immunization

Appendix E - Management of Biologicals

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1. The Cold Chain

"Cold chain" refers to the process used to maintain optimal temperature conditions during the transport, storage, and handling of vaccines, starting at the manufacturer and ending with the administration of the vaccine to the client.

Vaccines are sensitive biological products; protection of vaccine potency and stability is important. The recommended temperature for vaccine storage and handling is, at all times, between +2°C to +8°C. Biologicals may be inactivated by exposure to excess light or heat or freezing, depending on the nature of the product, the temperature reached and the duration of exposure. **Any loss of vaccine potency is permanent and irreversible. Damage from successive exposures to adverse conditions is cumulative.** It is important to know the correct storage conditions for each biological product and to ensure that each is kept under the recommended conditions.

As a general principle, **0°C to +2°C** is considered "refrigeration conditions", with due regard to the accuracy of the temperature reading device. Products exposed to a validated temperature in this range for any period of time, even for a series of exposures are not considered to have undergone a cold chain incident and do not need to be reported. The exception to this is Tubersol® for which exposures to temperatures in the 0°C to +2°C temperature range do constitute a cold chain incident and must be reported using the Cold Chain Incident Form.

It is extremely important to have a thermometer calibrated to an accuracy of +/- 1°C or better. Place the thermometer probe centrally (in the middle of the middle shelf) in the refrigerator, where temperatures are more constant and less likely to fluctuate.

When the refrigerator temperature is in the 0°C to +2°C range, adjust the refrigerator temperature and restore to the recommended (between +2°C to +8°C) range **immediately**. See Section 5. Management of a Cold Chain Incident for more information.

All biological products freeze at temperatures below 0°C; products that have been exposed to temperatures below 0°C may not be usable. Specific exceptions to this (e.g., lyophilized products) are provided in the Vaccine Stability Chart.

The Vaccine Stability Chart is a reference provided to Biological Products Consultants to guide product use when biologicals are exposed to temperatures outside the acceptable range. This chart contains updated stability information from the vaccine product monographs and the manufacturers. No vaccine should be removed from cold chain conditions nor returned to BCCDC until it has been determined that the product cannot be used.

2. General Recommendations

To facilitate cold chain management:

- Designate one person, at the Health Service Delivery Area (HSDA) level, as a Biological Products Consultant (BPC) to be responsible for decision-making regarding continued use of vaccines following cold chain incidents, based on known stability data. When the Vaccine Stability Chart does not contain sufficient information in order to make a determination about vaccine usage, the BPC will consult with BCCDC Vaccine and Pharmacy Services. The BPC will ensure that all staff who handle vaccines are trained in biological management procedures. The BPC will review

documentation for vaccine storage and confirm that conditions comply with the criteria established by Vaccine and Pharmacy Services for vaccines that are to be returned to BCCDC for redistribution.

- Designate one person, at the Health Unit office level, as the Biological Products Monitor (BPM) to be responsible for ordering, receiving and storing all biological products, auditing inventories, and tracking exposure history for every exposed product. The BPM is also responsible for twice-daily monitoring of the refrigerator internal temperature, and arranging for service calls and maintenance for the biological refrigerators. The BPM will maintain documentation at the office level to support storage conditions for vaccines that are returned to BCCDC for redistribution.
- Designate a backup for the BPC and the BPM.
- Designate an individual within the local office to review vaccine orders quarterly with the BPM. This individual should be familiar with immunization schedules and the frequency of immunization clinics, the birth cohort for the office, school programs and seasonal demands for vaccines. See Section 4.3 Vaccine Orders.
- Have written standard operating procedures for vaccine storage and handling available at each site to facilitate cold chain management by all staff.

Maintaining the quality of biological products is the shared task of manufacturers, vaccine handlers, and all health care professionals responsible for immunization delivery.

All staff must be aware of:

- the importance of the cold chain and the implications of cold chain incidents
- standard vaccine storage and handling practices
- the immediate and appropriate action to be taken in the event of a vaccine exposure to temperatures outside the standard storage conditions

3. Equipment

The essential cold chain equipment needed to transport and store vaccines includes:

1. Dedicated refrigerator(s) for storing biological products
2. A freezer
3. Temperature monitoring devices
4. Insulated containers (coolers)
5. Ice packs (frozen)
6. Gel packs (stored at biological refrigerator temperatures)
7. Insulating material

3.1 Refrigerators

- See National Guidelines, Section 3, for detailed information on refrigerators.
- Store biological products preferably in a **purpose-built refrigerator**, (also called a pharmacy, vaccine, biologicals, laboratory or industrial grade refrigerator).
- Domestic frost free refrigerators can be used, however, temperatures may fluctuate in different compartments of the refrigerator, and vaccines can only be stored in certain areas. For details, see National Guidelines or eziz.org references above.
- Pharmacy grade under-the-counter units are acceptable for vaccine storage.

