SUPPLEMENTARY NOTES FOR MANAGEMENT OF COLD CHAIN PRODUCTS/ MATERIALS

CHAPTER 15 GUIDELINES ON GOOD DISTRIBUTION PRACTICE (GDP)

(These notes are to be read alongside the Guidelines)

GLOSSARY OF TERMS USED

Active systems	Actively powered systems using electricity or other fuel source to maintain a temperature-controlled environment inside an insulated enclosure under thermostatic regulation (e.g. cold rooms, refrigerators, temperature-controlled trucks, refrigerated ocean and air container)
Cold chain	The process used to maintain optimal conditions during the transport, storage, and handling of cold chain products, from the point of manufacturer to the point of use.
Passive systems	Systems which maintain a temperature-controlled environment inside an insulated enclosure, with or without thermostatic regulation, using a finite amount of pre-conditioned coolant in the form of chilled or frozen gel packs, phase change materials, dry ice or others
Qualification	Documented testing that demonstrates, with a high degree of assurance, that a specific process will meet its predetermined acceptance criteria
Temperature-controlled	Includes any environment in which the temperature is actively or passively controlled at a level different from that of the surrounding environment within precise predefined limits
Temperature excursion	An excursion event in which a time- and temperature-sensitive products is exposed to temperatures outside the range(s) prescribed for storage and/or transport. These temperature range may be the same or different which are determined by the manufacturer, based on stability data
Temperature monitoring device	This includes temperature indicators such as data-loggers, cold chain monitors (CCM), vaccine vial monitors (VVM) and freeze watch indicator.
Validation	Documented testing performed under highly controlled conditions, demonstrating that processes, methods, and systems consistently produce results meeting predetermined acceptance criteria

Paragraph	Explanation
15.1 GENERAL INSTRUCTION	
15.1.1 List of products should be provided with cold chain storage temperature specifications for reference by personnel who handle the receipt of goods and related store personnel.	➢ Company should provide list of all cold chain products and its storage requirement (with reference to which standard used). ➢ The list should also include registration number of the products and its registration holder.
15.2 PERSONNEL	
15.2.1 Written procedures should be available and appropriate training should be provided for all staff involved in the handling, receipt, storage, packing and delivery operations for cold chain products/materials to ensure the quality of cold chain products/materials is maintained.	➢ All staffs involved with the management of cold chain products should be identified and trained. ➢ Company should provide training schedule and re-assessment to ensure staffs are equipped with specific knowledge and skills to handle cold chain products. ➢ All policies and procedures should be made aware to all staffs concerned. ➢ All policies and procedures should be available in writing and situated in accessible area for easy references by the staffs.
15.3 FACILITIES AND EQUIPMENTS	
15.3.1 Cold chain product storage facilities should be qualified prior to prevail that it is capable of storing the product in accordance with the specifications given situation. Qualification and validation records must be kept and cold chain products storage facilities must be able to operate at all time in accordance to the qualifying conditions.	➢ Company should provide qualification documents of the storage facilities and the validation documents of the temperature monitoring system ➢ Qualification should include consideration for holding time (Operational Qualification).

15.3.2 Suitability of locations for placing temperature sensors in a cold room used for storage of cold chain products should be subjected to temperature mapping study. Mapping studies should be conducted in accordance with written procedures and storage conditions determined before operation.	➢ See Chapter 3 ➢ Company should provide validation reports for temperature mapping of the facilities. ➢ Location of temperature logger should be identified.
15.3.3 Temperature and humidity (if needed) for cold room or refrigerator must be monitored and recorded continuously using temperature and humidity sensors.	➢ No clarifying remarks.
15.3.4 Maximum and minimum temperatures should be recorded, either electronically or manually at least once in the last 24 hours, with continuous review of records. Records must be kept for at least one year.	➢ No clarifying remarks.
15.3.5 Cold room or freezer must be fitted with an alarm system to alert staff if any occurrence of temperature beyond specifications. Action and warning limits should be established. Periodic testing programme on the alarm system should be established to ensure the alarm system is functioning.	➢ Alarm systems should include visual and audible alarms. ➢ Alarm systems should be able to alert staff during emergencies (including after working hours).

15.3.6 Alternative power systems should be established for cold rooms to ensure cold room temperatures remain and the temperature /humidity detector will continue functioning in the event of power failure. Periodic testing programme on alternative power systems should be established to ensure that it works. Alternative plan to provide alternative areas where storage temperature equivalent should be provided if no alternative power systems can be provided.	➢ Company should provide back-up power supply (e.g. uninterrupted power supply/ UPS system). ➢ Company to develop and maintain a contingency plan in the event of power failure or any other unforeseen situation that may cause products to be at risk.
15.3.7 Periodic maintenance programmes for air conditioning systems in a cold room and freezer must be established and implemented.	➢ No clarifying remarks.
15.3.8 Calibration and temperature monitoring functions of all equipment, including alarms and other related equipment, must be inspected at least annually.	➢ No clarifying remarks.
15.4 STOCK RECEIVING AND HANDLING	
15.4.1 Cold chain products should be identified immediately after receipt and stored under the storage conditions that comply with the directions on the product label. Written procedures should be provided to ensure that the activities of receipt, storage, and distribution is done without compromising on the quality, efficacy and safety products /	➢ No clarifying remarks.