- Standard “bar” fridges (small volume combination fridge/freezer with one exterior door) are not adequate because they do not maintain even temperatures.
- Refrigerators are “Vaccine Use” only. Do not store items such as food and beverages in vaccine refrigerators, to prevent unnecessary opening of the refrigerator.
- It is preferable to store laboratory specimens in a refrigerator other than a refrigerator dedicated to vaccine storage. If laboratory specimens must be stored in a vaccine refrigerator, these specimens should be stored in a separate, clearly-marked container.
- Choose an appropriate refrigerator size:
    - Consider the amount of vaccine that your health unit will use in your monthly order period.
    - Choose a refrigerator that can hold vaccines in the middle and upper shelves without crowding.
    - Consider seasonal fluctuations when more vaccine may be required, for example, during influenza season and for school immunization programs.
- The room in which the refrigerator is placed should have a thermometer to measure the ambient (room) temperature, and a thermostat to adjust the room temperature if required. In the absence of temperature monitoring, room temperature is assumed to be ≤ +24°C unless circumstances warrant consideration of higher temperature, such as direct sunlight or an additional heat source.
- Lock the refrigerator, or place the refrigerator in a room that can be locked, to prevent unauthorized access, product handling or refrigerator tampering.
- Close the refrigerator door tightly. Installing a Velcro latch can help ensure that the door isn’t accidentally left ajar during the day, or after hours.
- Maintain the refrigerator temperature between +2°C to +8°C. A temperature of **+5°C** provides a safety margin for temperature fluctuations.
- Place the refrigerator away from the wall or surrounding structures (according to manufacturer’s recommendations) to provide proper ventilation and air circulation on all sides.
- Ensure the area around (including behind and under) the refrigerator is clean and dust free. This will help to ensure that the refrigerator is working at optimal levels.
- Protect the refrigerator from direct sunlight.
- Connect the refrigerator to a dedicated electrical circuit that is not used for other appliances.
- Use a plug guard on the electrical outlet for the refrigerator to prevent accidental disconnection from power.
- Label the vaccine refrigerator’s power breaker switch in the electrical panel box: **“VACCINE REFRIGERATOR – DO NOT DISCONNECT / DO NOT SWITCH OFF”**.
- When refrigerators are newly installed or have been repaired, follow manufacturer’s instructions for establishing the appropriate temperature. Test that the refrigerator is maintaining the appropriate temperature before placing biologicals in the unit. When there are no manufacturer instructions, allow one week of twice daily refrigerator temperature monitoring before using the unit to store vaccines.
- Have a refrigerator maintenance check (cleaning coils, checking door seals) done regularly (at minimum, annually). See National Guidelines for a “maintenance” checklist.
- Documentation of maintenance will be critical when an equipment malfunction occurs. Keep records of all maintenance and service repairs for the lifetime of the refrigerator. Post the refrigerator maintenance and/or repair telephone number on the refrigerator for easy accessibility.

3.2 Backup Power Supply

It is best practice to have all refrigerators storing vaccines connected to a backup power supply, which comes on automatically in the event of a power outage. As of March 31, 2013, all refrigerators storing more than $10,000 of BCCDC-supplied biological products should be connected to a backup power supply.

A backup power supply may be a generator or battery-pack.

Backup generators automatically provide power to the refrigerators to maintain the recommended temperature in the event of power outages. Backup generators should be tested as required by local building and fire codes and should receive maintenance at least annually (check manufacturer's specifications for test procedures and maintenance schedules). Backup generators should have the capacity to run continuously for 72 hours if necessary, and an adequate supply of fuel in place for this.

Backup battery packs (uninterruptible power supply {UPS} units) are an alternative to generators. Considerations for use of UPS include the following:

- expected load (number and capacity {wattage}) of equipment backed up;
- amount of time that one chooses to provide backup power;
- features of the UPS (for example, some units come with electronic modules that adjust to various conditions in the power supply);
- site features (such as space and weight-bearing capacity).

Where a backup generator or backup battery packs cannot be installed, establish a written agreement with an alternate storage facility (e.g., local hospital) with a backup generator, where vaccines can be appropriately and securely stored and monitored.

Have a written plan for "urgent procedures" when weather conditions, natural disasters or other emergencies might affect vaccine storage conditions.

3.3 Temperature Monitoring

3.3.1 Temperature Alarms

Develop a 3-year plan for purchase and implementation of continuous-monitored alarm systems for all refrigerators storing BCCDC-supplied biological products. Prioritize the refrigerators to be monitored, considering the volume and costs of products stored in the units, and complete implementation by **March 31, 2014**.

A monitored alarm system can prevent substantial financial losses in the event of an equipment malfunction that occurs outside of regular working hours. Install a continuous-monitoring temperature alarm or notification system with 24 hour and 7 days a week monitoring for vaccine refrigerators. The system should sound an audible alarm and alert one or more external monitors at a specified phone or pager number. Provide a fan-out list of health unit office/health authority contacts to be used by the external monitor. The contact list should be reviewed quarterly and updated for accuracy. Develop a written protocol to facilitate determining the nature of the problem and the process to manage the incident, to be used by staff responding to a call from the external monitor.

An alarm is not necessary when there is a small quantity of vaccine in an office only for a clinic day, and vaccines are returned to a central depot when the office is unattended.

3.3.2 Minimum-Maximum Temperature Monitoring

- Use a constant temperature-recording device or digital minimum/maximum thermometer (with probe) to monitor both the current refrigerator temperature and the minimum/maximum temperatures reached.
- Thermometers should be calibrated to be accurate within +/- 1°C or better.
- Check equipment annually, or according to manufacturer's specifications, to ensure thermometer measurement is accurate, batteries are functioning, and cables/probes are undamaged. Maintain and change batteries as recommended by the manufacturer, keeping in mind warranty requirements.
- See the National Guidelines for detailed information on temperature monitoring devices.
- Place the thermometer probe centrally (in the middle of the middle shelf) in the refrigerator, not at the back, front or at the door.
- Have extra thermometers (ideally minimum/maximum thermometers) available for use in coolers that are being used to store vaccines for several hours (e.g., for use at an off-site mass clinic). It is not necessary to use a thermometer in insulated coolers being used to transport vaccine for a short duration (e.g., from the health unit to physician's office) or in small coolers used at a clinic work station.
- At the start and end of each work day, record the minimum and maximum temperatures reached since the last monitoring, on the Temperature Form (see Section 7. Forms). Record the temperatures on the form even when there is a continuous temperature recording device in use, or when the refrigerator is connected to an alarmed temperature system. Also record the current refrigerator temperature, ambient (room) temperature, and refrigerator dial setting. Reset the min/max thermometer once you have recorded the temperatures.
- Retain completed forms (and the weekly recording wheel from the continuous data logger, if used) in order to have a history of temperature maintenance for refrigerated biological products. Retain records for a minimum of three years, or for a longer period of time as determined by HA.

3.3.3 TempTale®

Many biologicals orders shipped from BCCDC to the field will contain an electronic monitoring device called a TempTale®. This device will indicate a cold chain incident if the temperature during delivery is below +0.5°C or above +8°C. The TempTale® provides time and temperature data for vaccine shipments from BCCDC to the field. Instructions for handling a TempTale® are included in Section 4.1 Vaccine Delivery to Health Units below.

Temperature indicator cards and freeze tags are no longer used by BCCDC pharmacy.

Refer to Section 5. Management of a Cold Chain Incident for management of vaccine exposures to temperatures outside of the appropriate range. No vaccine should be removed from cold chain conditions nor returned to BCCDC until it has been determined that the product should not be used. Do not return any vaccine unless directed to do so by your Biologicals Product Consultant or BCCDC Vaccine and Pharmacy Services.

3.4 Insulated Containers

- Insulated containers (coolers) are used to transport quantities of vaccine off-site during one working day, or to store quantities of vaccine needed for immunization onsite during a working day, thus avoiding frequent opening of the refrigerator.
- The cooler must be able to maintain vaccine temperature between +2°C to +8°C during transport and throughout clinics.
- The temperature inside the cooler is maintained with ice/gel packs, and insulating materials.
- The cooler should meet the following criteria:
    - large enough to store vaccines, ice/gel packs, and insulating materials during transport;
    - external surface material is strong and durable;
    - lid is tight fitting.

3.5 Ice Packs/Gel Packs

- Keep enough frozen ice packs and/or refrigerated gel packs (at +2°C to +8°C) ready to meet the vaccine transport needs of your clinic or health unit.
- Set ice packs on their edge and allow space between them for air circulation in the freezer. Stacking ice packs on top of each other in the freezer may result in uneven or partial freezing, and decrease the efficacy of the ice packs.
- Ensure that ice packs are completely frozen before use.

3.6 Insulating Materials

- Insulating materials are used as a barrier to prevent direct contact between vaccines and frozen ice packs.
- Insulating materials include flexible insulating blankets and gel packs at **refrigerator temperature**, bubble wrap, crumpled packing paper or Styrofoam peanuts.
- A layer of paper toweling is not sufficient as a barrier to protect vaccines from contact with frozen material.

4. Handling Biological Products

4.1 Vaccine Delivery to Health Units

Vaccine shipments require immediate attention.

- **Unpack and refrigerate biological products immediately upon their arrival.** Vaccines that are delivered by refrigerated truck are packed without any ice or gel packs; the temperature in the packing boxes will rise dramatically unless the vaccines are refrigerated promptly.
- The National Guidelines provide a resource for tracking vaccine inventory. The Vaccine Tally Sheet may be used to document arrival of a product, lot number and expiration date.
- Check for evidence of physical damage, freezing or excessive heat.
- Freezing affects the physical form of aluminum-adjuvanted adsorbed vaccines. It is thought that freezing causes the adsorbent to form larger, heavier granules that will gradually settle at the

bottom of the vial when the vial is shaken. The physical changes initiated by freezing provide the basis for the shake test. A World Health Organization (WHO) Bulletin describing validation of the shake test to detect freeze damage is available at Validation of the shake test for detecting freeze damage to adsorbed vaccines. A "Shake test learning guide" is available in Annex 1 (pages 59-62) of a WHO document. The shake test is not necessary when the vaccine is frozen solid, or when a homogenous solution cannot be obtained by vigorous shaking (white lumps/sediment cannot be separated from the walls of the glass vials), as this is a sign that the vaccine has frozen.

- If you notice evidence of damage, label the products as "Do not use", quarantine in the refrigerator, and contact your Biological Products Consultant for directions about vaccine use.
- In general, BCCDC will not accept vaccines from a manufacturer when a cold chain excursion has occurred, unless there is a significant reason to do so (e.g., the vaccine is in short supply and is deemed unaffected by the exposure). BCCDC Vaccine and Pharmacy Services will provide the details of this initial exposure when these vaccines are shipped to the field.

TempTale®4 USB (TT4USB) instructions:

1. Remove the TT4USB device from shipping box immediately.

2. Check the LCD window display:
   - If a SUNSHINE symbol appears in the top left corner, this indicates that the device is still recording temperature. Proceed to STEP 3.
   - If no SUNSHINE symbol appears, it is likely that the TT4USB was not started at BCCDC or stopped accidentally during transit. Quarantine the contents of the shipment immediately in the refrigerator and label "DO NOT USE". Inform the BPC, but do NOT complete a Cold Chain Incident form. Contact the Biologicals Desk (604-707-2582) who will review the refrigerated truck record and provide direction regarding vaccine use. Proceed to STEP 6 to return the TT4USB to BCCDC Pharmacy.

3. Firmly press and hold the red "STOP" button, located in the bottom right corner of the TT4USB for at least 3 seconds.

   A "STOP" icon will appear in the top right hand corner, indicating that the device has stopped recording the temperature.

   - If no other symbol appears on the display window, this indicates the shipment has been maintained under cold chain conditions and is okay to use. Proceed to Step 4.
   - If a BELL (alarm) symbol appears along with the "STOP" icon, this indicates the shipment was exposed to temperatures outside of the +0.5°C to +8°C range.

   Quarantine the contents of the shipment immediately in the refrigerator. They cannot be used until further notice from BCCDC. Keep the contents segregated from other useable inventory while you await a BCCDC response. If the shipment is urgent but has a bell you may choose to plug the TT4USB into a local PC USB port and save both files to your computer and then contact BCCDC Pharmacy (604-707-2580). If more than one box needs to be quarantined, keep them separated from each other as well. Proceed to Step 4.

4. Press the green “Start” button to view and record the transit temperature history. Information will appear in the window.

   The numbers indicate:
   a) average temperature
   b) high (Hi-) temperature
   c) low (Lo-) temperature

   Record the information from (a) through (c) on the TT4USB form. Pressing the “Start” button again will repeat the display of the readings. Complete the entire form.

5. Fax the TT4USB form immediately to the Biologicals Desk at 604-707-2582.

6. Return the TT4USB monitor(s) immediately to BCCDC in the provided prepaid bubble envelope. Enclose a copy of the completed TT4USB form.

7. Once BCCDC receives the TT4USB the information is downloaded and a consult will be provided back to the health unit office as early as possible, if required. Record the information provided by BCCDC on the TT4USB form that has been retained at the originating office.

If unsure of proper procedure for the TempTale® device, store the shipment and the TempTale® in the refrigerator until Biological Products Monitor or designate is available.

See Algorithm 2: Cold Chain Incident from BCCDC to Health Authority.