materials that should be stored under cold conditions.	
15.4.2 Inspection upon receipt of products / materials should be done to prevent signs of aggression, destruction and non-conformance along the cold chain storage and distribution, as well as physical damage to the packaging materials, labels and quantity of the product compared to the information in the purchase order. These inspections shall be conducted under the recommended storage conditions as on the product label.	➢ No clarifying remarks.
15.4.3 If the storage temperature is found to have deviated from the storage specifications, manufacturer for the products / materials should be contacted to confirm the suitability of the use of products / materials and the decision recorded.	➢ Products that are subjected to investigation (e.g. breach in cold chain) should not be disposed of until the investigation is complete.
15.4.4 All cold chain products (e.g. removed, quarantined) must be stored under the storage conditions stated on the label other than the product which will be disposed off.	➢ No clarifying remarks.
15.5 DOCUMENTATION	
15.5.1 Procedures must be implemented to handle the returned products and also the products / materials that have been stored under out of the specified storage condition	➢ Company should provide written procedure for handling products SOP returned by customer. ➢ Company should provide written SOP for handling out-of-specification situation (e.g.

	during the reception, storage and distribution of products / materials.	temperature excursion).
15.5.2	Written procedures should be available to explain the packing materials required, packing configuration of transportation container for cold chain products / materials and labels to identify these products as products that require special storage /shipping conditions. Packaging operations for cold chain products should be recorded and should have the second person conformance to ensure that the packaging operations carried out in accordance following written procedures.	➢ Company should provide qualification for transportation container (active or passive container). ➢ Company should provide validation report for packing configuration used. ➢ Written procedure should include type of packaging material used, number of ice pack/dry ice used, detailed step of the packing process (including conditioning of the ice pack) and temperature monitoring device used.
15.5.3	Outer packing / shipping containing cold chain products/ materials should be labelled: ❖ "Cold but not freezing" for medicines that require maintenance of temperature in the range of +2ºC to +8ºC, or ❖ "Refrigerate the contents of the package" for medicine transported in packaging that needs to be removed before the medicines be placed in the refrigerator, or ❖ "Keep frozen" for medicines that require maintenance in the range of temperatures below 0 º C.	➢ No clarifying remarks.

15.5.4 Packing and handling of cold chain medicines should put a warning to acknowledge the recipient that it is a cold chain medicines and receiver must put the medicines in appropriate storage facilities as soon as possible.	➢ No clarifying remarks.
15.5.5 Medicines labelled "Keep Frozen" should be transported in such a manner to ensure that it remains frozen.	➢ No clarifying remarks.
15.6 TRANSPORTATION	
15.6.1 Written procedures should be established to ensure that the cold chain products / materials received are distributed under storage conditions comply with the directions on the label of products based on product stability testing results. Companies should use the temperature 'data logger' or other temperature recording devices to verify that the desired temperature has been maintained during the delivery of each consignment received. In addition, simulation studies can be conducted to validate the delivery conditions, taking into account the possibility of the worst situation.	➢ Company should provide written SOP to ensure that management of cold chain is maintained throughout distribution. ➢ Any temperature excursions outside of the labeled storage conditions, for brief period, may be acceptable provided stability data and scientific/technical justification is available to ensure that product quality is not affected. ➢ Temperature monitoring devices or indicators should be used when appropriate (based on validation study done). ➢ Temperature monitoring devices should be calibrated at predetermined intervals. If single use monitoring devices are used, it should also be qualified.
15.6.2 Refrigerated vehicles or containers to transport cold chain products should be mapped and monitored.	➢ Cold chain transport packaging systems must be qualified for both active and passive shipping/transport configuration.

15.6.3 Necessary precaution steps should be implemented when using dry ice during transportation in order to avoid a direct contact with the product and consequently caused coagulation of products / materials.	➢ No clarifying remarks.
15.6.4 Delivery route planning for cold chain products should be created to prevent the risk of exposure to the cold chain products beyond the control of the ambient temperature. Cold chain medicines should be clearly identified from other items in the same distribution activities.	➢ No clarifying remarks.
15.6.5 For each delivery, evaluation and validation of methods of delivery temperature control system to be used must consider the time required for delivery, weather conditions and any future risk exposure.	➢ Company should ensure that delivery/transport system should be continuously monitored by calibrated monitoring system.

REFERENCES:

1. Australian Code of Good Wholesaling Practice for Medicines in Schedule 2,3,4 and 8. National Coordinating Committee on Therapeutic Goods, April 2011.
2. Guidance Notes on Good Distribution Practice. Health Sciences Authority Regulatory Guidance , August 2010.
3. Guidelines for Temperature Control of Drug Products During Storage and Transportation. Health Canada's GUI 0069, April 2011.
4. Guidelines on the International Packaging and Shipping of Vaccines. WHO, December 2005.
5. Model Guidance for the Storage and Transport of Time-and-Temperature-Sensitive Pharmaceutical Products, Annex 9. WHO Technical Report Series, No.961, 2011.
6. National Vaccine Storage and Handling Guidelines for Immunization Providers. Public Health Agency of Canada, 2007.