4.2 Vaccine Storage

- See Section 8. Resources, How to store Vaccines in the Refrigerator, for diagram illustrating placement of biological products in the refrigerator.
- Use vaccines that have experienced a cold chain incident and have been determined to be usable **at the first opportunity**.
- **“First to expire, first out”**: rotate vaccine stock according to expiry date (placing vaccine with the shortest expiry date at the front of the shelf, and longest expiry date at the back) so that vaccine closer to the expiry date will be used first.
- The expiry date is the date by which a vaccine or diluent should be used. When the date is marked as a month and a year, the vaccine or diluent may be used up to and including the last day of the month. Note: some component vaccines and diluents may be assembled into one package with a labeled expiry date on the outer carton. This date is the shorter of the two dates of either the component vaccine or the diluent in the package.
- Check biological products inventory on the last working day of each month. Remove expired products to prevent the administration of expired product to a client.
- Check the expiry date on multi-dose vials which have been opened. Note vial(s) that will need to be removed when the post-puncture expiry date is before the end of the next month, and remove the vial(s) on that date. Multi-dose vials are dated when first opened, and should be used within 30 days of first puncture unless the product monograph specifies a shorter time period for use (e.g., some influenza vaccine in multi-dose presentation must be used within 7 days of first puncture).
- **Return all expired products** to BCCDC Vaccine and Pharmacy Services (see Section 7. Forms, Field Return Form). Do **not** discard expired products locally.

- Check for product(s) that will expire within three months and if use is unlikely within that time in the local office, determine if another office within the region could use the product. Redistribute within the Health Authority as needed to avoid wastage.
- Keep a separate tray or container in the refrigerator for products that have been partially used or previously taken from the refrigerator for a clinic (protect from light, if applicable). Use these vaccines before opening new vials or packages.
- Group the same biological products together and space the products to allow air circulation between rows.
- Keep all vaccines in their original packaging unless circumstances warrant providing less than a full package to a community provider to avoid wastage.
- Store vaccines **only** on the upper and middle shelves in the refrigerator.
- Do not use refrigerator door shelves and crispers for vaccine storage as these areas are more susceptible to temperature fluctuations.
- Store sealed bottles of water in the refrigerator to provide cold mass that will help to maintain internal temperatures and delay temperature changes in the event of a power or refrigerator failure.
- Store flexible insulating blankets or gel packs that will be used as insulating material during vaccine transport in the refrigerator.
- Diluent for vaccines can be stored at room temperature to conserve refrigerator space, unless the product insert specifies refrigeration.
- Store epinephrine at **room temperature** (15°C to 30°C) and protect from heat, light and moisture. Do not store epinephrine in the refrigerator.
- Open the refrigerator door **only** when necessary, and close it as soon as possible.

4.3 Vaccine Orders

- Review inventory on hand and order vaccines as per the shipping schedule provided by BCCDC Vaccine and Pharmacy Services for your office. Weekly ordering is recommended for large health unit offices, biweekly for medium-sized offices, and monthly for small and isolated offices.
- Establish a base order for all vaccines or minimum quantity to be kept on hand at all times, considering the following:
    - the size of the age cohort (i.e., the number of births in the community, or the number of students in a school-based program grade);
    - the doses in a “routine” immunization schedule (no seasonal fluctuations, e.g., two doses of MMR vaccine/infant);
    - seasonal and program demands (influenza clinics, kindergarten clinics, school-based programs: hepatitis B, meningococcal C, HPV, varicella, TdaP);
    - frequency of delivery from BCCDC or RHA central depot;
    - small buffer amount to accommodate any unexpected demand.
- Review base order quantities quarterly, and revise as needed (for example, if there is a large supply of vaccine on hand on a regular basis, this may indicate over-ordering). Base orders will need to be adjusted when there is a program change to the number of doses in a recommended immunization schedule or when a new combination vaccine is introduced (e.g., use of INFANRIX hexa® rather than PEDIACEL® and hepatitis B vaccine).

- Consider quantity on hand when ordering.

  Example: monthly base order, minus quantity of the vaccine on hand, = amount to order. Consider delivery date to the office when placing orders. Base order of 100 doses, minus 20 doses on hand = 80 doses would be ordered.
- For school-based programs, order only the quantity needed for the **first** dose in a vaccine series (grade 6 hepatitis B, HPV); order subsequent doses at a later date as needed according to series schedule. Consider coverage level reached with dose #1 to estimate vaccine amount needed for dose #2.
- Avoid over-ordering or early ordering. Do not stockpile vaccines. Any loss will be more costly in the event of a power outage or refrigerator failure, and the risk of wastage from expired product is increased.
- Alert staff when an order is placed, and when order is expected to arrive. All staff need to be aware of procedures to follow when a biologicals order is received and the Biological Products Monitor or designate is not available.
- For Public Health only, use the Biologicals Order Form (see Section 7. Forms) to order biological products from BCCDC.
- Physicians, pharmacists, private clinics and facilities order public-funded vaccines through their local health unit office.

4.4 Principles of Vaccine Handling

- Keep vaccines in the refrigerator or in a cooler until ready to administer.
- Use small coolers at work stations during mass immunization clinics. This will reduce the number of times that the refrigerator or larger cooler will be opened and closed during the day, thus reducing temperature fluctuations and exposures to adverse conditions (see Section 8. Resources, Mass Clinics – Vaccine Handling Tips).
- Biological products are not hazardous waste. Empty multi-dose vials may be placed in the regular garbage for disposal.

4.5 Transportation and Management of Vaccines for Clinics

Consider the amount of vaccine to be transported, the external air temperature, and the length of time the vaccine will be in an insulated container. This will help to determine packing requirements.

Packing vaccines for clinic use:

- Keep vaccines in original packaging.
- Place a thermometer with the vaccine in the cooler when vaccine will be in the cooler for more than 4 hours. Note: A minimum/maximum thermometer is recommended for monitoring temperature inside large coolers during mass immunization clinics.
- Provide a protective barrier of insulating material such as a flexible insulating blanket, between the vaccines and the frozen packs.
- Place frozen packs at the top of the cooler.
- See Section 8. Resources, Packing an Insulated Container. Specific packing configurations should be developed at the local level, considering locally available equipment and supplies.
- Consider local testing of packing configurations using available supplies and monitoring the temperatures in a cooler over time to determine the appropriate vaccine load and packing

requirements that will maintain the temperature within the +2°C to +8°C range. Consider the length of times vaccines may be in the field in your specific region (locations of outside clinics and travel times to clinics).

- Packing configurations will vary on a seasonal basis. **It is most important to prevent vaccines from freezing.** In winter conditions, fewer or no frozen packs may be needed to maintain the required temperature; more frozen packs may be needed for summer conditions.
- Maintain the packing configuration when removing vaccines from or returning vaccines to the cooler.
- Refrigerate diluent for 24 hours in the refrigerator if you are planning on transporting it in the cooler with the vaccines. Diluent that is not refrigerated before being placed in a cooler may warm the temperature in the cooler. If you have not refrigerated the diluent, transport diluent separately from vaccines.
- Keep coolers out of direct sunlight. Do not place coolers in the trunk of a car where temperatures cannot be monitored and may be significantly different from interior vehicle temperatures.
- When weather temperatures are below +2°C, transport in a vehicle where the temperature can be kept higher than +2°C to avoid freezing. Do not place coolers by the car heater.
- Check the temperature readings hourly to ensure the vaccines are maintained within cold chain parameters.

Packing single-dose vaccines for clinic use:

A request for a single dose of a vaccine is not expected to occur frequently, but when requested, supplying a single-dose or less than a complete package may be appropriate, to avoid unused vaccines expiring in the field.

It is important to package a single-dose of vaccine that will clearly identify the vaccine and will protect product integrity during transit.

Packaging process:

- When possible, provide the vaccine in an original box that has the correct lot number and expiry date for the product.
- A package insert (copy or original) should be provided. You do not need a product monograph.
- INFANRIX hexa® **must** be supplied in an original box because PEDIARIX™ is added as a diluent to the vial containing a Hib pellet. The two components are lot specific with respect to the final “combined” product.
- When live vaccines such as MMR and varicella are packaged with the appropriate diluent, a lot number is only required for the MMR or varicella antigens. The number of vials of vaccine should be equal to the number of vials of diluent, and the correct diluent should be included for each product.
- If a vaccine cannot be supplied in its original box, single doses should be carefully wrapped in bubble wrap and placed in a padded envelope. This protects the vaccine from breakage, light, prevents direct contact with ice packs and reduces the variability of the temperature close to the vaccine.
    - The envelope should be labeled with the name of the vaccine, lot number and expiry date.
    - To maintain the vaccine temperature between +2°C to +8°C refrigerate the diluent prior to packaging. Wrap both the diluent and the vaccine and place in the same envelope.

4.6 Mass Immunization Clinics

Monitor the temperature in larger coolers used for mass clinics. Check the temperature in the large monitored cooler before removing vaccines at the clinic. When there is concern that products may have been exposed to adverse temperatures, do not use the vaccine until you have received instructions from your Biological Products Consultant.

The British Columbia Mass Immunization Cold Chain Project (2005-2006) provided recommendations for insulated coolers that would maintain the cold chain during vaccine transport and handling in mass clinic settings. The project provided data for a small number of specific packing configurations and vaccine loads, under summer and winter conditions and over extended periods of time. These data will be useful if your circumstances (ambient temperatures and travel times) match those of the project. The project report is available on the BCCDC website (see Section 8. Resources, BC Mass Immunization Clinic Cold Chain Project) and contains the specific packing configurations for large and small coolers for mass clinics under summer and winter conditions.

If vaccines are transported to mass clinics in numerous coolers, use all the vaccines in one cooler before opening the next cooler.

4.7 Returning Biological Products

- Check inventory and return products to BCCDC Vaccine and Pharmacy Services **monthly**.
- Return only BCCDC-supplied products.
- Encourage community immunization providers to return damaged/wasted vaccines to public health for forwarding to BCCDC.
- Complete a Field Return Form (see Section 7. Forms), indicating the product, lot number, expiry date, reason for return, quantity (in doses), and the contact person at the health unit. Accurate and complete information is required to facilitate analysis of returns and determine underlying causes of vaccine wastage.

For products that **do not** require return under cold chain conditions:

- Fax the completed form to the Biologicals Desk at 604-707-2581 to obtain a Field Return authorization number. Biologicals Desk will fax the Field Return Form with the authorization number to the health unit office. No Field Return authorization number will be provided unless all required information in the Field Return form is complete.
- Enclose a copy of the Field Return form with the authorization number in the vaccine shipment, and retain a copy in the health unit office.

For products that **do** require return under cold chain conditions:

- Follow the steps outlined above to obtain a return authorization number. No Field Return authorization number will be provided unless all required information in the Field Return form is complete.
- Complete the Biologicals Return and Redistribution Requirements Form, if needed.
- Contact the Biologicals Desk for packing instructions and to obtain a TempTale® from BCCDC to accompany the shipment.
- Return the vaccines in an insulated container, packed as specified by BCCDC and monitored with the TempTale® device.

Do not return vaccines for redistribution without consultation and authorization by BCCDC Vaccine and Pharmacy Services. **All** of the following criteria must be met:

- The cold chain was maintained between +2°C to +8°C for these products, throughout their storage at the site.
- Products were received directly from BCCDC, and were maintained at all times at the site, with no transfer to/from other site(s) prior to being shipped back to BCCDC.
- Products are in their original packaging: sealed, unopened and unused.
- Products were stored in a safe and secure location with no public access.
- The refrigerator temperature was logged at the start and end of each business day.
- The products have **at least 3 months dating** before the expiry date is reached.

The redistribution form must be signed by the Biologicals Products Consultant for the region, **and** the Biological Products Monitor at the local health unit. Include the form with the vaccines being returned. See Section 7. Forms, for the Biologicals Return and Redistribution Requirements Form.

To facilitate the tracking of vaccine returns, use the following "Reasons for Return" codes:

Reason for Return Codes	Code
Cold Chain Incident: Power Outage	A
Cold Chain Incident: Equipment Malfunction	B
Cold Chain Incident: Handling Error (human error – vaccine left out of fridge, fridge door left open)	C
Damage To Product (packaging, syringes, vials, ampoules broken/crushed)	D
Expired Product	E
Vaccine Returned to BCCDC for Redistribution	F*
Wrong Product Shipped by BCCDC/Requested by HA/HU	G*
Product Recall by Manufacturer	H*
Annual Influenza Harvest	I
Cold Chain Incident: In Transit BCCDC to HA/HU	J
Cold Chain Incident: In Transit Within HA	K

*Indicates product to be returned under cold chain conditions, with a temperature monitoring device.

Use **one** Reason for Return Code only: choose the primary reason for return.

5. Management of a Cold Chain Incident

See Algorithm 1: Cold Chain Incident Within Health Authority and Algorithm 2: Cold Chain Incident from BCCDC to Health Authority.

All biological products are licenced for use under storage conditions of **+2°C to +8°C**.

As a general principle, **0°C to +2°C** is considered "refrigeration conditions" with due regard to the accuracy of the temperature reading device. For example, with a thermometer calibrated for accuracy at +/-1°C, a

reading of +0.5°C could be as high as +1.5°C or as low as -0.5°C. The decision about use of the product will be based on the temperature range, and the "worst case scenario", which in this example would be -0.5°C. Products exposed to a validated temperature in the 0°C to +2°C range for an exposure of any period of time, even for a series of exposures, do not constitute a cold chain incident and do not need to be reported. The **exception** to this is Tubersol®, for which exposures to temperatures in the 0°C to +2°C temperature range do constitute a cold chain incident and must be reported using the Cold Chain Incident Form.

It is extremely important to adjust the refrigerator temperature and restore the temperature to within the recommended +2°C to +8°C range **immediately**, because further temperature declines to below 0°C could result in freezing of vaccines.

Any temperature outside of the +2°C to +8°C temperature range requires immediate action.

- Check that your thermometer is working correctly; you may need to change the battery. Check manufacturer's specifications for battery life.
- On the Temperature Log, record the date, time and 3 temperatures (the current refrigerator temperature, the minimum temperature reached since last check, and the maximum temperature reached since last check). Also record the refrigerator dial setting. Reset the thermometer after recording these temperatures.
- If the **current** refrigerator is malfunctioning, move all of the vaccines to a properly functioning, monitored refrigerator.
- Adjust your refrigerator temperature setting and monitor the effect of this measure, or have the refrigerator serviced, and check that the temperature is between +2°C to +8°C, ideally at +5°C, before returning any vaccine to the refrigerator.
- Place exposed vaccines in a container; clearly label as **"DO NOT USE"**, and mark the date and time. Place this container with the exposed vaccines into a functioning refrigerator, ensuring that the exposed vaccines are separate from any non-exposed vaccines. It is important that the exposed vaccines are returned to acceptable temperatures (+2°C to +8°C) as soon as possible.
- When the temperature is outside the 0°C to +8°C range (+2°C to +8°C for Tubersol®), the BPM will complete the Cold Chain Incident Form (see Section 7. Forms).
- Contact your Biological Products Consultant for direction about use of the vaccines.
- Do **not** discard any vaccines until this consultation and determination of use has been made.
- Clearly label biological products that have had a cold chain incident, but are subsequently deemed to be usable. Use these vaccines as soon as possible. Develop a system to track vaccines exposed to a cold chain incident, including the temperature and the duration of the exposure.
- Biological products that have been exposed to a temperature outside the recommended range in transit from BCCDC to the field should be labeled with a dot and the date of the exposure. Retain the original TempTale® as a record of the temperature and duration of the incident.
- Develop a protocol within the HA for labeling products that undergo subsequent cold chain incidents. This is particularly important in instances where a vaccine will remain "good to use" with multiple exposures (e.g., a specific vaccine may be "stable at +25°C for one or a series of exposures not exceeding a total time of 72 hours").
- Return to BCCDC the exposed vaccines that have been determined by the Biological Products Consultant to be non-usable.

Any cold chain incident provides an opportunity to review cold chain management and modify practices that may be contributing to cold chain incidents.

When the information in the Stability Chart is insufficient to make a decision, the Biological Products Consultant will contact BCCDC Vaccine and Pharmacy Services for assistance in determining if vaccines can be used.

Consult with Vaccine and Pharmacy Services when products have had a **second** exposure to temperatures outside of the recommended range and second exposure information for a particular vaccine is missing in the Stability Chart.

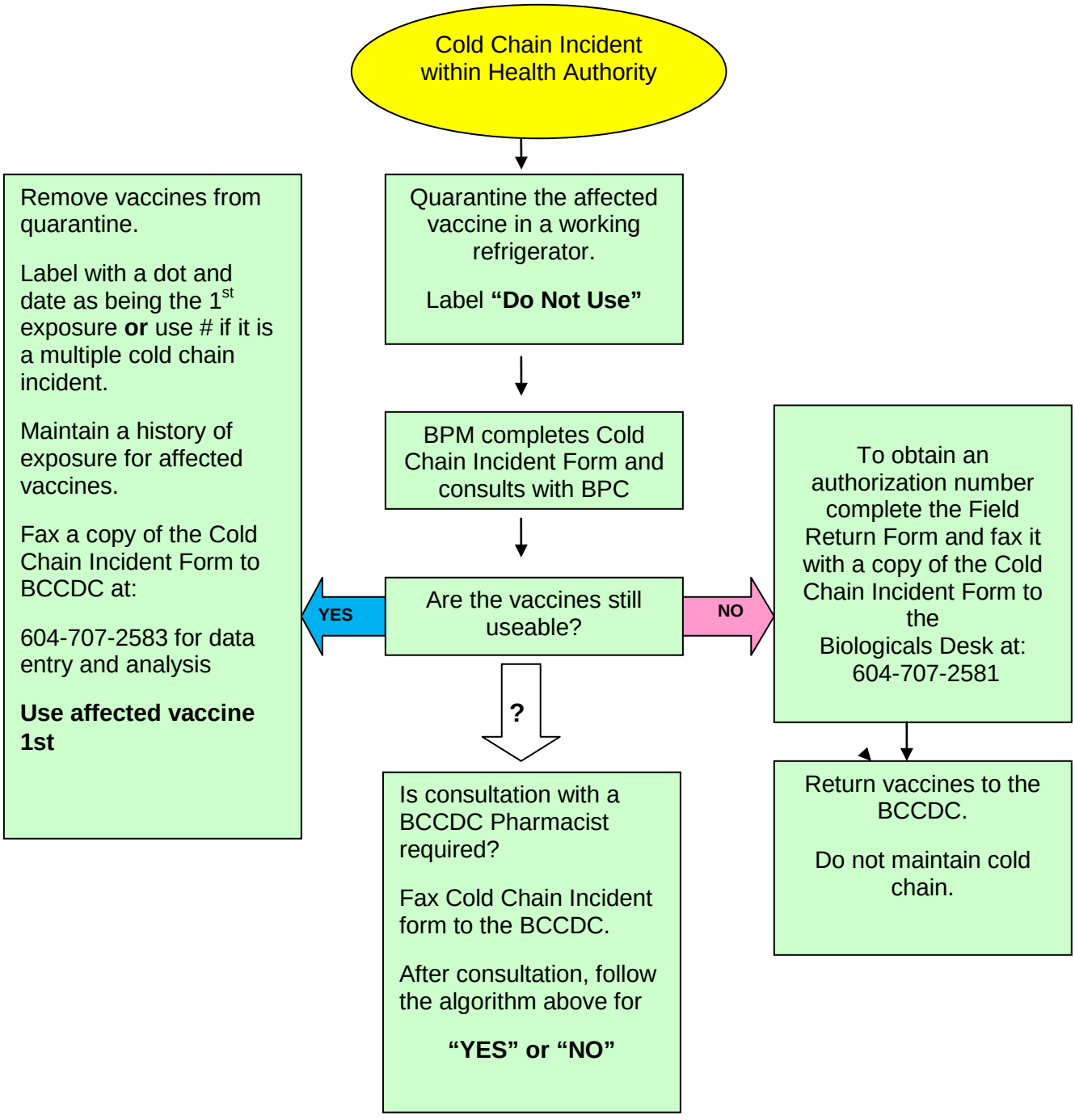
5.1 Power Failure

- Establish an office-specific emergency plan for power failures or equipment malfunction.
- Identify a backup refrigerator that is accessible, monitored and functional at all times.
- On the Temperature Form (see Section 7. Forms), record the refrigerator temperature (minimum, maximum, and current), room temperature, and time, as soon as possible after the start of the power failure. Reset the thermometer.
- Place a "**DO NOT USE**" sign on the refrigerator. Do **NOT** open the refrigerator except to remove vaccines for alternate storage.
- On average, the temperature in a powerless refrigerator will increase approximately +1°C per hour. However, the rate of temperature increase will depend on factors such as the type of refrigerator or room temperature. The refrigerator is insulated and able to maintain its temperature, especially if it contains cold ballast (bottles of water).
- If power is expected to be restored within 4 hours or less, keep the vaccines in the refrigerator and keep the refrigerator doors closed. Refer to BC Hydro information on power outages.
- If a longer power outage is expected, or if the refrigerator temperature is going out of range quickly, move vaccines to a cooler with ice packs and insulating material. Take the vaccines to a facility that has a functioning monitored refrigerator (i.e., that has power or a backup generator) as per the local emergency plan.
- Continue to monitor and record refrigerator temperatures for the duration of the outage. If power failures are a common occurrence, centralize vaccine storage to a more power-stable facility.
- Record the time and refrigerator temperatures (current, minimum, and maximum) when the power is restored.
- Complete the Cold Chain Incident Form and contact your Biological Products Consultant if products have been exposed to temperatures outside of the 0°C to +8°C range (+2°C to +8°C for Tubersol®).

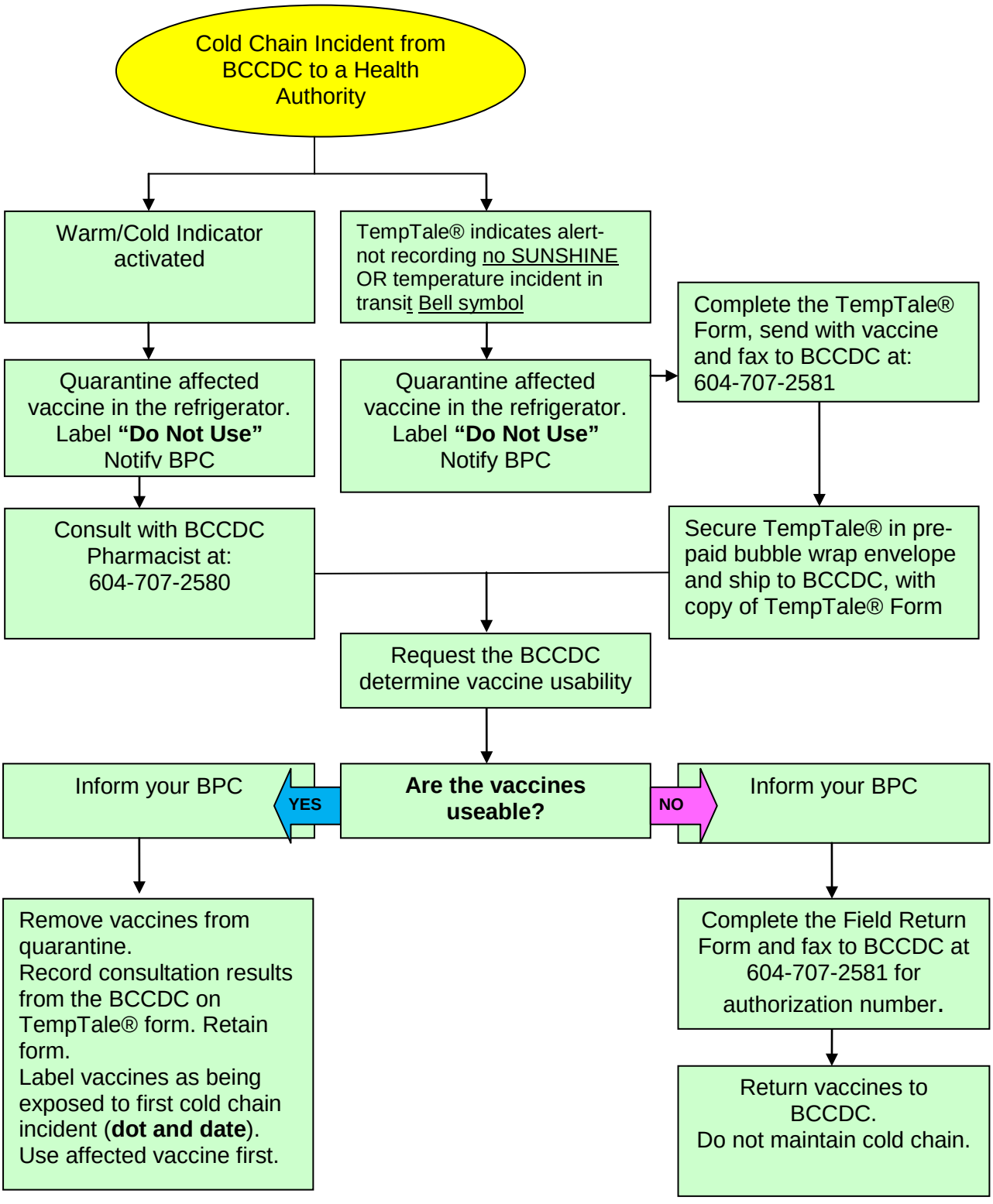
5.2 Equipment Malfunction

Regular maintenance promotes proper functioning of the refrigerator and maintenance of the required temperature, and extends the useful life of the unit. However, refrigerator malfunction **can** and does occur. Each office should have a plan in place to deal with equipment malfunction. The most important action to take should this happen is to protect the vaccine supply as quickly as possible. Move vaccines to a properly functioning refrigerator at the appropriate temperature. Do not place "warm" vaccine in a refrigerator with other vaccines, as this warmth of the vaccines will increase the refrigerator temperature, thus risking exposure of vaccines already in the unit to compromise. After the vaccine is secure, attempt to find the cause of the malfunction and correct it.

5.3 Algorithm 1: Cold Chain Incident within Health Authority



5.4 Algorithm 2: Cold Chain Incident from BCCDC to Health Authority



6. Vaccine Stability Chart Information

BCCDC has developed a Vaccine Stability Chart for **PUBLIC HEALTH USE ONLY**. It contains guidance for use of vaccines exposed to specific time/temperature scenarios.

Using the Vaccine Stability Chart

1. Staff person identifies that there has been a break in the cold chain.
2. Staff person contacts Biological Product Monitor (BPM).
3. BPM completes the Cold Chain Incident Form and contacts the Biologicals Product Consultant (BPC).
4. BPC reviews the completed Cold Chain Incident Form and uses the Vaccine Stability Chart to determine whether vaccines are usable. If all decisions are made at the local level, retain original form and fax a copy of the incident form to the Biologicals Desk.
5. If the information contained in the Vaccine Stability Chart does not match the circumstances of the reported cold chain failure, the BPC can contact the BCCDC Vaccine and Pharmacy Services at 604-707-2580 and speak with a Pharmacist. A copy of the Cold Chain Incident Form is needed by BCCDC Vaccine and Pharmacy Services to assist with the assessment of the stability of the vaccines in question.
6. The completed Cold Chain Incident Form, with actions taken, is retained by the health unit, and copied to BCCDC Vaccine and Pharmacy Services for data entry and analysis.
7. Clearly label vaccines that have been exposed to a cold chain incident and have subsequently been determined to be usable. Use these products at the first opportunity.

7. Forms

The following forms for public health use are available on the BCCDC, Vaccine and Pharmacy Services website.

- Biologicals Order Form
- Field Return Form
- Biologicals Return and Redistribution Requirements Form
- Cold Chain Incident Form
- Temperature Form
- TempTale® 4 Monitoring Device Form for REFRIGERATED TRUCK deliveries
- TempTale® 4 Monitoring Device Form for COURIER deliveries

Note: all forms now indicate **doses** rather than units.

8. Resources

The BCCDC website has resource material for community vaccine providers and public health on the Vaccine Management page.

Cold Chain Resources for Community Providers

1. How to Store Vaccines in the Refrigerator
2. Packing an Insulated Cooler
3. Handle Vaccines with Care
4. Equipment Malfunction or Power Failure
5. Temperature Form
6. Cold Chain Checklist

Cold Chain Resources for Public Health

1. How to Store Vaccines in the Refrigerator
2. Packing an Insulated Cooler
3. Cold Chain Checklist
4. Mass Clinic – Vaccine Handling Tips
5. Mass Clinic Project Report
6. TempTale® Directions
7. Cold Chain Incident Algorithms

Training videos for Biologicals Management are available on the BCCDC Vaccine Management page.

9. References

California Vaccines for Children (VFC) Online Immunization Training available at http://eziz.org/vaccine-storage/ (see Vaccine Storage and Handling)

Department of Health and Ageing (2005) National Vaccine Storage Guidelines: Strive for Five. Canberra, Australia available at http://www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/D7EDA378F0B97134CA257D4D0081E4BB/$File/strive-for-5-guidelines.pdf

Public Health Agency of Canada. (2006). Canadian Immunization Guide (7th ed.) available at http://publications.gc.ca/site/eng/308837/publication.html

Public Health Agency of Canada (2007). National Vaccine Storage and Handling Guidelines for Immunization Providers available at http://healthycanadians.gc.ca/publications/healthy-living-vie-saine/vaccine-storage-entreposage-vaccins/index-eng.php

World Health Organization Bulletin (2010). Validation of the shake test for detecting freeze damage to adsorbed vaccines. Vol.88:624-631. Available at http://www.who.int/bulletin/volumes/88/8/08-056879.pdf

World Health Organization (2006). Temperature sensitivity of vaccines. Available at http://apps.who.int/iris/bitstream/10665/69387/1/WHO_IVB_06.10_eng.pdf (see Annex 1)

World Health Organization (2002) User's handbook for vaccine cold rooms and freezer rooms, available at http://apps.who.int/iris/bitstream/10665/67801/1/WHO_V-B_02.31_eng.pdf